Chapter 77

Scientific Evidence for the Use of Homeopathy for the Prevention and Treatment of COVID-19

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ABSTRACT
As of November 2, 2022, according to the World Health Organization (WHO), the total number of confirmed cases of COVID-19 in the world passed 620 million, and the total number of deaths due to the infection passed 6.5 million. Today, specific drugs against SARS-CoV-2 are still under study or starting to be marketed. In contrast, homeopathy is a long-established medical rationale, and is based on the patient's symptoms and individuality when choosing a medicine. Thus, the aim of this literature review was to gather available scientific evidence on the effectiveness of homeopathy in the prevention or treatment of COVID-19. We found 3 randomized clinical trial articles, 1 cohort study, and 7 descriptive observational studies. Of these, 73% repertorized the patients' symptoms and the prescription was individualized. The remaining articles were concerned with the analysis of homeopathic medicines as epidemic genius. Compiling the findings, it could be observed that homeopathy does indeed have a high beneficial adjuvant potential in the treatment of COVID-19 in mild, moderate and severe cases of the disease. However, more robust clinical trials and cohort studies are needed to investigate the prophylactic power of homeopathy in this case. Furthermore, *Arsenicum album* and *Bryonia alba* were the most prescribed drugs, with better results both in prevention and adjuvant treatment to allopathy, and therefore, are the ones suggested in this study as the epidemic genie.

Keywords: COVID-19, Homeopathy, Pandemic, Epidemic genie.

1 INTRODUCTION

The emergence of SARS-CoV-2 was first observed when new cases of pneumonia were reported in the city of Wuhan, China (HUANG et al., 2020). During the first weeks of the epidemic in Wuhan, an association was identified between the first cases and the Wuhan Huanan Seafood Wholesale Market. Authorities closed the market on January 1, 2020 for environmental sanitation and disinfection, however, retrospective investigations identified additional cases with disease onset in December 2019 (NISHIURA; LINTON; AKHMETZHANOV, 2020).

The genetic sequencing of the virus suggested that it is a betacoronavirus belonging to the subgenus Sarbecovirus of the family Coronaviridae, being the seventh coronavirus known to infect humans (BRAZIL, 2021). As of November 2, 2022, according to the World Health Organization (WHO), the total number of confirmed cases in the world passed 620 million, and the total number of deaths due to infection passed 6.5 million.

The signs and symptoms of COVID-19 infection vary. Most people have fever (83-99%), cough (59-82%), fatigue (44-70%), anorexia (40- 84%), shortness of breath (31-40%), and myalgia (11-35%). Other nonspecific symptoms, such as sore throat, nasal congestion, headache, diarrhea, nausea, and vomiting, have also been reported (HUANG et al., 2020; CHEN et al., 2020; WANG et al., 2020; EASTIN et al., 2020). Loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms have also been reported (SPINATO et al., 2020; COSTA et al., 2020; TONG et al., 2020).

According to The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020), while most people with COVID-19 develop only mild or moderate disease (80%), approximately 15% develop severe disease requiring oxygen support, and 5% have critical illness with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiple organ failure including acute kidney injury and cardiac injury.

The Homeopathic Science was born in the year 1796 after the publication of the scientific article "Essay for discovering the curative virtues of medicinal substances, followed by some comments on the curative principles admitted until our days days", by the German physician Cristiano Frederico Samuel Hahnemann, creator of homeopathic therapeutics (BRAZIL, 2013).

Homeopathy is a medical rationale based on three fundamental principles: the law of similars, experimentation on "healthy" men, and the use of ultra-dilutions or infinitesimal doses. The Law of Similars (Similia Similibus Curantur) establishes that the substances existing in nature (of vegetal, mineral and/or animal origin) have the potentiality to cure the same symptoms that they are capable of producing, that is, the medicine chosen to treat the sick causes the same symptoms of this disease when administered to a healthy being. Conversely, it is capable of improving the symptoms in sick patients, through the reestablishment of vital energy, balancing the individual in an integral way - body, emotions, and mind. From the experimentation of the specific homeopathic medicine on the "healthy" man, all signs and symptoms observed were carefully and precisely registered, constituting the Homeopathic Materia Medica. The homeopathic medicines are rigorously manipulated based on the homeopathic harmacopoeia, and this manipulation is based on successive dilutions and dynamizations as many as necessary according to each clinical situation. At the end of the preparation, there should be no identification of the active molecule, but the registration of its energy (BRASIL, 2012).

In the current situation, when specific drugs for COVID-19 infection are still under study or at the beginning of commercialization (such as nirmatrelvir) (BRASIL, 2022), based on the knowledge of the symptomatology and individuality of the patient, homeopathy, which is already well established, can be considered in the prevention and treatment of this global public health emergency.

According to Samuel Hahnemann (2013), in his work "Organon of the Art of Healing", every epidemic must be treated as if it were something new and unknown. A homeopath does not immediately perceive the complete picture of the epidemic in the first case he treats: one must closely observe series of

cases since each collective disease reveals itself in the totality of its signs and symptoms. The characteristic symptoms peculiar to the epidemic are important elements in the totality of a symptomatic picture.

Instead of helping an individual to increase his self-healing power, one should aim to treat the whole epidemic region as one patient: that is, the whole "pattern energy" can only be revealed by different patients with the same disease, but different constitutions. By identifying the peculiar and uniform characteristics for most patients in the same outbreak, we can identify one or several drugs that are most consistently useful in the epidemic for all affected persons. To this drug, or set of drugs most effective in treating the epidemic, Hahnemann gave the name "epidemic genius" (EG), establishing the criteria for both its choice and the use of the same drugs in each stage of the epidemic, as well as prophylactic agents (LEITÃO et al., 2020).

