Treatment of a Woman With Glycyrrhiza glabra for Acute Sinusitis: A Case Report



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Abstract

Objective: The purpose of this case report is to describe the treatment of a patient with acute sinusitis using *Glycyrrhiza glabra*.

Clinical Features: A 26-year-old woman presented with acute sinusitis of 10-day duration. Her symptoms included facial pressure and soreness around the frontal and maxillary sinuses, a headache, pharyngitis, a fever, rhinorrhea, nasal congestion with postnasal drip, a productive cough, myalgias, and fatigue.

Intervention and Outcome: After administration of 12 to 15 drops of a 2 000-mg tincture of *G glabra* twice a day, improvements were noted. Resolution of her symptoms occurred after 3 days of treatment.

Conclusion: For the treatment of acute sinusitis, *G glabra* may be a natural therapeutic remedy. (J Chiropr Med 2018;17:268-274)

Key Indexing Terms: Sinusitis; Infection; Chiropractic

INTRODUCTION

Acute sinusitis is a common condition seen by general practitioners worldwide. It is estimated that the incidence of sinusitis is 35 million people each year in the United States, contributing to between 15 and 40 cases per 1 000 patients.¹ Episodes of acute sinusitis are more prevalent in adults and are the second leading cause of infectious disease encountered in clinical practice.² Women have a greater incidence of the infection than men and have a higher probability of seeking care.^{3,4}

Acute sinusitis is an infection and inflammatory process affecting the nasal passages and paranasal sinuses. Common symptoms include facial pain, rhinorrhea, pressure or fullness in the sinuses, and nasal obstruction that can last up to 4 weeks.⁵ Acute sinusitis is diagnosed by clinical signs and symptoms, most importantly the presence of purulent nasal discharge.⁵ It is commonly caused by a virus and is a self-limiting condition and in most cases can be treated symptomatically. The viruses that are transmitted inducing acute sinusitis are the same as those associated with the common cold.⁶ These viruses are the rhinovirus, influenza virus, and parainfluenza virus. However, not all cases of acute sinusitis are initiated by a virus. The

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bacterium *Haemophilus influenzae* can convey the infection as well. This bacterium produces toxins that interfere with ciliary movement and damage the mucosa.⁷ The stagnation of secretions caused by decreased ciliary movement creates a perfect culture medium for viral or bacterial growth.⁸ People at higher risk for contracting acute sinusitis include those who are immunocompromised and those who work closely with other people.

The conventional medicine treatment strategy for acute sinusitis emphasizes the use of antibiotics. In the United States, 85% to 98% of sinusitis patients are prescribed antibiotics.⁶ However, evidence shows that most cases of acute sinusitis are viral in origin and only a marginal number of cases develop a secondary bacterial infection.⁹ Other pharmaceutical agents that are employed for the treatment of acute sinusitis are oral or topical decongestants, topical anticholinergics, antihistamines, mucolytics, nasal corticosteroids, and hypertonic saline nasal irrigation.⁷

However, the research related to the efficacy of the other forms of therapy for acute sinusitis is limited. In most of the studies, antibiotics are combined with decongestants or nasal irrigation and in some cases corticosteroids were prescribed as well.¹⁰⁻¹² These studies were shown to reduce the severity of symptoms. In 1 study conducted by Bahtouee et al, administering a nasal decongestant with the antibiotics amoxicillin-clavulanic acid, pseudoephedrine, and intranasal saline produced no additional benefit.¹⁰ In addition, a study by Ragab et al determined that nasal irrigation was as effective as systemic antibiotics after 14 days of treatment.¹³ However, a systemic review analyzed the effectiveness of saline nasal irrigation for the treatment of acute sinusitis and the authors concluded that there was some evidence of symptom relief, but the studies did not have a

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large enough study group and there was a high risk of bias.¹⁴ Because most cases of acute sinusitis are viral in nature and antibiotics are used to prevent secondary infections, the actual efficacy of using antibiotics as the primary therapeutic approach is questionable. In addition, there are a small number of studies administering anticholinergics and antihistamines for the treatment of acute sinusitis. Of these studies, most are typically used for allergic rhinitis rather than acute viral sinusitis.¹⁵ Lastly, Venekamp et al performed a meta-analysis and found that oral corticosteroids as a monotherapy are ineffective.¹⁶ Although viral acute sinusitis is self-limiting, without treatment complications may ensue.¹⁷ The complications that occur most often are orbital cellulitis, orbital abscess, epidural empyema, and subdural empyema.⁹

A natural alternative to antibiotics for the treatment of either bacterial or viral sinusitis is Glycyrrhiza glabra, also known as licorice root, sweet root, or sweet wort.¹⁸ It grows in Southwest and Central Asia and Europe.¹⁹ This herb is a perennial that can reach heights of 1 to 2 m and is anchored in the ground by a taproot, which can reach 1.25 m in length. Each year a new stem grows with branches that can give rise to flowers, leaves, or fruit. The inflorescence of the plant have a spike like appearance with bluish to light purple flowers.¹⁸ G glabra is one of 30 different species of plants in the Glycyrrhiza genus and family Leguminosae.²⁰ The first documented use of G glabra for medicinal purposes dates back to ancient Assyria and Egypt around 2500 BC.²⁰ The part of the plant that is used medicinally is the roots and stolons.²⁰ Traditionally, G glabra is used for reducing inflammation, preventing ulcers, acting as a mucolytic, blocking calcium channels, and inhibiting microbial growth.²⁰

