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Herbal Medicine on Response Immune Patient with COVID-19 Infection a Scoping Review

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Abstract

BACKGROUND: COVID-19 has spread through the world and has caused a global pandemic. There is a lot of evidence that taking herbal medicines could increase the immune response but otherwise, the relation of herbal medicine and inflammation factors that lead to cytokine storm is still discussing.

AIM: The purpose of this article is to review the evidence of herbal medicine that use in COVID-19 patients and the effect on the immune response of patients with COVID-19 infection.

METHOD: We conducted a scoping review on the PubMed and Science Direct databases from January 1 to July 2020 using searching terms "COVID-19", "SARS-CoV2 Infection", "Herbal Medicine" AND "Immune Response" Or "Humoral Immune, Response". We use only scientific articles that discuss herbal medicine and its effect on the immune response. There were eight articles included in the analysis, many types of herbal medicines are used to maintain symptom management and to enhance the patient's immune response, including, Echinacea, QPD (qingfei paidu) and Western medicine, Jiedu Capsule (SFJDC), Yidu-toxicity blocking lung decoction and Ayush Kwath, nagella sative, and LHQW.

RESULTS: This article concludes that several alternative herbal medicines affect the immune response in COVID-19 patients, especially in reducing inflammatory agents, cytokine levels, and immunomodulators. Echinacea, Jiedu Capsule (SFJD), QPD (qingfei paidu) and Western medicine, and Ayush Kwath, nagella sative, and Lianhuaqingwen (LHQW) are the alternative herbal medicines that could provide benefits for COVID-19 patients, although research on the target mechanism must need more exploration.

Introduction

COVID-19 has become a global pandemic that is spreading very fast around the world. COVID-19 can cause acute respiratory infections and cause severe cytokines storms. Several herbal remedies are used to relieve severe symptoms due to cytokines storms and have an effect on immune response, but some evidences have not shown a significant effect; therefore, we aim to review the scientific evidences regarding the effect of presenting herbal medicines on COVID-19 patients.

Methods

Study design

This study used a scoping review design. This design was chosen because this design provides a wide scope for a specific field. This scoping review procedure goes through several stages. The first is formulating clear research questions and objectives, then identifying appropriate research, then sorting research articles, then extracting and charting data then concluding and analyzing the results of the research [1].

Literature search strategy

The literature searches were carried out on several databases. The search was carried out by two researchers (RWR and TIYLP) who conducted separate searches on PubMed and Science Direct on the literature published from January 1 to July 2020. The keywords used are a combination of Medical Subheading (MESH) using Boolean's Logic to find the right article and specifics. The combination of MESH terms we use are: (9 "COVID-19" OR "SARS-CoV2 Infection") AND ("Immune Response").

Identification and selection of relevant articles

The search results of the two researchers were then compared and then discuss if there were any differences which were then discussed and made a decision to get the same number of searches. The duplication of articles is then removed. Articles that meet the criteria were herbal medicine intervention, outcomes related to immunity response, in English, participant in adults and available in full text then included in the (PRISMA) chart to report the search progress (Figure 1).