In different epidemic areas, there are differences in climate, diet, collective emotional state, virus strains, etc., and therefore the named disease may present with different symptomatology in different regions, which will require different homeopathic remedies. James Tyler Kent, renowned American homeopath, has also described a semiotic protocol for identifying the GE group of remedies and emphasizes that although the application of GE in choosing homeopathic remedies requires a lot of work, it has spectacular results (KENT,2002).

Homeopathy has long been used in the management of epidemics throughout the world, with quite significant results. "Hahnemann, in 1799 used belladonna in the control of an epidemic of scarlet fever, and later, treated an epidemic of Typhus having achieved approximately 99% successful results." (BRAZIL, 2013).

Daruiche (2012) conducted a survey proving the effectiveness of homeopathic action on epidemic populations in Germany, France, Spain, the US, and Mexico, including the Spanish flu that decimated much of the world's population in the early 20th century.

In his review, Shalts (2005) mentions that during the Asian cholera epidemic in Germany (1831-1832) the mortality rates in European homeopathic hospitals were 7-10%, while with conventional treatments they reached 40-80%. Homeopathy was also effective in the cholera epidemic that ravaged Rio de Janeiro in 1855 (LEITÃO et al., 2020), as well as in recent decades it has been successfully applied in Brazil in epidemics of meningitis and dengue fever (DARUICHE, 2012; BAROLLO, 2007).

Seeing the beneficial effect of homeopathy in these various epidemics, this paper aims to search for scientific evidence of its use for both prevention and treatment of the current pandemic of COVID-19 in the world, available in the literature.

2 OBJECTIVES

2.1 GENERAL OBJECTIVE

✓ To gather scientific evidence available in the literature on the effectiveness of homeopathy in preventing or treating COVID-19.

2.2 SPECIFIC GOALS

✓ Select the randomized clinical trial articles of the use of homeopathy in the prevention or treatment of COVID-19;

✓ Select the cohort study articles of the use of homeopathy in the prevention or treatment of COVID-19;

✓ Select the articles from descriptive observational studies of the use of homeopathy in the prevention or treatment of COVID-19;

✓ Propose a drug or group of drugs epidemic genius.

3 METHODOLOGY

A literature search was conducted in PubMed, Scopus, Embase, Cochrane and BIREME databases, with the following search strategy: homeopath* AND (covid OR "coronavirus disease 2019" OR "COVID-19" OR "SARS- CoV-2").

Next, scientific articles of randomized clinical trials, cohort trials, and descriptive observational studies (case series and case report), in which patients used homeopathy for the prevention or treatment of COVID-19, published until September 2022, were selected. For selection, there were no restrictions on age, sex, ethnicity, social status, comorbidities, or disease severity of study participants.

Due to the potential seriousness of the disease, studies in which the drug treatment offered to the participants was only homeopathy were not required in this selection. Only articles in English and available through subscription by the Portal Periódicos CAPES were included. Exclusion criteria were pre-clinical trials, post-IVID-19 sequelae treatment studies, clinical trials in which the comparator was not placebo, and case reports of self-medication.

Although case series and case reports are not evidence of efficacy in this case, because COVID-19 is a new, pandemic disease, a review of these types of studies is necessary, both to establish a possible GE drug and to guide future clinical trials.

4 SCIENTIFIC EVIDENCE FOR THE USE OF HOMEOPATHY IN THE PREVENTION OR TREATMENT OF COVID-19

4.1 ARTICLE SELECTION

The total number of results found in each database using the established search strategy is described in table 1.

Table 1 - Total result of the database search.

Databases	PubMed	Scopus	Embase	Cochrane	BIREME
Total no. of results	87	145	170	30	375

Among the results obtained, 11 evidences were found: two clinical trials for treatment of the disease, one clinical trial assessing prevention, one retrospective cohort study assessing prevention, six case series on treatment, and one case report on treatment. Table 2 summarizes the selected studies.

Regarding the choice of drug used, only three studies did not individualize the treatment. Adler et al. (2022) tested Natrum muriaticum LM2 as an epidemic genie; Daruiche et al. (2022) evaluated the use of Arsenicum album 30CH as an epidemic genie; and Talele et al. (2021) tested the efficacy of the drugs Arsenicum album 30CH, Bryonia alba 30CH, a combination (Arsenicum album 30CH with Bryonia alba 30cH, Gelsemium sempervirens 30CH and Influenzinum 30CH); a nosode of coronavirus CVN01 30CH and Camphora 1M in the prevention of COVID-19, in a randomized fashion.

It is also worth noting that all participants in the studies cited here had not received at least one dose of the vaccine for COVID-19.

Table 2 - Selected studies.

Clinical Trials				
Author	**Country**	**Title**	**Year**	**Goal**
Adler *et al.*	Brazil	Homeopathy for COVID-19 in primary care: A randomized, double-blind, placebo-controlled trial (COVID-Simile study).	2022	To investigate the efficacy and safety of *Natrum muriaticum* LM2 in the treatment of mild cases of COVID-19 in a primary care setting.
Nayak *et al.*	India	Efficacy of individualized homeopathy as an adjunct to standard of care of COVID-19: A randomized, single-blind, placebo-controlled study.	2022	To evaluate the efficacy of adjuvant individualized homeopathic medicine in adults (aged ≥18 years) admitted to Chirayu Hospital, a hospital designated for treatment of COVID-19.
Talele *et al.*	India	Randomized double-blind, placebo-controlled feasibility study, evaluating the efficacy of homeopathic medicines in the prevention of COVID-19 in a quarantined population.	2021	To evaluate any potential sign of efficacy of commonly recommended homoeopathic drugs for the prevention of COVID-19 in a high-risk population in a government-run quarantine facility for a COVID-19-exposed population, as well as to assess the number of subjects hospitalized and days to recovery.
Cohort studies				
Daruiche *et al.*	Brazil	Homeopathy for COVID-19 prevention: Report of an intervention at a Brazilian service sector company.	2022	Comparing the incidence of confirmed/suspected cases of COVID-19 between those who did or did not receive the homeopathic remedy *Arsenicum* epidemic genius *album* 30CH.
Case Series				
Devos *et al.*	Belgium	Retrospective observational survey on a series of 183 consecutive homeopathically-treated patients during the first COVID-19 peak in Belgium.	2021	To describe the homeopathic medicines prescribed by Belgian physicians for patients with probable SARS-CoV-2 infection, or confirmed by PCR, and the average time of resolution of the symptoms.
Jethani *et al.*	India	Clinical characteristics and remedy profiles of patients with COVID-19: A retrospective cohort study.	2021	To identify the clinical presentation of laboratory-confirmed COVID-19 patients and the group of homeopathic medicines indicated based on their symptomatology profile. To identify the percentage of individuals with symptom resolution and mean time to resolution after the use of allopathic medicines + homeopathics.

