



The medicinal plants for Covid-19 treatments: an integrative literature review

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Abstract

It's well know that the use of medicinal plants for treatment of diseases are tradicional practice and started at the beginning of medicine and the knowledge the went through generation to generation. Goal: Analyze studies about the use of medicinal palnts to treatment and prevantion for COVID-19 inside the national and internacional scientific journals in the last three years. Method: It's an integrative literature review which analyzed the quantitatives data. The Virtual Library Health was used for research during the months of October to November. Results:About the mean question was found just fews studies that could answer this research goals, 8 (0,65%) researchs show that the use of medicinal palnts need be more explore for achieved

a better understament. Coclusion: the data collect show that some plants like Turmeric working a positive way for treating symptoms of COVID-19, also was found another kinds of plants, we have the exemplo of the maoto as a pre-exposure treatment measure for the virus. So medicinal plants have the potential to be used as a treatment for COVID-19 but we need more research about the properties of these plants.

Keywords: Medicinal Plants, COVID-19, Treatment.

1. Introduction

It is known that the use of medicinal plants for curative purposes is a therapeutic form of very ancient origin, belonging to the beginning of medicine and coming from the accumulation of knowledge and information passed from generation to generation. Over the centuries, the cultivation of various plant species has established the basis for the treatment of different diseases (Brazil, 2015).

In recent years, several plant species are becoming the object of research in order to evaluate the therapeutic efficacy and guarantee their use in a wide range of studies that search for substances produced by plants to protect against viruses, bacteria and fungi, since the demand for phytotherapeutic products in the sense of prevention and treatment has been increasing considerably (Lisboa et al.,2017).

During the pandemic of Covid-19 the use of medicinal plants has become more present for some population groups, who seek alternative solutions to prevent and/or alleviate the symptoms of the disease, as they feel that the only available resource is self-help, self-care, and self-medication (Villena-Tejada et al., 2021).

Regarding the treatment of Covid-19, despite numerous trials in development with various drugs, it has not yet been possible to determine an official treatment against the coronavirus. What is being performed is an early treatment measure in order to reduce the symptoms while the body itself reacts against the infection (Gardin & Braga, 2021).

Different researchers have suggested herbal medicine as a potential option to cure or prevent COVID-19, mainly because many plants are employed for diseases with symptoms similar to COVID-19. Countries such as China and India integrating their use into Western medicine to boost the immunity power of COVID-19 patients (Khadka et al., 2021).

Self-medication with medicinal plants in times of COVID-19 has been a recurring attitude among the population, using plants with great potential, but without proven methods, to improve and/or prevent the symptoms related to COVID-19 (Villena-Tejada et al., 2021).

The present study aims to analyze in national and international scientific databases information about studies that address the use of medicinal plants as treatment and/or prevention of COVID-19 published in scientific journals in the last 3 years.

2. Methodology

This is an integrative literature review with quantitative data analysis, which is considered the broadest methodological approach to reviews, allowing the inclusion of experimental and non-experimental studies for a complete understanding of the analyzed phenomenon.

The review was conducted following the steps proposed by Sousa et al. (2017) in the first step, the theme was identified, medicinal plants for COVID-19, with the following research question: what is the evidence in the literature on the use of medicinal plants for treating COVID-19?

In the second step, the eligibility criteria for the studies were established; the inclusion criteria were articles, whose focus was related to the use of medicinal plants for treating symptoms of covid-19, available in full, in any language. The exclusion criteria were studies with inconclusive results, those that did not describe the steps in detail, secondary studies, in silico, theses and other documents.

Still in this step, the databases were selected, the search was conducted in the Virtual Health Library during the month of October and November 2022. For the search refinement, the descriptors Medicinal Plants, COVID-19, Pharmacological Treatment with the AND Boolean operator were used (Figure 1).

The initial sample with the use of the descriptors and qualifier in the advanced search was 541 studies, which after applying the database filter resulted in 1222 articles, 71 articles selected according to the title and abstract, and by reading the articles in full, 8 articles were included that composed the review.