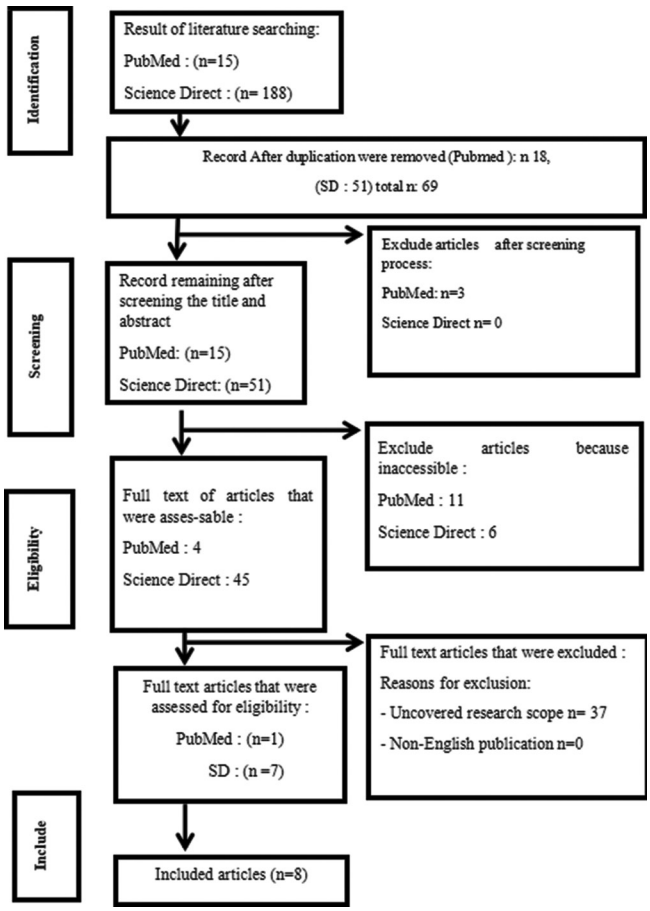

Figure 1: PRISMA flow chart for scoping review

Inclusion criteria

These studies have several inclusion criteria:

1. Herbal medicine interventions, of any duration and follow-up
2. Outcomes related to immunity response
3. Studies in English
4. Participants in adult
5. Articles with full-text

Exclusion criteria

We exclude articles with animal study.

Data extraction

Articles under the inclusion criteria extracted on an excel worksheet. The data such as title, author, date of publication, country and region, research objectives, study design, targets of study, number of samples, study settings, data collection, key findings, and research domain were extracted.

Summarizing the findings

All articles within the inclusion criteria are then summarized by taking into findings the effect of herbal medicine on the immune response. The methodological characteristics of the articles were also evaluated using an Excel spreadsheet. Each article will be assessed about the study design, target of study, sample size, and setting. Then, the data were classified and presented in the percentage.

Results

Characteristic of published articles

We included eight articles based on inclusion and exclusion criteria. Most of the articles came from Biomedicine and Pharmacotherapy (37/5%, n = 3) Advance Integrative Medicine (18%, n = 1), then Journal of Ayurveda and Integrative Medicine (18%, n = 1), Journal Farmacopunture (18%, n = 1), Journal of Pharmacological research (18%, n = 1). These articles are from China (62,5%, n = 5), US/Canada (18%, n = 1), Nepal (18%, n = 1), and United Arab Emirate (18%, n = 1). Most of research have study design systematic reviews (50%, n = 4), non-systematic reviews (18%, n = 1), and original articles (33/34%, n = 3).

Data extraction of the included articles

The article data information is detailed in Table 1, all articles discuss the effect of herbal therapy on the immune response in COVID-19 patients; however, some articles do not explain in detail the method and number of samples the articles would be extracted when it explains the aim of the study. The information would be explained clearly in Table 1.

Discussion

The current COVID-19 pandemic requires researchers to find effective management symptoms so that the patient's condition could improve. The absence

Table 1: Data extraction of the included articles (n = 8)