Funijo *et al.*	Brazil	Homeopathic treatment in patients with COVID-19: Analysis of clinical evolution and comparison between cases in 2020 and 2021.	2022	Compare the outpatient homeopathic treatment of symptomatic cases of COVID-19 at the Instituto Hahnemanniano George Galvão (IHGG), São Paulo, in March and April 2020 with symptomatic cases seen at the same institution in March and April 2021.
Kurd *et al.*	Israel	Homeopathic treatment for COVID-19-related symptoms: A case series.	2022	To present 5 cases of patients with COVID-19, who were successfully treated with homeopathy, hospitalized at a tertiary medical center in Jerusalem for moderate to severe symptoms related to COVID-19. Each of them requested homeopathic treatment in addition to conventional therapy from the Center for Integrative Complementary Medicine at the hospital.
Takacs *et al.*	Austria	Adjunctive homeopathic treatment of hospitalized COVID-19 patients (COVIHOM): A retrospective case series.	2022	To present the clinical experience with homeopathic treatment of patients with COVID-19 admitted consecutively at the Lienz Hospital in Austria.
To and Fok	Hong Kong	Homeopathic clinical features of 18 patients in COVID-19 outbreaks in Hong Kong.	2020	To report on the symptomatic symptom sets identified in 18 symptomatic patients with COVID-19 in Hong Kong who used homeopathy as a adjuvant treatment for symptom relief.
Case Report				
Glas	Slovenia	Individualised homeopathic treatment of nausea and vomiting in the first trimester and of COVID-19 in the third trimester of pregnancy - A case report.	2022	To describe the case of a thirty-something woman treated with individualized homeopathy for nausea and vomiting in pregnancy in her first trimester and for COVID-19 symptoms in her third trimester, three weeks and a half before the scheduled cesarean delivery.

4.2 CLINICAL TRIALS OF THE USE OF HOMEOPATHY IN THE PREVENTION OR TREATMENT OF COVID-19

All selected clinical trials were randomized and placebo-controlled. Two of them were double-blind (ADLER et al., 2022; TALELE et al., 2021) and one single-blind (NAYAK et al., 2022).

Adler et al. (2022) evaluated the use of Natrum muriaticum LM2 compared to placebo in symptomatic, COVID-19 positive patients 18 years of age or older in home isolation, with severe acute respiratory syndrome (a condition leading to hospitalization) as the exclusion criterion. The primary endpoint was recovery time, defined as the number of days until all disease symptoms were reported as mild or absent. The secondary endpoint was the time to reduce the number of symptoms or score by 50%, as a symptom rating scale was also used (0 = absent, 1 = mild, 2 = moderate, and 3 = severe). The length of the follow-up period ranged from 3 to 21 days among participants who received homeopathy and from 2 to 27 days among those who received placebo, as well as 23 individuals in the homeopathy group (23/42 = 54.8%) and 33 in the placebo group (33/44 = 75%) reported taking other medications during the treatment period, however, with no evidence of a difference between the groups (p-value = 0.07). There was no difference in the primary endpoint (time to recovery) between the groups receiving homeopathic medicine and placebo in either the patient population with mild cases of COVID-19 (p = 0.56) or those with at least 5 moderate or severe symptoms at inclusion (p = 0.06). There was no statistically significant difference for the secondary endpoint considering all participants and those with at least 5 moderate or severe symptoms (p = 0.38 and 0.07, respectively). However, for patients with moderate to severe symptoms, a 50% reduction in symptom severity (score) was achieved significantly earlier in the homeopathy group (p = 0.04). Over the course of this study, four participants were admitted to the hospital, one from the homeopathy group and three from the placebo group (2.4% vs 6.8% respectively, p = 0.62), with no statistically significant difference.

Finally, regarding the quality of the study, the analysis of the results was per protocol, in which only the individuals who reached the end of the process are considered, which compromises the observation of the real efficacy or inefficacy of the treatment employed. In addition, the relatively small sample size (smaller than the necessary previously calculated to obtain relevant effect) is the main limitation to the power of conclusion (β error, type 2). Thus, further studies with larger sample sizes and participants with greater symptom severity are needed in order to evaluate the efficacy of Natrum muriaticum LM2 for COVID-19, since in patients with mild symptoms, the disease is usually self-limited.

Nayak et al. (2022) evaluated the efficacy of individualized homeopathic adjuvant treatment in adults (age ≥ 18 years) admitted to Chirayu Hospital (Madhya Pradesh, India) for management of COVID-19 between July and October 2020. As exclusion criteria, patients with severe heart, lung, kidney, brain, blood or other major systemic diseases, patients on ventilatory support, immunocompromised patients

evident in medical history, pregnant and lactating women, and also patients deemed unable to complete the study were considered.