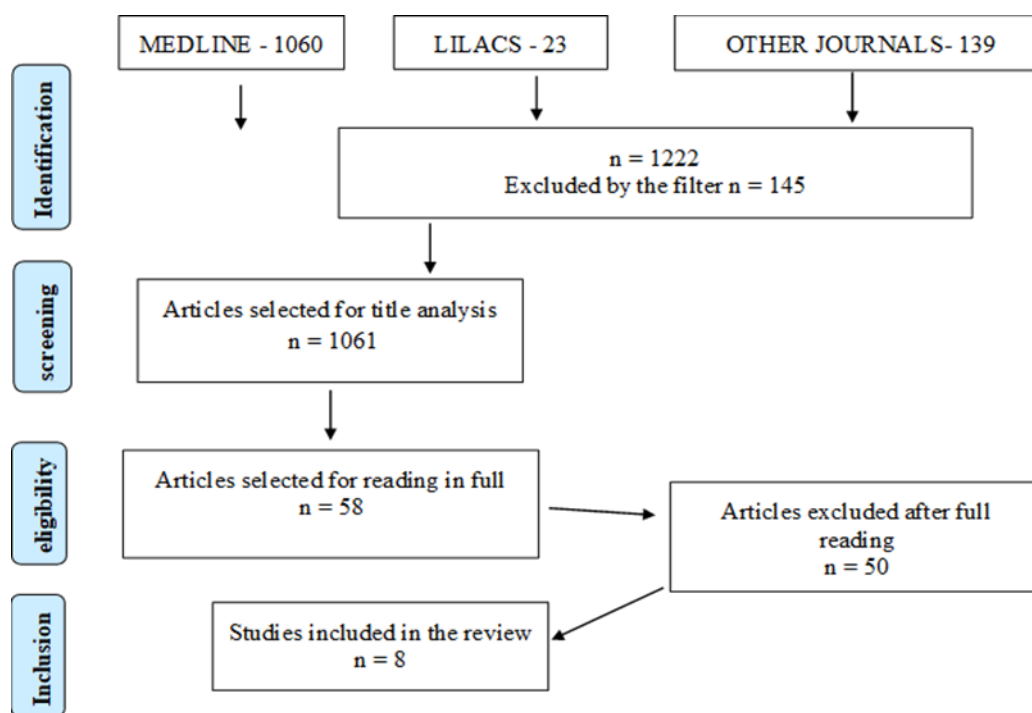


Figure 1. Flowchart of the article selection process for the integrative review.

Source: Research data, adapted from Moher et al ¹⁰.

3. Results

On the theme in question, few studies matched the theme and objectives of the research, only 8 (0.65%) of the research found in the databases searched, demonstrating that the use of medicinal plants needs to be better addressed and understood (table 1). As for the year of publication only 1 (12.50%) was in 2020 (Villena-Tejada et al.,2020), 3 (37.50%) in 2021 (Gardin & Braga, 2021, Hassaniazad et al, 2021, Khadka et al., 2021)

and 4 (50%) in 2022 (Nabeshima et al., 2022, Askari et al., 2022, Pranskuniene, Balciunaite, Simaitiene, Bernatoniene, 2022, Shafie et al., 2022).

The countries in which the studies were conducted stands out Iran with 3 (37.50%) (Hassaniazad et al., 2021, Askari et al., 2022, Shafie et al., 2022), 1 (12.5%) in Brazil (Gardin & Braga, 2021), 1 (12.5%) Lithuania (Pranskuniene et al., 2022), 1 (12.5%) Japan (Nabeshima et al., 2022), 1 (12.5%) Nepal (Khadka et al., 2021), 1 (12.5%) Peru (Villena-Tejada et al., 2020).

