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RESEARCH ARTICLE

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Greater celandine (*Chelidonium majus* L.) for COVID-19: A twenty-case series

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In December 2019, an outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, China, with a rapid increase in cases worldwide. Until now, among several drugs tested, none demonstrated sufficient efficacy for its etiological treatment. Greater celandine (*Chelidonium majus* L.) is a well-known medicinal plant, traditionally indicated for digestive disorders and topically to remove warts. This study, performed at private offices in São Paulo and Aracaju (Brazil), describes 20 consecutive COVID-19 outpatients treated with greater celandine and their clinical evolution. The patients, aged 14–71 years (median of 41 years), were treated with *Chelidonium majus* 10% mother tincture, 20–30 drops three times a day for 3–12 days (median of 5 days). Clinical features were assessed during the treatment and at least until 1 week after its end. These cases were considered mild, as most COVID-19 cases. The symptoms were mainly fever, fatigue, cough, sore throat, coryza, anosmia, ageusia, and headache. Ten patients had comorbidities, such as hypertension, diabetes, and overweight. Complete or almost complete clinical improvement occurred within 1–9 days of treatment (median of 3 days). There were no adverse events. This casuistry, although small, may inspire other researchers to continue investigating *Chelidonium majus* as a healing treatment for COVID-19.

KEYWORDS
case series, *Chelidonium majus*, COVID-19, greater celandine, phytotherapy

1 | INTRODUCTION

Since December 2019, the world has been facing a new disease caused by a β-coronavirus, initially called 2019 novel coronavirus, originated in Wuhan, China. The presenting clinical features of coronavirus disease (COVID-19) range from an influenza-like illness to a severe acute respiratory syndrome (SARS). The COVID-19 pandemic has caused thousands of deaths, disrupted global healthcare networks, and brought international economic recession.

Several drugs are being used on patients with COVID-19, inspired by empirical or hypothetical bases. So far, none of them has proved sufficiently effective as a form of etiological treatment.

Greater celandine (*Chelidonium majus* L.) is a medicinal plant of the family *Papaveraceae*, native to temperate and subarctic regions of Asia and from the subarctic to Mediterranean Europe. It is traditionally indicated for abdominal cramp pains in the bile ducts and in the gastrointestinal tract (Blumenthal et al., 1998), for the symptomatic treatment of mild spasms in the upper gastrointestinal tract and slight biliousness, and for dyspeptic complaints such as flatulence (ESCOP, 2003). As an old topical indication, there is its reputed power to remove warts. Other indications of external use are corns, tinea infections, eczema, and tumors of the skin (Orland, Knapp, König, Ulrich-Merzenich, & Knöß, 2014). In homeopathy, according to the German Commission D, *Chelidonium majus* is indicated for liver and gallbladder disorders, respiratory inflammations, and rheumatism (Kommission, 1985). In anthroposophic medicine, its indications are as follows: stimulation of metabolic processes, especially in the case of disorders of the liver–bile–pancreas system and their accompanying psychological symptoms (Kommission, 1999). In traditional Chinese medicine, it is mainly used to treat blood stasis, to relieve pain, to

promote diuresis in edema and ascites, to treat jaundice, and to relieve cough (Gilca, Gaman, Panait, Stoian, & Atanasiu, 2010).

More recently, its in vitro and in vivo antiviral activity has been studied (Gerencer et al., 2006; Lozjuk, Lisnyak, & Lozjuk, 1996; Nawrot et al., 2020), a fact that encouraged the authors to use greater celandine for patients with COVID-19.

2 | CASES PRESENTATION

The 20 consecutive outpatients with COVID-19 described below were treated in private offices, in two cities (São Paulo and Aracaju) in Brazil, in April, May, and June 2020. All adult patients in this study and the parents of a minor patient gave written and signed consent to publish the data.