During the research, in some cases, more than one homeopathic medicine was needed and used non concomitantly. All homeopathic medicines were prescribed in the centesimal potency scale and the scheduling was as decided by the responsible homeopathic physician, following the homeopathy guidelines for centesimal potencies from the 5th edition of the Organon of Medicine. All patients received supportive care according to the Madhya Pradesh government recommendation for COVID-19: azithromycin 500 mg (once daily), pantoprazole 40 mg (once daily), calcium 500 mg (twice daily), montelukast 10 mg/levocetirizine 5 mg (once daily), zinc 50 mg (once daily), and vitamin D3 60,000 IU (weekly), for 5 days. Other allopathic medications for treating symptoms such as cough, pain, and fever were also administered.

The primary endpoint of the study was clinical recovery estimated through the change in total symptom score. Patients were asked by homeopathic physicians to rate their symptoms experienced in the past 24 h, with 0 being no symptoms and 10 being the worst imaginable suffering from the symptom. The scores were summed to obtain total points per patient. The secondary endpoints were

the time to fever resolution and the time to clinical recovery (total symptom score equal to zero). Time to fever clearance was defined as the time from the first dose of study drug until the temperature dropped to ≤ 37.5 °C and remained below that temperature for at least 48 h.

After randomization, the homeopathy group (H) and the placebo group (P) received 151 and 149 participants, respectively. At enrollment 62.91% (n = 95) had pneumonia in the H group, and 51% (n = 76) in the P group. Patients with severe, moderate, and mild signs and symptoms were distributed comparably between the groups.

As a result of the primary endpoint, there was a statistically significant difference in the comparison of the mean total symptom score between the groups over 10 days of follow-up (p = 0.0001). There was a greater trend towards a decrease in the mean total symptom score of the patients using homeopathy. Regarding secondary outcomes, it was observed that in group H, the time to clinical recovery was about 2 days earlier than in group P (p = 0.0001). Fever resolution was 20h earlier in group H (p = 0.04), and a logistic regression performed showed that the chance of patients being symptom-free was 8 times higher in group H than in group P (adjusted odds ratio = 8.36; 95% CI: 4.63 to 15.07; p = 0.0001). At hospital discharge, 63% of the P group had at least one symptom, while in the homeopathic treatment group, only 24% had some residual COVID-19-related symptom. Regarding specific symptoms, there was a significant difference in favor of the H group in the proportion of patients with resolution of dyspnea (p = 0.003); sputum production (p = 0.0001); fatigue (p = 0.0001); and cough (p = 0.0001).

Among the forty homeopathic medicines prescribed, the three most prevalent were: Arsenicum album with 9.93% of patients (n = 15), Bryonia alba and Phosphorus with 7.94% (n = 12) of patients each.

These drugs are highly recommended in the homeopathic literature for diseases with similar presentations, such as influenza.

About the quality of the trial, being a single-blind study, it has its limitation due to the experimenter's bias, since the physicians responsible for the allocation and homeopathic treatment were aware of the group assignment. However, the analysis of the study was by intention to treat, which gives robustness to the evaluation, because it considers all the individuals who were randomized, even those who discontinued the study or died, keeping the necessary amount of individuals established in the sample calculation.

Talele et al. (2021) evaluated the potential efficacy of commonly recommended homeopathic medicines for the prevention of COVID-19 in a population previously exposed to confirmed cases of COVID-19 by RT-PCR. Participants were isolated in a quarantine facility run by the government of India. The survey also assessed the number of subjects hospitalized and days to recovery (absence of symptoms).

Participants were divided into 6 groups for observation of the following interventions: Arsenicum album 30CH, Bryonia alba 30CH, a combination remedy (Arsenicum album 30CH with Bryonia alba 30CH, Gelsemium sempervirens 30CH, and Influenzinum 30CH), coronavirus nosode CVN01 30CH, Camphora 1M, and placebo group. The group randomized to receive the combined remedy had twice as many participants as the other groups. The dosage employed was six tablets, twice a day, for 3 consecutive days. In total, there were 2,294 enrolled and randomized into the study from June 4, 2020 to July 27, 2020. Exclusion criteria included: individuals detected as positive for SARS-CoV-2 at the start of the trial; inability to follow up during the trial period; individuals who took any homeopathic preventive medication immediately prior to enrollment; and individuals scheduled to receive any other experimental medication during the study.

Participants were advised to report, via telephone contact or in person, to the quarantine center coordinator if they experienced any COVID-19 symptoms or potentially unpleasant side effects during the month of the study period. Individuals with symptoms were tested for SARS-CoV-2 and positive cases were sent for further treatment according to standard protocol. These were followed up by telephone on day 15 and day 30, and completed a questionnaire about symptom severity, well-being, and duration of treatment. Individuals who were asymptomatic or who did not test positive for COVID-19 and who took the homeopathic medicines remained in the quarantine facility for 14 days and were closely monitored by medical staff. On day 15, participants who were asymptomatic and not exposed to positive cases during those last 15 days were released from the quarantine facility. Due to the confinement restrictions, and thus avoiding the need for physical presence, participants were contacted by telephone at the time of the scheduled 30-day visit.

The analysis of the study result was per protocol, which considered the 2,233 patients who completed the survey.

As a result, the groups that had a lower incidence of COVID-19 by day 30 of the study, relative to the placebo group, were those that used Bryonia alba 30CH (p = 0.018) and the coronavirus nosode CVN01 30CH (p = 0.036). Presenting the results as odds ratios, Bryonia alba 30CH was the only one that showed statistical significance (OR = 0.318; CI = 0.11-0.94; p = 0.04). In this case, the group that used this drug had a 68% reduction in the chance of developing COVID-19 when compared to the placebo group.