Table 1. Estudo Relacionado ao Tema

Authors /year	Plant used	Relevant Result
Villena-Tejada et al. (2020)	The most commonly used plants are eucalyptus, ginger, peppercorns, chamomile, and garlic.	The present study reported an association between the use of 17 medicinal plants and the treatment or prevention of respiratory symptoms related to COVID-19.
Gardin e Braga (2021)	Celandine (Chelidonium majus)	But in this case series, there was complete or near complete resolution of symptoms with the institution of treatment in 1 to 9 days (median 3 days), with total symptom duration ranging from 2 to 22 days (median 8 days)
Hassaniazad et al. (2021)	Turmeric	Administration of nano-curcumin in the inflammatory phase of COVID-19 may accelerate recovery from the acute inflammatory phase by modulating inflammatory immune responses.
Khadka et al. (2021)	Lemon, Curcuma angustifolia Roxb., Turmeric, Allium sativum L. Garlic	The study found that the use of medicinal plants increased during COVID-19 and most respondents recommended medicinal plants to prevent COVID-19.
Nabeshima et al. (2022)	Maoto granules	During the 1-week observation period, significantly fewer subjects were diagnosed with COVID-19 in the maoto group (N = 3, 7.1%) than in the control group (N = 6, 46.2%). The prophylactic efficacy of maoto was 84.5%.
Askari et al. (2022)	Turmeric	The results of the present study showed that curcumin-piperine co-supplementation in

		COVID-19 outpatients can significantly reduce weakness.
Pranskuniene, Balciunaite, Simaitiene, Bernatoniene (2022)	Thymus vulgaris L., Tilia cordata Mill., Matricaria recutita L.	Trends in the ethnopharmacological choices of the modern consumer and analysis of archival sources can be a great source of ideas for new herbal pharmaceutical preparations.
Shafie et al. (2022)	Turmeric	Because nanocurcumin may be effective in increasing O ₂ saturation and reducing the severity of symptoms in patients with COVID-19, it could probably be used as a complementary agent to speed patients' recovery.

As for the type of research method, 3 (37.50%) used placebo-controlled randomized controlled trial (Askari et al., 2022, Shafie et al., 2022, Hassaniazad et al., 2021), 1 (12.5%) qualitative (Pranskuniene et al, 2022), 1 (12.5%) Cutting study (Nabeshima et al., 2022), 1 (12.5%) cross-sectional study (Villena-Tejada et al.,2020), 1 (12.5%) web survey (Khadka et al., 2021), 1(12.5%) case series (Gardin & Braga, 2021).

The total sum of the eight studies was 2,760 participants, a number considered expressive, little information about the characteristics of the participants could be extracted, because some studies did not provide a description of such information. Regarding gender, in 4 studies (50%) had more men with participants (Askari et al., 2022, Shafie et al., 2022, Hassaniazad et al., 2021, Khadka et al., 2021) and 4(50%) had more women (Gardin & Braga, 2021, Nabeshima et al., 2022, Villena-Tejada et al.,2020, Pranskuniene et al., 2022).

As for the age range of the participants, in 4 (50%) the mean age was between 40 and 49 years (Gardin & Braga, 2021, Nabeshima et al., 2022, Askari et al., 2022, Hassaniazad et al, 2021), 2 (25%) between 50 and 59 years (Pranskuniene et al., 2022, Shafie et al., 2022), 1 (12.5%) between 20 and 29 years (Khadka et al., 2021) and 1(12.5%) between 30 and 39 (Villena-Tejada et al.,2020). Participants' education was not described in 3 (37.50%) (Nabeshima et al., 2022, Hassaniazad et al., 2021, Shafie et al., 2022), 4 (50%) university level (Villena-Tejada et al.,2020, Nabeshima et al., 2022, Askari et al., 2022, Khadka et al., 2021), 1 (12.5%) secondary level (Pranskuniene et al., 2022).

The most cited plants in the studies were turmeric 4 (50%) of the studies (Khadka et al., 2021, Shafie et al., 2022, Hassaniazad et al., 2021, Askari et al., 2022), 2 (25%) Garlic (Khadka et al, 2021; Villena-Tejada et al.,2020), 1 (12.5%) Celandine (Gardin & Braga, 2021), 1(12.5%) Maoto granules (Nabeshima et al., 2022) and 1 (12.5%)Thymus vulgaris (Pranskuniene et al., 2022).

About the use of medicinal plants for COVID-19 cases, 4 (50%) of the studies reported that it was to treat symptoms of patients already diagnosed with the disease (Gardin & Braga, 2021, Askari et al., 2022, Hassaniazad et al, 2021, Shafie et al., 2022), and 4(50%) to prevent the disease in participants with no prior

diagnosis (Nabeshima et al., 2022, Pranskuniene et al., 2022, Villena-Tejada et al.,2020, Khadka et al., 2021).