All patients took *Chelidonium majus, planta tota* (the whole plant collected during flowering time) orally, 10% mother tincture, with 50% alcohol content (Schraiber Homeopatia Laboratory, Cotia, SP, Brazil), from homeopathic pharmacies. *Chelidonium majus* extract was manufactured through percolation; the final product (mother tincture) contains 0.06–0.15% of alkaloids calculated as chelidonine. The dosage was 20–30 drops taken with water, three times a day (approximately every 8 hr) for 3–12 days, according to the persistence of symptoms.

All patients were followed up for at least 1 week after the end of treatment.

Patient 1: A 40-year-old male presented with fever (38°C, 100.4 °F—axillary temperature) and pruritic erythematous papules on the trunk and face. After 4 days, the patient developed anosmia and dysgeusia, sore throat, coryza, cough with productive sputum, and fatigue. The patient is overweight. On physical examination, the patient presented a moderate oropharyngeal hyperemia and edema of the nasal turbinates. At that moment, *Chelidonium majus* was started, 30 drops three times a day. All symptoms completely disappeared on the second day. The medication was interrupted on the third day. Three weeks after the onset of symptoms, his blood tests (IgM and IgG antibody test) were positive (rapid IgM-IgG combined antibody test for COVID-19, immunochromatography based test).

Patient 2: A 38-year-old female, wife of Patient 1, informed a similar picture: fever (38°C, 100.4 °F), dysgeusia, coryza, sore throat, gradually increasing cough with productive sputum, and headache—for 10 days. There were no comorbidities. The only change on physical examination was a moderate oropharyngeal hyperemia. The patient took *Chelidonium majus* 30 drops three times a day, for 4 days. After 1 day, the patient had no more cough; after 3 days the patient felt well, with no other symptoms, except for a little respiratory phlegm that the patient considers "normal" due to the variation in the climate. The result of her nasopharyngeal swab test for COVID-19 (RT-qPCR, real-time reverse transcription polymerase chain reaction) was positive.

Patient 3: A 47-year-old female complained of headache, myalgia, arthralgia, fever (37.6°C, 99.8 °F), anosmia, ageusia, anorexia, epigastric pain, dry cough, and sore throat. The patient has hypertension and a very recent diagnosis of breast cancer, which has not been treated yet. Two days after the onset of symptoms, her nasopharyngeal swab test for COVID-19 (RT-qPCR) was positive. The patient took dipyrone 500 mg for pain. On physical examination, there was a moderate oropharyngeal hyperemia and a moderate pain on epigastric palpation. Seven days later, with the same symptoms, except for fever, the patient started treatment with *Chelidonium majus* 30 drops three times a day. A day later, the patient had only headache. After 2 days of treatment, the patient was completely asymptomatic. The medication was maintained for another day.

Patient 4: A 42-year-olf female had complained of anosmia, sore throat, and anorexia for 4 days. There were no comorbidities. On physical examination, there was only a moderate oropharyngeal hyperemia. Her nasopharyngeal swab PCR test for COVID-19 was positive. After 3 days, with *Chelidonium majus* 30 drops three times a day, the patient was asymptomatic. On the fifth day, the medicine was interrupted.

Patient 5: A 45-year-old male with sickle cell trait presented with a 5-day history of anosmia, fatigue, dyspnea, cough, back pain, headache, arthralgia, and fever (37.8°C, 100.1 °F). His nasopharyngeal swab PCR test for COVID-19 was positive. On physical examination, the patient had only fever. He took *Chelidonium majus* 30 drops three times a day. On the sixth day, the patient was asymptomatic except for mild fatigue, which disappeared the next day.

Patient 6: A 40-year-old female had had chest pain, coryza, sore throat, cough, and headache for 5 days. On physical examination, the patient had a moderate oropharyngeal hyperemia. There were no comorbidities. Her nasopharyngeal swab PCR test for COVID-19 was positive. The patient took *Chelidonium majus* 30 drops three times a day for 5 days. On the third day, the patient was asymptomatic.