As for hospitalizations, only the Bryonia alba 30CH group had no participant who was hospitalized. Regarding the time in days for recovery (absence of symptoms) after confirmation of the diagnosis of COVID-19, the only group with statistically significant fewer days when compared to the placebo group was the coronavirus nosode CVN01 30CH (mean placebo = 13 days; mean nosode = 5 days; p = 0.03).

Because the group that used Bryonia alba 30CH had only 310 subjects, its prophylactic potential should be explored in larger scale studies.

1. Cohort studies

The cohort study found was conducted by Daruiche et al. (2021), in which available data from all employees of a company were retrospectively analyzed for 3 months (from April 28 to July 30, 2020) in order to compare the incidence of confirmed or suspected cases of COVID-19 among those who received or did not receive the homeopathic medicine GE Arsenicum album 30CH. As exclusion criteria, employees diagnosed with COVID- 19 in the period of the beginning of the research were considered.

In the retrospective analysis of Occupational Health records, 3 subgroups of employees were identified: (1) telecommuting workers;

(2) workers whose tasks required daily commuting to the company's construction sites in the city of São Paulo; and (3) workers allocated to company facilities outside the city of São Paulo.

All employees were followed up weekly by the Occupational Health sector using telemedicine resources. Workers with symptoms similar to COVID-19 were referred to health services for to be submitted to diagnosis (RT-PCR) for confirmation. All symptomatic cases in any group were prescribed the homeopathic medicine GE with therapeutic intent and evaluated daily through telemedicine resources.

The intervention consisted of administering two drops of the drug weekly for prevention, or daily with therapeutic intent. For logistical reasons, only employees who remained working on company premises in the city of São Paulo (G2) could receive the intervention (n=405, 24.66%).

Direct participant observation was not possible and therefore, the use of the homeopathic medicine was evaluated based on the employee's self-report.

The primary outcome was the incidence of COVID-19 during the study period, including both confirmed (RT-PCR positive) and suspected cases. The secondary endpoint was the need for hospitalization and/or ICU. Laboratory operational workers in G2 and G3 did not differ significantly in age group (20 to 60 years), type of work, educational level, or income. The risk of exposure to SARS-CoV-2 was similar for

both, as all of these employees used the public transportation system to go to work and were subjected to similar working conditions, protective measures, and monitoring. On the other hand, G1 (administrative employees who worked at home) was exposed to the same risk of transmission as the general population; the age range was 16 to 77 years, and also included all employees over 60 years old (high-risk group).

About the equivalence of the groups, except for cardiovascular disease and history of cancer, the proportion of cases was uneven. There was a higher proportion ($p < 0.05$) of participants with hypertension, chronic obstructive pulmonary disease, and diabetes mellitus in the group that underwent the intervention (G2) when compared to the two groups that did not use homeopathy (G1 and G3).

In G1, 117 subjects (13.36%) were diagnosed positive for COVID-19 at some point. In G3, 361 subjects (67.87%) were also diagnosed positive for COVID-19. However, in G2 (who received homeopathy), only 3 cases (0.74%) were positive, who had only mild symptoms and were treated at home. The pairwise comparisons of disease incidence were all significant: G1xG2; G1xG3; and G2xG3; $p < 0.001$), demonstrating the prophylactic efficacy of both the use of Arsenicum album 30CH (G1xG2 and G2xG3) and home isolation (G1xG3). The odds ratio of being infected in G3 versus G1 is 13.70 (95% CI, 10.21 to 18.39), that is, 13.70 times greater chance of being infected in group 3 (no social isolation); in G3 versus G2 is 283.02 (95% CI, 88.98 to 900.18), a 283.02 times greater chance of being infected when not using the intervention; and in G1 versus G2 is 20.66 (95% CI, 6.53 to 65.39), a 20.66 times greater chance of being infected when not using the intervention but doing home isolation.

None of the sick workers in G1 or G2 required hospital admission. In turn, 3/245 (1.22%) sick G3 workers were admitted to the ICU - but without the need for intubation or mechanical ventilation.

2. Descriptive observational studies

Devos et al. (2021) retrospectively collected data from 183 mild cases of COVID-19 treated by 6 Belgian homeopathic physicians from February to April 2020. Both patients with confirmed diagnosis by RT-PCR and patients with some of the following concomitant symptoms were included: cough, dyspnea, fever, pain, exhaustion, chest pain, and anosmia. Patient follow-up occurred remotely, due to the requirement of social isolation to prevent the spread of the virus.

The authors considered 11.5 ± 5.7 days to be the average duration of symptoms of mild cases of the disease. Therefore, they established that if all symptoms disappeared in less than 8 days, the shortening of the duration may have been influenced by the homeopathic approach.

Of all patients, 2 (1.1%) required hospitalization, but were able to return home after some time. For 51.4% (n=94), a single medication, chosen individually for the totality of the symptomatic picture, was prescribed mostly in 30K, with the posology of 3 globules twice daily. For 23% (n=42) two successive remedies were required; for 16.4% (n=30) three different homeopathic remedies were required, and for 9.2% (n=16) more than 3 different remedies were used. In those cases of change, the reasons were

inefficiency within 24 hours of administration, worsening of symptoms, or appearance of new symptoms. Ninety-seven different homeopathic medicines were prescribed. 60.1% (n=109) of the patients became asymptomatic in less than 5 days after administration of the homeopathic remedy, and 23% (n=42) in less than 8 days. Table 3 summarizes the most commonly prescribed drugs and the respective percentage of patients who achieved cure in less than 8 days.

Table 3 - Most prescribed homeopathic medicines for COVID-19 and the respective percentage of cure in less than 8 days.