Regarding the presentation of the plants, in 5 (62.50%) they were used in a manipulated way (Gardin & Braga, 2021, Askari et al., 2022, Hassaniazad et al., 2021, Shafie et al., 2022, Nabeshima et al., 2022), in 3 (37.50%) the participants cited using plant in natura (Pranskuniene et al., 2022, Villena-Tejada et al.,2020, Khadka et al., 2021).

Studies evaluating the use of some plant species to treat symptoms of COVID-19 in symptomatic patients have found promising results, with the reduction of weakness caused by the disease (Askari et al., 2022), reduction of cases of hypoxia (Shafie et al, 2022), reduction of symptoms in a short period (Gardin & Braga, 2021), increase in lymphocytes during infection (Hassaniazad et al., 2021), reduction of virus infection in healthcare workers (Nabeshima et al., 2022).

3. Discussion

The use of medicinal plants is something very recurrent in traditional medicine, dating back to the dawn of humanity, with the pandemic of COVID-19, a new disease, which so far does not have a specific treatment and known cure, resulted in part of the population seeking alternative therapies, either for prevention of the disease or treatment of symptoms.

The data indicate that research on the theme medicinal plants and COVID-19 is still scarce, as can be observed by the amount of research found in the databases and published in the last three years. It is noteworthy that there has been a small increase in studies that address the topic, so much so that in the year 2022, four published studies were found.

It is noteworthy that one of the countries that have done the most research on the subject in question was Iran, where three randomized clinical trials were found on the properties of turmeric for symptoms of COVID-19. The studies were conducted in many different regions of the globe, demonstrating that worldwide pattern in the use of traditional medicine for COVID-19.

The methodologies employed in the studies were the most diverse, being predominant the randomized clinical trial with use of placebo, which is considered an excellent scientific method for evaluation, for following protocols at the time of the evaluation of the variables to be studied (Hassaniazad et al., 2021).

As for the profile of the participants, in half of the studies there was a predominance of women and in the other half of the studies of men. In the studies that evaluated the frequency of medicinal plant use, and were not necessarily controlled clinical trials, a predominance of women occurred. Some authors claim that women are more versed in the properties of medicinal plants and that they usually use medicinal plants to care for the health of their family members (Villena-Tejada et al., 2020).

In the study conducted in Lithuania on medicinal plant use the authors reported that the percentage of men and women was unequal because traditionally, knowledge of herbal medicine in the country is passed down through the female line and even today, herbalists are usually women (Pranskuniene et al., 2022).

Regarding the age of the participants, there was a predominance of mature adults, followed by older adults, who are usually the ones who most use medicinal plants as alternative treatment, studies have reported that the elderly are more prone to indiscriminate use of medicinal plants (Villena-Tejada et al., 2020).

Another difference in the studies analyzed was regarding the education of the participants, a significant number did not describe this information, and in the rest, university education prevailed among the participants. This differs somewhat from other findings, because people with professional training are more likely to use a scientifically validated treatment, abandoning the use of medicinal plants (Villena-Tejada et al., 2020).

About the plants used, turmeric stood out, being cited in half of the studies, it is also noteworthy that three randomized clinical trials employed components of this plant for their patients (Shafie et al., 2022, Hassaniazad et al., 2021, Askari et al., 2022), and another study in which a web search was conducted with 774 participants, the most cited plant was turmeric.

Several *in silico* trials have been conducted demonstrating the curative properties of curcumin for treating covid-19 symptoms. The medicinal properties of turmeric as a source of curcumin have been known for thousands of years; however, only recently have the exact mechanisms of action and its bioactive components been investigated (Shafie et al., 2022).

Another plant mentioned was garlic, which has several medicinal properties already documented in the current literature. Studies point out that garlic (*Allium sativum* L.) exhibited an inhibitory effect on SARS-CoV-2 replication, thus, it can be considered a promising agent against COVID-19 (Villena-Tejada et al., 2020). *Allium sativum* contains sulfoxide, proteins and polyphenols as sulfur-containing bioactive compounds that are antiviral with immunostimulatory potential (Khadka et al. 2021).

Half of the studies found the medicinal plants were used to treat patients diagnosed with COVID-19, some of them, were able to demonstrate the medicinal properties of these plants for reducing some symptoms of the disease, as was the cases of the use of turmeric, Celandine (*Chelidonium majus*). One of the studies used Maoto granules as a preventive measure, and the research was carried out with health professionals (Nabeshima et al., 2022).