Patient 7: A 37-year-old female presented with anosmia, ageusia, fever (39°C, 102.2 °F), body aches, mild dyspnea, and fatigue. The patient took paracetamol 500 mg for pain. The patient is overweight. The only change on physical examination was a mild oropharyngeal hyperemia. On the seventh day of symptoms, the patient started taking *Chelidonium majus*, 30 drops three times a day, for 5 days. After 2 days, there were only anosmia and dysgeusia (which gradually normalized), with no other symptoms.

Patient 8: A 37-year-old male gave an 8-day history of fatigue, body aches, headache, anosmia, and ageusia. The patient is overweight. On physical examination, there was a mild oropharyngeal hyperemia. The patient took *Chelidonium majus*, 30 drops three times a day, for 5 days. After 3 days, the patient had only anosmia and dysgeusia (which gradually normalized), no other symptoms. This patient is married to Patient 7. Their diagnoses (Patients 7 and 8, as well as 9 and 11) were based on symptoms and exposures, no test was performed because testing capacity is insufficient to meet the current needs in Brazil.

Patient 9: A 64-year-old female presented with a 24-hr history of coryza, sneezing, body aches, malaise, fatigue, dyspepsia, and insomnia for fear of COVID-19. The patient reported previous contact with persons with laboratory-confirmed COVID-19. The patient has hypertension. On physical examination, there was a mild edema of the nasal

turbinates. *Chelidonium majus*, 30 drops, was given from the beginning of the second day of symptoms and maintained three times a day for 3 days. On the second day of treatment, the patient was asymptomatic.

Patient 10: A 14-year-old male, overweight, had an acute onset of diarrhea, anorexia, nausea, malaise, and indisposition in the morning. The only change on physical examination was a moderate diffuse pain on abdominal palpation. At the end of the day, the patient started taking *Chelidonium majus*, 20 drops three times a day, for 3 days. After 1 day, the patient was completely asymptomatic. After 7 days, his blood tests for COVID-19 showed a positive IgM and a negative IgG.

Patient 11: A 53-year-old female had a 4-day history of fever (38°C, 100.4 °F), fatigue, sore throat, anosmia, anorexia, diarrhea, and dyspepsia. The patient is overweight. As a health professional, the patient had some previous contact with patients with laboratory-confirmed COVID-19. On physical examination, there was a moderate oropharyngeal hyperemia and a mild diffuse pain on abdominal palpation. The patient took *Chelidonium majus*, 20 drops three times a day, for 3 days. On the third day, the patient was asymptomatic, except for slight fatigue.

Patient 12: A 36-year-old female presented with headache, thoracolumbar pain, and fermentative dyspepsia for 10 days. Her nasopharyngeal swab PCR test for COVID-19 was positive. Then, the patient received azithromycin for 7 days, prescribed by another doctor, with no clinical improvement. On physical examination, the patient had intense borborygmus on abdominal auscultation. Two days later, she started taking *Chelidonium majus*, 30 drops three times a day, for 7 days. After 3 days, the patient was asymptomatic.

Patient 13: A 53-year-old female gave a 3-day history of profuse and cold sweating, coryza, sneezing, tearing, fatigue, postural dizziness, and dysuria. There were no changes on physical examination. The patient had a positive nasopharyngeal swab PCR test for COVID-19. She took *Chelidonium majus*, 30 drops three times a day, for 7 days. After 3 days, the patient was asymptomatic.

Patient 14: A 45-year-old female presented with a 7-day history of coryza, dry cough with chest pain, odynophagia, eructation, fermentative dyspepsia, anorexia, body aches, cooling in the lower limbs, and fear of dying. There were no comorbidities. Although the patient did not have hypertension previously, on physical examination her blood pressure was high (150/90 mmHg) and the abdomen was slightly distended, with a slow peristalsis. Her nasopharyngeal swab PCR test for COVID-19 was positive. The patient took *Chelidonium majus*, 30 drops three times a day, for 7 days. After 5 days, the patient was asymptomatic, with resolution of changes in physical examination.