Homeopathic Medicine (prescription prevalence)	**% of individuals cured in < 8 days**
Bryonia alba (28%)	70%
Arsenicum album (18%)	64%
Phosphorus (11%)	70%
Gelsemium sempervirens (8%)	70%

Source: Devos et al., 2021.

Regarding the limitations of the study, it is worth noting that the population that had access to homeopathy during this epidemic period was younger than the general Belgian sick population, and they consulted their doctors early.

Jethani et al. (2021) collected the data of RT-PCR positive patients for COVID-19 admitted to Nehru Homeopathic Medical College and Hospital (NSMCH), which has been designated as the Health Center for treatment of COVID-19 in India, during the period between April 29, 2020 and June 17, 2020.

A total of 196 patients were admitted to the hospital during the study period, however, 58 patients did not give consent to receive complementary homeopathic treatment. Most patients (90.8%) were experiencing mild symptoms (n = 178) and the remainder (9.2%) were classified as moderate (n = 18). Homeopathic treatment was provided to 138 patients according to symptom repertorization, along with standard conventional allopathic treatment. The symptom repertorial analysis of these patients indicated a total of 28 medicines. The drugs were administered in different potencies (LM, 30CH, 200CH), with Bryonia alba (33.3%), Arsenicum album (18.1%), Pulsatilla nigricans (13.8%), Nux vomica (8%), Rhus toxicodendron (7.2%) and Gelsemium sempervirens (5.8%) being the most used. The most used potency was 30CH (n = 120).

The overall recovery rate for COVID-19 positive patients treated with homeopathy was 78% (n=107) and the average length of stay in the hospital was 13 days. A top 5% (5.1%) of patients worsened during the study and were referred to a tertiary care center with ventilatory support.

Regarding the limitations of the study, although most cases improved and were discharged, the positive outcome cannot be attributed to homeopathic medicines alone, since the patients also received

conventional allopathic medicines. In addition, this disease is also known for its self-limited course of 5 to 14 days in mild cases, and there was no control arm to evaluate the efficacy of homeopathy.

Fujino et al. (2022) conducted a retrospective descriptive observational study based on the analysis of medical records of patients from Instituto Hahnemanniano George Galvão (IHGG), São Paulo, with symptoms compatible with COVID-19 and positive RT-PCR test results, during the period from March to April 2020 and in the same months of 2021. For the purpose of study homogeneity, medical records with incomplete registration data were excluded.

After selecting the medical records, the data were collected, tabulated and analyzed in Microsoft Excel spreadsheets, recording the symptoms and medications prescribed every 3 days, with Day 0 (D0) being the day of the initial consultation when the patients were evaluated and when they received the homeopathic medication.

In each case, only one homeopathic medicine was prescribed at a time, chosen according to the symptoms presented. In one situation where symptoms changed during the course of the condition, it was necessary to change the prescribed medicine, and these different medicines were used sequentially, and never simultaneously. All patients were followed up until evident clinical improvement; no adverse events were observed, and the patients recovered with resolution. In none of the cases was hospitalization required.

Fifty-four medical records were selected, with an equal number of patients in the 2 years. Of the 27 cases studied in 2020, 81.48% were female and 18.52% were male, with a mean age of 53 years, and five patients were 65 years or older. In 2021, of the 27 cases analyzed, 70.37% were female and 29.63% were male, with a mean age of 45 years, with two patients over 65 years old. None of these data show a statistically significant difference between the two groups ($p > 0.05$).

In 2020, considering the total number of patients, there was improvement of symptoms from day 3 and resolution of the condition on day 9, with 82% of patients without clinical symptoms. The researchers divided the participants into three groups according to the frequency of symptoms: G1 patients with more frequent symptoms; G2 patients with moderately frequent symptoms; and G3 patients with uncommon symptoms. Also in 2020, in G1 there was a statistically significant and progressive reduction in the number of symptoms over the course of days, from day 3 of drug use ($p < 0.001$). In G2, this reduction was significant only from day 6 (D6) ($p < 0.001$) between D3 and D6. Symptoms belonging to G3 only had a significant reduction in frequency between D0 and D3 ($p = 0.0097$), showing improvement on the third day after homeopathic medication. From D3 on, the improvement was not significant: these symptoms persisted.

By 2021, the G1 group had a statistically significant reduction in the number of symptoms as of day 6 (between D0 and D6, $p = 0.0003$; between D6 and D9, $p = 0.0074$). In the group of symptoms that appeared at moderate frequency (G2), there was also a significant reduction in the number of symptoms as

of day 6 (between D0 and D6: p = 0.0306), with an exponential decrease. Symptoms belonging to G3 only had a significant reduction in their frequency as of day 12, p = 0.0215 between D0 and D12.

Considering the total number of symptoms in each sample (2020 and 2021), there was a highly significant difference (p < 0.001) in the reduction of symptoms between the two samples from the third day after use of the homeopathic drug, with a greater decrease in the number of symptoms between D0 and D3 in the 2020 sample compared to 2021. Furthermore, there were no adverse events reported during treatment in 2020 or 2021.

About the prescribed medications, in 2020, Antimonium tartaricum was the most prescribed medication on the third (59.26%) and sixth (78.6%) day of evaluation. In 2021, the most frequently prescribed medication before resolution of the condition was Arsenicum album.

Kurd et al. (2021) presented the cases of 5 patients hospitalized in Jerusalem for moderate to severe symptoms related to COVID-19. Each of them requested homeopathic treatment in addition to conventional therapy from the hospital's Center for Integrative Complementary Medicine. All patients had more than 18 years of age and had a confirmed diagnosis of COVID-19 upon admission to the hospital.