Whereas the methodology of others was to investigate the use of medicinal plants by participants who did not have a diagnosis of COVID-19, and the results showed that many people used the plants to treat the symptoms of the disease, based on prior knowledge passed down from generation to generation for viral diseases that had similar symptomatology (Pranskuniene et al., 2022, Villena-Tejada et al., 2020, Khadka et al., 2021).

The way the plants were used also differed, with many participants reporting that they used them *in natura*, often being planted and harvested from their backyards. In the study conducted in Nepal most respondents obtained medicinal plants from gardens or farms, the authors further reiterate that interesting to find that people are growing more medicinal plants during COVID-19, which is a positive sign for the development of gardening or farming practices in the country (Khadka et al., 2021).

Often the use of medicinal plants turned out to be the only access that people have to healthcare during the COVID-19 pandemic, which can lead to risks, as there is still a popular belief, that because it is nature, plants have no health risks. Therefore, the overuse of medicinal plants, however, can be problematic and is cause for concern. Easy access to social media, which often publishes unreliable advertisements, may play a role in the increasing use of medicinal plants (Khadka et al., 2021).

The vast majority of studies used specific parts of plants, so that it was possible to increase the bioavailability of certain specific compounds and increase the absorption rate, or use based on alternative health practices,

with the use of extracts of some plants (Gardin & Braga, 2021).

In addition, it is noteworthy that some of the clinical studies that evaluated the use of medicinal plants for COVID-19 were able to achieve expressive results for treating the symptomatology of the disease. As was the case with the use of turmeric in the study by Askari et al. (2022) in which participants in the intervention group received two curcumin-piperine capsules; each capsule contained 500 mg curcumin plus 5 mg piperine, the control group had significant reduction in weakness due to curcumin-piperine co-supplementation when compared to the placebo group.

Whereas Shafie et al. (2022) in the Iranian randomized controlled study, the treatment group received 160 mg of nano-curcumin (4 capsules of 40 mg) daily for 6 days, the mean differences in O₂ saturation were significantly greater in patients receiving nanocurcumin supplements ($p = 0.02$).

In another study that also used the authors concluded that administration of nano-curcumin in the inflammatory phase of COVID-19 may accelerate recovery from the acute inflammatory phase by modulating inflammatory immune responses (Hassaniyazad et al., 2021).

In Gardin and Braga's (2021) study participants were treated with *Chelidonium majus*, the authors noticed complete or near complete clinical improvement occurred within 1-9 days of treatment (median 3 days) and there were no adverse events.

As for the use of medicinal plants by Nabeshima et al. (2022) for post-exposure prophylaxis of COVID-19 in healthcare workers with the use of maoto granules, the results showed that the prophylactic efficacy of maoto was 84.5%.

Thus, it is emphasized that no treatment is available to cure or prevent COVID-19, only the current vaccines are indicated for the prevention of the most severe symptoms of the disease. However, medicinal plants are alternative treatments for symptoms and need to be evaluated for this use.

Furthermore, understanding which medicinal plants are being used by the population is a way to reduce health risks, such as poisoning. Most plants used for therapeutic and prophylactic purposes during a pandemic of COVID-19 may contain toxic substances that can cause a variety of health problems if overdosed, making research-based use important (Pranskuniene et al., 2022).

5. Final Considerations

The studies show that the use of medicinal plants is still something very common by the population, who use previous knowledge to treat symptoms of COVID-19, such situation needs to be evaluated, due to the risk of intoxication. However, few scientific studies were found on the topic in question, something that needs to be reevaluated.

The data show that some plants show promise for treating symptoms of COVID-19, such as turmeric, included in three randomized studies, as well as other plants that are used to treat symptoms of the disease, and for prevention. One of the studies pointed to the efficacy of maoto as a pre-exposure treatment measure for the virus. Thus, medicinal plants have the potential to be used as a treatment for COVID-19, so there is a need for research that addresses the properties of these plants.

Thus, the present study was able to achieve the proposed results; moreover, it is possible to observe the need

for further research on the use of medicinal plants for COVID-19 in different populations, so that it is possible to evaluate the risks involved with self-medication.

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