Patient 15: A 36-year-old female gave a 3-day history of chest pain, fatigue, tremors, cooling in lower limbs, and fear of dying. The patient had a previous diagnosis of panic disorder. There were no comorbidities and no changes on physical examination. Her nasopharyngeal swab PCR test for COVID-19 was positive. The patient took *Chelidonium majus*, 30 drops three times a day, for 7 days. After 5 days, the patient was asymptomatic.

Patient 16: A 71-year-old female presented with a 24-hr history of dry cough, odynophagia, fatigue, body aches, dysuria, and anorexia. The patient has hypertension and type 2 diabetes. On physical examination, there was a moderate oropharyngeal hyperemia and the breath sounds were diminished at the apices. The patient took *Chelidonium majus*, 30 drops three times a day, for 7 days. After 5 days, she was asymptomatic, with resolution of changes in physical examination. Ten days after the onset of symptoms, her blood tests for COVID-19 showed a positive IgM and a negative IgG.

Patient 17: A 28-year-old female had had only fatigue and malaise for 5 days. There were no comorbidities and no changes on physical examination. The patient took *Chelidonium majus*, 30 drops three times a day, for 7 days. After 5 days, the patient was asymptomatic. Two weeks after the onset of symptoms, her blood tests for COVID-19 showed a positive IgM and a negative IgG.

Patient 18: A 61-year-old female presented with a 24-hr history of fever (38°C, 100.4 °F), headache, anosmia, ageusia, odynophagia, fatigue, and anorexia. There were no comorbidities. On physical examination, there was a moderate oropharyngeal hyperemia and fever. The patient took *Chelidonium majus*, 30 drops three times a day, for 12 days. This patient was the one who took the longest to become asymptomatic (9 days) and the only one who needed more than 8 days of medication. Fourteen days after the onset of symptoms, her blood tests for COVID-19 showed a negative IgM and a positive IgG.

Patient 19: A 59-year-old female gave a 24-hr history of severe headache, coryza, odynophagia, body aches, fatigue, and fever (39°C, 102.2 °F). There were no comorbidities. On physical examination, there was an intense oropharyngeal hyperemia and fever. Her nasopharyngeal swab PCR test for COVID-19 was positive. The patient took *Chelidonium majus*, 30 drops three times a day, for 8 days. After 7 days, she was asymptomatic.

Patient 20: A 34-year-old female presented with a 4-day history of dry cough, dyspnea, odynophagia, myalgia, and fever. The patient has chronic bronchitis. There were no changes on physical examination. Her nasopharyngeal swab PCR test for COVID-19 was positive. The patient took *Chelidonium majus*, 30 drops three times a day, for 5 days. After 3 days, she was asymptomatic.

None of the 20 patients reported any medication-related adverse event.

Table 1 summarizes the main data from the 20 cases.

3 | DISCUSSION AND CONCLUSIONS

This case series is notable because it shows a significant clinical improvement in a few days, most of the time. It is known that the natural course of COVID-19 is quite variable. Symptoms usually tend to resolve after 10 days (Siordia Jr., 2020). But in this case series, there was complete or almost complete symptoms resolution with the institution of treatment in 1–9 days (median of 3 days), with a total duration of symptoms ranging from 2 to 22 days (median of 8 days).

TABLE 1 Clinical features of 20 patients with COVID-19 treated with *Chelidonium majus*