Case 1 was a 44-year-old morbidly obese woman (BMI = 54) with uncontrolled diabetes mellitus and hypothyroidism (Hashimoto's disease) who was admitted to the emergency room with fever, dyspnea, dry cough, and diarrhea. She was diagnosed with severe viral pneumonia and a high-risk hypercoagulable state. In addition to conventional allopathic treatment, she was started on Arsenicum album every 2h. She was discharged from the ICU on day 4. On day 5, his respiratory condition improved greatly, with oxygen saturation at 97% without supplemental oxygen. On the 14th day he was discharged with good health.

Case 2 was a 36-year-old obese woman (BMI = 32) who presented with cough, dyspnea, oxygen saturation of 90% on room air, fever (38.7°C), myalgia, intense weakness, headache, dizziness, nausea, hematemesis, and agenusia. She had given birth 10 months ago and was still breastfeeding. She was diagnosed with severe pneumonia related to COVID-19. In addition to conventional allopathic treatment, she was started on Arsenicum album every 2h. On the second day, the administration of Arsenicum album was alternated with Phosphoric acid every 2h. By the third day, the patient had slept without supplemental oxygen and was virtually free of chest pain on inhalation. Her oxygen saturation was 98% on room air and her sense of taste was returning. Also on the third day, she was given alternating phosphoric acid and Bryonia alba. On the fourth day he had no fever, his breathing was better, his appetite was good, and his sense of taste continued to improve. He was discharged on the fifth day.

Case 3 was a 40-year-old, obese man (BMI = 31), admitted after a week of headache, fever (39 °C), muscle aches, and dyspnea with an intense, choking cough, aggravated by speech. On admission, he collapsed. He was extremely weak and suffered from back pain and muscle stiffness, improved by a very hot bath. He had lost his sense of smell and taste, and had no appetite. The patient was diagnosed with severe pneumonia related to COVID-19. In addition to conventional allopathic treatment, he started

Arsenicum album every 2h. On the fourth day, the patient felt better, free of fever and body aches. His appetite was good, and his cough had reached a point where it no longer bothered him. The medication was changed to Stannum 4 times a day. By the fifth day his dyspnea had improved significantly, he felt well and slept soundly. He was discharged on this day.

Case 4 was a 35-year-old obese man (BMI = 33) with diabetes mellitus and hypertension. He presented with fever unresponsive to antipyretic therapy, was very weak, with severe diarrhea, dry cough, and dyspnea, with oxygen saturation of 93% on room air. His respiratory condition worsened in the Emergency Room, with oxygen saturation dropping to 87%, requiring supplemental oxygen via nasal cannula. Besides the conventional allopathic treatment, he started phosphorus every 2 hours. On the second day, the medication was replaced by lobelia purpurascens every 2h. Still on the same day, the cough had practically disappeared, and her chest constriction and dyspnea had completely disappeared. On the fourth day lobelia purpurascens was replaced by ozone every 2h. The patient's cough improved immediately, and the medication was continued 4 times a day. He was discharged from hospital 2 days later.

Case 5 was a 62-year-old man hospitalized with fever and severe dyspnea. He was diagnosed with COVID-19 related critical pneumonia and acute respiratory distress syndrome with hypoxemic respiratory failure (oxygen saturation of 70%). Due to refractory hypoxia, the patient was transferred to the ICU to be intubated and mechanically ventilated. The patient received conventional allopathic treatment, and at the request of his family, started homeopathic treatment on his 12th day in the ICU. He then started arsenicum album every 3h, and calmed down after the first dose. On the third day of treatment, he was extubated without complications and transferred to an isolation ward. He was discharged on the seventh day to continue his recovery at home.

The data from the five patients reveal a much shorter ICU and hospital length of stay than the overall average for patients with COVID-19: 22 days of hospital stay and 11.6 days of ICU stay (BRASIL, 2021). Takacs et al. (2021) presented their clinical experience with homeopathic treatment of patients with COVID-19 at the Lienz Hospital in Austria between March 20 and April 20, 2020. The homeopathic physician in charge of treatment was instructed by the hospital on March 27, 2020 to treat all inpatients with COVID-19. The progress of 13 patients who received homeopathic treatment in addition to conventional therapy was reported. At the beginning of treatment, each patient received influenzinum, either in the 200CH potency or, in case of a very critical condition, in the 10,000CH potency, on the first day. Afterwards, the prescription was adapted according to the clinical evolution. All patients were over 18 years old, with a mean age of 73.4 ± 15.0 (SD) years. Only one patient died, and this had been admitted to the hospital ICU with prolonged septic shock which was not manageable by conventional or homeopathic medicine. Six of the 13 patients (46.2%) were transferred to the ICU. The mean ICU stay of the 5 surviving patients was 18.8 ± 6.8 days (13-30 days). The 12 surviving patients were discharged without sequelae after 14.4 ± 8.9 days.

In this study, the authors used the modified Naranjo algorithm (LAMBA et al., 2020) (Table 4) to assess the causal attribution of clinical outcome to homeopathic intervention. Six points were assumed as thresholds for potential association between homeopathic therapy and symptom improvement or cure in acute cases. The algorithm score was between +7 and +8 points in 11 patients (84.6%), one patient with a score of +3 and the non-survivor with a score of -3 points.