Author (s) and date of publication	Country/ region	Aim of study	Type of herbal medicine	Data collection	Findings
Aucoin *et al.*, August 1, 2020 [4]	US/Canada	The purpose of this study was to determine the role of Echinacea in the prevention and treatment of COVID-19 patients and to determine whether Echinacea supplementation can increase the risk of cytokine storm in human clinical trials.	*Echinacea*	Search strategy using Medline (Ovid), AMED (Ovid), CINAHL (EBSCO), EMBASE (Ovid)	1. The impact of Echinacea supplementation on cytokine storm that much evidence suggests that Echinacea decreases the number of proinflammatory cytokines. 2. The benefits of echinacea to provide clinical benefits are still being discussed in animal studies can reduce the production of IL-1α, IL-6, and TNFα cytokines and increase the survival rate in mice infected with severe influenza, and SARS-CoV. 3. Research of the use of Echinacea in cytokine storms may be warranted.
Xin *et al.*, July 4, 2020 [5]	China	The purpose of this study is to explore the effect of combine therapy QPD and Western medicine on COVID-19 Infection	*QPD (qingfei paidu) And Western medicine*	63 Patients with COVID-19 infection who were treated with worsening symptoms were given combination therapy between Western medicine (antivirus interveron and lopanivir, arbidol) and QPD together. Then, it was evaluated the clinical characteristics such as routine blood, biochemical index, inflammatory factors, and lung severity score of each patient by looking at computerized tomography.	1. QPD decoction and Western medicine are beneficial for COVID-19. 2. Combine therapy improves anti-inflammation in patients with COVID-19 3. Combined therapy may mitigate the extent of multiorgan impairment in COVID-19
Tao *et al.*, 2020. October 12, 2020 [15].	China	The purpose of this study is to explore the effect of combine therapy QPD and Western medicine on COVID-19 infection	*Jiedu Capsule (SFJDC)*	Search strategy using Encyclopedia of traditional Chinese medicine (ETCM), Integrative Pharmacology-based Research Platform of Traditional Chinese Medicine (TCMIP), and TCM Systems Pharmacology Database (TCMSP). The chemical structures were obtained from the NCBI PubChem database, and all structures of these compounds were optimized for each backbone structure along with energy minimization by using Autodock 4.1 and GROMACS 2019 software for subsequent analysis.	1. A systematic study integrated is proposed to illustrate the potential immune and anti-inflammatory mechanisms of SFJDC against COVID-19 2. SFJDC regulates related targets, showing the potential anti-novel coronavirus effect 3. The work can provide a better understanding of the therapeutic mechanism of SFJDC for treating COVID-19.
Zhao *et al.*, 2020. June 19, 2020 [6].	China	This study aims to investigate differences in changes in inflammatory agents, immune function, and evaluation of differential leukocyte counts in COVID-19 patients with Yidu Toxicity administration.	*Yidu-toxicity blocking lung decoction*	Total of 40 patients with severe pneumonia of COVID-19 admitted to the respiratory departments and infectious disease departments of the First Affiliated Hospital of Anhui Medical University were selected	1. The data derived from Chinese medicine prescription according to the fifth National recommendations during the COVID-19 pandemics 2. The alterations of inflammatory agents, immune function, and leukocyte differential count in severe pneumonia of COVID-19 patients after yidu-toxicity blocking lung decoction were given. 3. The inflammatory agents, IL-6 and TNF-α, were found to be decreased by Yidu-toxicity blocking lung decoction *in vitro* 4. Yidu-toxicity blocking lung decoction could relieve inflammation of COVID-19 patients and offering another option in clinical settings.
Gautam *et al.*, 2020. August 17, 2020 [7].	Nepal	To validated scientifically Ayush Kwath to boost immunity and can be used as prevention and control of COVID-19	Ayush Kwath	Unavailable Information	Ayurveda concepts and biomolecular studies, these Ayurveda herbs are seen to have rich sources to fight against the immuno-pathogenesis process of viral diseases, but to date, no study has been found about its effectiveness against COVID-19. Ayush Kwath due to its antiviral, immune-modulatory, antioxidant, anti-inflammatory, anti-platelet, anti-atherosclerotic, hepato-protective, reno-protective properties; seems to be effective in regulating immunity for the prevention and reduction of viral disease complications. As there is a lack of enough evidence to support its specific role against corona virus, there is a requirement to validate the effectiveness of these formulations with extensive biotechnological, pharmacological, and clinical research.
Maideen, Juni 2020 [16].	United Arab Emirates	This study is to review the potential of nigela sativa to treat the patient with COVID-19 infection as antiviral, antioxidant, anti-inflammatory, anticoagulant, immunomodulatory, bronchodilator, antihistamic, antitusive, antipyretic, and analgesic activities.	Nigella sativa	Medline/PubMed, Central Pubmed, Google Scholar, Science Direct, DOAJ, and reference list about nigella sativa.	1. Many studies confirmed that nigela sativa has antiviral, antioxidant, anti-inflammatory, immunomodulatory, bronchodilatory, antihistaminic, antitussive activities related to causative organism signs and symptoms of COVID-19. 2. It also has anti-hypertensive, anti-obesity, anti-diabetic, anti-hyperlipidemia, anti-ulcer, and antineoplastic activities which could help patient with comorbidities. which would help the COVID-19 patients with comorbid conditions.
LI *et al.*, July 3, 2020 [17].	China	This article purpose is to review the preclinical evidence of LHQW in lung protection and antiviral activities	LHQW	Academic databases (up to August 8, 2020) including PubMed, CNKI and Web of Science, on ethnobotany and ethno medicines	This study has conclude that LHQW has benefit to treating virus infection especially COVID-19 and it has potential to become candidate to complementary strategy.
Xiong *et al.*, June 12, 2020 [18].		This article purpose is to evaluate the efficacy Baidu Decoction (XBD) combine with conventional drug and compare with conventional drug alone I patient with COVID-19 infection	Xuanfei Baidu Decoction	42 patient with covid19 infection randomly assigned to XBD and conventional medicine and conventional medicine alone.	XBD combine conventional medicine may significantly improve patient clinical symptoms, increase immune response, and significantly reduce C-reactive protein.