Patient	Age (years)	Gender	Symptoms	Changes on physical examination	Comorbidities	Number of days with symptoms before starting Chel.	Number of days until resolution of the clinical features after the introduction of Chel.	Number of days with Chel.	Diagnostic test
1	40	M	Fever, pruritic erythematous papules, anosmia, dysgeusia, sore throat, coryza, cough, fatigue	Oropharyngeal hyperemia, edema of the nasal turbinates	Overweight	4	2	3	IgM +, IgG +
2	38	F	Fever, dysgeusia, coryza, sore throat, cough, headache	Oropharyngeal hyperemia	No	10	3	4	Nasopharyngeal swab PCR test +
3	47	F	Headache, myalgia, arthralgia, fever, anosmia, ageusia, anorexia, epigastric pain, dry cough, sore throat	Oropharyngeal hyperemia, epigastric pain	Hypertension	10	2	3	Nasopharyngeal swab PCR test +
4	42	F	Anosmia, sore throat, anorexia	Oropharyngeal hyperemia	No	4	3	5	Nasopharyngeal swab PCR test +
5	45	M	Anosmia, fatigue, dyspnea, cough, back pain, headache, arthralgia, fever	Fever	Sickle cell trait	5	7	7	Nasopharyngeal swab PCR test +
6	40	F	Chest pain, coryza, sore throat, cough, headache	Oropharyngeal hyperemia	No	5	3	5	Nasopharyngeal swab PCR test +
7	37	F	Anosmia, ageusia, fever, body aches, dyspnea, fatigue	Oropharyngeal hyperemia	Overweight	7	2	5	No
8	37	M	Fatigue, body aches, headache, anosmia, ageusia	Oropharyngeal hyperemia	Overweight	8	3	5	No
9	64	F	Coryza, sneezing, body aches, malaise, fatigue, dyspepsia, insomnia	Edema of the nasal turbinates	Hypertension	1	2	3	No
10	14	M	Diarrhea, anorexia, nausea, malaise, indisposition in the morning	Diffuse abdominal pain	Overweight	1	1	3	IgM +, IgG -
11	53	F	Fever, fatigue, sore throat, anosmia, anorexia, diarrhea, dyspepsia	Oropharyngeal hyperemia, abdominal pain	Overweight	4	3	3	No

(Continues)

TABLE 1 (Continued)

Patient	Age (years)	Gender	Symptoms	Changes on physical examination	Comorbidities	Number of days with symptoms before starting Chel.	Number of days until resolution of the clinical features after the introduction of Chel.	Number of days with Chel.	Diagnostic test
12	36	F	Headache, thoracolumbar pain, fermentative dyspepsia	Intense borborygmus	No	19	3	7	Nasopharyngeal swab PCR test +
13	53	F	Profuse and cold sweating, coryza, sneezing, tearing, fatigue, postural dizziness, dysuria	No	No	3	3	7	Nasopharyngeal swab PCR test +
14	45	F	Coryza, dry cough, chest pain, odynophagia, eructation, fermentative dyspepsia, anorexia, body aches, cooling in the lower limbs, fear of dying	High blood pressure, abdomen distended, slow peristalsis	No	7	5	7	Nasopharyngeal swab PCR test +
15	36	F	Chest pain, fatigue, tremors, cooling In lower limbs, fear of dying	No	No	3	5	7	Nasopharyngeal swab PCR test +
16	71	F	Dry cough, odynophagia, fatigue, body aches, dysuria, anorexia	Oropharyngeal hyperemia, breath sounds diminished (apices)	Hypertension, type 2 diabetes	1	5	7	IgM +, IgG -
17	28	F	Fatigue, malaise	No	No	5	5	7	IgM +, IgG -
18	61	F	Fever, headache, anosmia, ageusia, odynophagia, fatigue, anorexia	Oropharyngeal hyperemia, fever	No	1	9	12	IgM -, IgG +
19	59	F	Headache, coryza, odynophagia, body aches, fatigue, fever	Oropharyngeal hyperemia, fever	No	1	7	8	Nasopharyngeal swab PCR test +
20	34	F	Dry cough, dyspnea, odynophagia, myalgia, fever	No	Chronic bronchitis	4	3	5	Nasopharyngeal swab PCR test +

Note: Chel. = *Chelidonium majus;* F: female; M: male; +: positive; —: negative.

In the 20 cases mentioned, *Chelidonium majus* was the only medication used to treat COVID-19, alongside symptomatic medicines (paracetamol and dipyrone).

This paper has some limitations. The main one is the small number of cases, which could not be considered as a proof of efficacy. Larger studies are needed, especially randomized clinical trials. But the starting point could be a case series. Another limitation is that some patients started the treatment with *Chelidonium majus* after a week or more with symptoms (1–19 days, median of 4 days).