Table 4 - Modified Naranjo's algorithm for homeopathy (MONARCH)

Criteria for assigning causality	**Yes**	**No**	**Maybe or N/A**
1. There was an improvement in the main symptom or condition for the which homeopathic remedy was prescribed?	+2	-1	0
2. Clinical improvement occurred within a plausible timeframe in relation to taking the medicine?	+1	-2	0
3. Was there an initial worsening of the symptoms?	+1	0	0
4. The effect covered more than the main symptom or condition (i.e., other symptoms were improved or altered)?	+1	0	0
5. Has the general well-being improved?	+1	0	0
6A. Sense of healing: some symptoms improved in the order inverse of the development of the symptoms of the disease?	+1	0	0
6B. Direction of healing: at least two of the following applied to the order of symptom improvement: – from organs of greater importance to those of less importance? – from the deepest to the most superficial aspects of the individual? – from top to bottom?	+1	0	0
7. The "old symptoms" (defined as symptoms that are not seasonal and non-cyclical that were previously thought to have were resolved) temporarily reappeared during the course of improvement?	+1	0	0
8. Are there alternative causes (other than the medication) that, with high probability, could have caused the improvement? (Consider the known course of the disease, other forms of treatment and other clinically relevant interventions)	+3	+1	0
9. Has the improvement in health been confirmed by any objective evidence? (for example, laboratory test, clinical observation, etc.)	+2	0	0
10. Repeated dosing, if performed, created clinical improvement similar?	+1	0	0

Source: LAMBA et al., 2020.

To and Fok (2020) reported 18 cases of patients diagnosed with COVID- 19, who had homeopathic consultation online and treated the disease with allopathic medicines or traditional Chinese medicine in addition to homeopathy, except for 1 patient who used homeopathy alone.

The case series comprised 10 young men, 6 young women and 2 middle-aged women with mild symptoms. The most commonly indicated medications by symptom repertorization for the 18 cases were Gelsemium sempervirens (n = 12) and Bryonia alba (n = 4), followed by Eupatorium perfoliatum (n = 1) and Arsenicum album (n = 1).

Of the 18 patients, 14 (77.7%) reported 80% or more improvement of symptoms on the third day of homeopathic treatment. The patient with the slowest rate of clinical recovery reported more than 60% improvement of symptoms on the third day. Two patients reported being symptom free on the third day.

Although the report shows good results, it is limited due to the age range of the participants involved - 15 patients (83%) between 18 and 24 years old - who, because they are young, may have a naturally faster recovery, and the fact that they are cases with mild symptoms.

Glas et al. (2022) reported the case of a pregnant woman who contracted SARS-CoV- 2 late in her pregnancy, more precisely three and a half weeks before the planned cesarean section. The patient presented with headache, nasal obstruction with discharge, and complaints of hyposmia and insomnia. The pregnant woman was immediately seen by homeopathic tele-consultation and all her symptoms were repertorized for the choice of the most appropriate medication, which in this case was Sepia officinalis LM6. After initiation of treatment, symptoms improved rapidly. The authors further used Naranjo's algorithm modified for homeopathy to analyze the attribution of causality of the clinical outcome to the homeopathic intervention. The score obtained was +8, suggesting that homeopathy contributed to clinical improvement.

It is worth noting that descriptive observational research has no power as evidence of efficacy, even though rapid healing of a significant percentage of patients can be considered an interesting indicator. For evidence of efficacy and health care decision making, randomized clinical trials are prioritized. However, because this is a new disease, the review of successfully treated case series serves as a guide for the planning of new clinical trials, and with this, the establishment or not of the effectiveness of the specific treatment.

3. Arsenicum album and Bryonia alba

Arsenicum album and Bryonia alba were the most prescribed homeopathic medicines for the treatment of COVID-19, based on the repertorization of the patients' symptoms, and the ones that presented the best results. Thus, we can also suggest them as epidemic genius medicines.

The materia medica (ABRAHCON, [18--?]) of Arsenicum album refers to the outwardly organized and inwardly disorganized individual. To that individual with the psyche who finds error in everything, wakes up feeling miserable, as if life is a burden, and believes that it is useless to take medicine, that he is

incurable, and that he will certainly die. The central idea is a deep-seated insecurity. In general, as far as the physical is concerned, it is also suitable for influenza.

Bryonia alba is the first medicine to be considered when the patient needs to lie still and suffers a lot from any movement. In the materia medica of pure experimentation, it presents a general action known and consecrated by clinical materia medica of several authors, which is its characteristic of drying the mucous membranes and inflame the serous producing in these, exudates and transudates in healthy individuals (LEITÃO et al., 2020). It is indicated to help in the treatment of previously diagnosed bronchitis symptoms, rheumatism symptoms, joint, bone and muscle pain, limb pain, sore throat, help relieve symptoms related to flu and acute inflammatory diseases of the respiratory system, watery runny nose with nasal obstruction and prostration during the flu, in relieving spasmodic, productive or dry, irritative coughs (BRAZIL, 2018).

Leitão et al. (2020) conducted a study in order to define the homeopathic epidemic genius (GE) of COVID-19 in Brazil, identifying a medicine or the group of homeopathic medicines corresponding to it. They followed the methodological guidelines presented by Kent (2002), Hahnemann (2013) and in the Minor Writings (HAHNEMANN and DUDGEON, 2006). As a result, they identified seven medicines, and both Arsenicum album and Bryonia alba are in this group, corroborating the findings found in this literature review.

5 FINAL CONSIDERATIONS

From the selection and analysis of the evidence found, we could observe that homeopathy does indeed have a potential beneficial adjuvant effect in the treatment of COVID-19 in mild, moderate and severe cases of the disease. However, more robust clinical trials with intention-to-treat analysis, considerable numbers of participants, and double-blinding are needed. The number of cohort studies performed is also very small and should be further explored, especially regarding the evaluation of the use of homeopathy in the prevention of the disease, since it may offer data on risk or chance of contracting the virus. On the other hand, several descriptive observational studies were found, which are of utmost importance, since they present the whole symptomatology of a series of cases and the individualized choice of the medicine. Thus, they allow a broad view of the various manifestations of the pathology in different individuals, which enables the visualization of the pandemic profile and the choice of the epidemic genie drug(s). In this sense, Arsenicum album and Bryonia alba were the most prescribed drugs with the best results in both prevention and adjuvant treatment to allopathy. Therefore, they are the ones suggested in this study as genius epidemic.

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