of official medicines for COVID-19 made the herbal medicines the best choice in efforts to seek treatment for COVID-19 and the patient's immune response. Herbal medicines include herbs, herbal materials, herbal preparations, and finished herbal products that contain as active ingredients parts of plants, or other plant materials, or combinations [2]. It has many active agent that provides the benefit for human health [3]. The utilization of herbal medicine with the evidence and scientifically to explore the effects of herbal medicine. The use of herbal medicine is expected to provide positive effects without deterioration condition patients with COVID-19 infection.

The results of the literature analysis on the effect of herbal medicine on patients infected with COVID-19 from the study [4], [5], [6], [7] it is known that each study has similarities and differences regarding the benefits of several herbal medicines on the immune response in infected patients COVID-19. This scoping review shows that many types of herbal medicine are used to maintain symptom management and to enhance the patient's immune response.

Some of the herbal medicines discussed in this literature study include the role of Echinacea in cytokine storms, in the study of [4] it was stated that the role of Echinacea was to reduce levels of proinflammatory cytokines in cytokines storms. Furthermore, [5] study on the combination of QPD and Western medicine in the treatment of COVID-19 patients found that the combination of QPD with Western medicine provided benefits for patients infected with COVID-19 and the combination of drugs. This therapy increases anti-inflammatory in COVID-19 patients and there is no effect of the combination of QPD therapy and Western medicine on mortality, but this combination therapy needs to be studied further with the incidence of multiorgan implants.

Furthermore, herbal medicine called Shufeng Jiedu Capsule (SFJDC) which is included as TCM (Traditional Chinese Medicine) has been widely used to treat upper respiratory tract infections because of its ability as an immunomodulators and anti-inflammatory, this herbal therapy regulates targets related to the impact of the new coronavirus.

Ayush kwath is also effective to regulate immunity and prevent and reduction of complications of viral diseases [6]. The results showed that there were changes in inflammatory agents, immune function, and leukocyte counts in severe pneumonia of COVID-19 patients after being given Yidu toxic lung inhibitors, especially IL-6 and TNF-inflation agents were found to decrease, when decoction of inhibitors of lung toxicity is reduced.

Validation of giving Ayush kwath to improve prevention and control of immunity in COVID-19 patients, it was found that Ayurveda is a collection of herbal plants that are rich in resources to fight COVID-19 [7]. Yidu Toxicity Blocking Pulmonary decoction conduce the changes in inflamatory agents, immune function, and leukocyte count in pneumonia from COVID-19 patients [6]. There are many studies with drug candidates used as antivirals or immunomodulators, herbal medicines may have the ability to regulate the production and release of proinflammatory cytokines, interfere with viral development in host cells, and modify certain molecular [8].

Nigella sativa is also one of herbal medicine that provides many advantages to human health. Nigella sativa has active agent such as thymohydroquinon and thymoquinone that have benefit as antibacterial and anti-inflammatory agent [9]. Inflammation is usually occurred when the tissue is damage [10]. Thymoquinone in *N. sativa* could reduce the IL-6 level that promotes the inflammation symptoms [11].

Clinical evidence from a range of studies of herbal medicine in the treatment of COVID-19 has shown significant results and supported the idea that herbal medicine has a beneficial effect in the treatment and prevention of epidemic diseases [12]. A Cochrane systematic review reported that herbal medicine combined with Western medicine may improve symptoms and quality of life in COVID-19 patients [13]. The combined therapy of herbal medicine with Western medicine has shown significant results in increasing the effective rate and improving the symptoms disappearance rate, TCM syndrome score, and complete blood count, compared to the effects of Western medicine monotherapy [14].

Conclusion

This article concludes that several alternative herbal medicines affect the immune response in COVID-19 patients, they provide reducing inflammatory agents, reducing cytokine levels, and immunomodulators. Echinacea, Jiedu Capsule (SFJD), QPD (qingfei paidu) and Western medicine, and Ayush Kwath are the alternative herbal medicines that could provide benefits for COVID-19 patients, although research on the target mechanism must need more exploration.

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