All of these 20 cases can be classified as mild, with absent or mild pulmonary involvement. Precisely for this reason, it is not possible to infer how the response to this medication would be in severe cases.

In this case series, 10 patients had at least one comorbidity: hypertension, type 2 diabetes mellitus, chronic bronchitis, sickle cell trait, and overweight. We can consider overweight a comorbidity, because according to some authors, overweight patients with COVID-19 are at a higher risk of developing severe pneumonia compared with patients of normal weight (Cai et al., 2020).

From the perspective of all 20 patients, the treatment was considered effective, well-tolerated, and easy to comply.

The medical and pharmacological literature indicates that the main chemical constituents of greater celandine are alkaloids, principally of the benzylisoquinoline type (e.g., coptisine, chelidonine, sanguinarine, berberine, protopine, and chelerythrine), chelidonic, and caffeic acid derivatives (such as caffeoylmalic acid) (Blumenthal et al., 1998; Wu, Wang, Xu, Liu, & Di, 2019). Its latex has the wart-removing property, attributed to its proteolytic enzymes (Pelikan, 1997). *Chelidonium majus* stimulates catabolic processes, such as bile production and excretion, and vitalizing processes, such as hepatic protein synthesis (Gardin, 2007).

The antiviral effect of *Chelidonium majus* has been reported in previous in vitro and in vivo studies (Gerencer et al., 2006; Lozjuk et al., 1996; Nawrot et al., 2020). Such inhibitory activity against papillomavirus, adenovirus, herpesvirus, and poliovirus is majorly attributed to its alkaloids.

There have been reports of increased liver enzyme activity, increased serum bilirubin, and jaundice with a high alkaloid daily dose (15–25 mg of alkaloids), especially during acute liver and biliary inflammation. After discontinuing the use of greater celandine, the values decreased. However, no side effects are expected with a maximum daily alkaloid dose of 2.5 mg (Blumenthal et al., 1998). Greater celandine should not be taken with an acute cholecystitis or if the bile ducts are obstructed, at least not at a dose of 2.5 mg of alkaloids (Blumenthal et al., 1998). Sanguinarine, the other important component, was toxic in rats with a lethal dose (LD_{50}) of 18 mg/kg body weight (Golob et al., 2008). These toxic doses are not achieved by the recommended dosage in this case series. Greater celandine may be prescribed at a maximum dosage of 2 g three times per day (Bone & Mills, 2013). It can be estimated that 30 drops of the 10% mother tincture result in a dose of 150 mg of *Chelidonium majus*. There is no experience on its safety during pregnancy, lactation, or for children under 12 years old (Blumenthal et al., 1998). There are no known unfavorable drug interactions.

Although this is a small casuistry, it is hoped that such case series may inspire other researchers to continue investigating this medicinal plant in healing COVID-19. According to Kienle and Kiene (2009), case reports and case series are very important means by which physicians scientifically report their experience, thereby contributing to the progress of medical knowledge. These papers have a central value in the discovery of new diseases, new treatments, unexpected effects, and adverse effects, as well as for medical education. Several therapeutic innovations start with a case report and a case series.

It is also well known that many drugs originate from medicinal plants. There are countless examples. One of them is shikimic acid, a chemical intermediate from *Illicium verum* used in the synthesis of oseltamivir.

In the authors' view, the populations at risk for COVID-19 are not exactly those with impaired immunity, but rather with impaired vitality. *Chelidonium majus* is a medicinal plant whose central action occurs in the liver, the seat of vitality—according to the fundamentals of anthroposophic medicine. Along with its probable antiviral effects, this medicinal plant can support the liver in its task of providing vitality to the body, thus favoring the overcoming of the disease.

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ETHICS STATEMENT

Written consent was obtained from all patients for publication of the data. Copies of the written consents are available for review by the Editor of this journal.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHORS CONTRIBUTION

NEG treated Patients 1–9 and he was a major contributor in writing the manuscript. AJB treated Patients 10–20 and she analyzed and interpreted the patients' data. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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