G glabra is considered to be generally safe. However, prolonged use of this agent is not recommended because it can result in hypertension, edema, cardiac symptoms including cardiomyopathy and arrhythmias, pseudohyperaldosteronism in conjunction with hypercortisolism with polyuria, myopathies, lethargy, headaches and tetany, retention of sodium and a severe disruption of electrolyte balance.¹⁸ Chronic consumption has resulted in hypertensive encephalopathy in 2 cases.¹⁸ Excessive dosages have been associated with hepatotoxicity, metabolic alkalosis, a reduction in testosterone, and visual disturbances.¹⁸ G glabra is contraindicated in individuals with chronic hepatitis, diabetes mellitus, severely impaired renal function, neuromuscular disorders with hypertonicity, cardiac dysfunction with arrhythmias, hypertension, hypertonia, and hypokalemia.¹⁸

G glabra is an herb that has the ability to act as an antiviral against hepatitis B and C, influenza A, herpes simplex virus, severe acute respiratory syndrome, the coronavirus, and the respiratory syncytial virus.²⁰ The antiviral components of *G* glabra are glycyrrhizin or glycyrrhizic acid and glycyrrhetinic acid.²⁰ Several antivi-

ral actions for *G glabra* have been established, which are specific for the virus it encounters.²⁰ It has been shown to prevent the fusion of the virus with the membrane of the host cell, increasing the synthesis of interferon γ in T lymphocytes and inhibiting enzymatic activity of viruses, impairing replication.²⁰

One of the antiviral functions of *G glabra* discussed previously is the potentiation of the production of interferon γ by T lymphocytes, which activates and mobilizes immune cells to combat the infection.²¹ Another effect of *G glabra* is the suppression of the enzymatic activity of neuraminidase.²² Neuraminidase is found on the surface of the virus and facilitates the cleavage of sialic acid residues, allowing the active form of the virus to detach from the virally infected host cell.²² Separating from the infected host cell is required for viral replication and transmission.²² There are 11 components in *G glabra* that inactivate viral neuraminidase activity in several strains of influenza including the H1N1 virus and an oseltamivir-resistant strain of H1N1.²²

There are a few studies that demonstrate the antimicrobial and antiviral properties of *G glabra*. ^{19,23,24} However, at present, there are no studies demonstrating the efficacy of *G glabra* for the treatment of acute sinusitis. Furthermore, no studies that determine the effectiveness of *G glabra* against the rhinovirus, the parainfluenza virus, or the *H influenzae* bacterium exist, and the few studies that elucidate the antiviral activity of *G glabra* against influenza are in vitro or use *G. glabra* as part of a formulation. The purpose of this case report is to discuss the treatment of a young adult female with acute sinusitis with the administration of *G glabra*.

Case History

A 26-year-old white woman presented with facial pressure and soreness around the frontal and maxillary sinuses, a headache, pharyngitis, a fever, rhinorrhea, nasal congestion with postnasal drip, a productive cough, myalgias, and fatigue. Nociceptive sensation inducing her headache was experienced predominately in the frontal and maxillary sinuses bilaterally with small amounts of clear nasal discharge. The primary symptoms she was experiencing that were the most severe were cough, fatigue, rhinorrhea, and facial tenderness and pressure. On a numeric scale from 1 to 10 with 1 being the least severe and 10 being the most severe, she described her cough, fatigue, rhinorrhea, and facial tenderness and pressure as 10, 7, 9, and 7 of 10, respectively. Her cumulative numeric score for her overall level of illness was 8 of 10.

She had been experiencing the symptoms for 10 days. She performed self-care for the first 3 to 6 days of her infection by adding up to 5 cloves of *Allium sativum* to her breakfast and lunch and a few drops of a tincture of *Origanum vulgare* oil to water. She switched from the tincture to 200-mg capsules owing to difficulty tolerating the tincture. She ingested the capsules $5 \times a$ day for 3 days and began supplementing with 100 mg of zinc and Emergen-C (Alcer Corporation, Carlisle, Pennsylvania) $2 \times a$ day at the same time. All the supplements were purchased at a store specializing in vitamins and supplements and were not professional grade. She also received acupuncture twice that week for her infection. She experienced mild 1 to 2 of 10 improvement in her sinus pressure and nasal congestion, but her relief was transient. The patient is a full-time student who is highly active competing in amateur fitness competitions. She performs strength training exercises 5 days per week and endurance exercises 6 to 7 days per week. Her symptoms were preventing her from participating in her daily exercises, which affected her progress for her next competition.

Past Medical History and Examination

She had a past medical history of sinusitis that occurs multiple times a year since her early childhood. She usually experienced an infection about once every 2 to 3 months. Earlier in December 2016, the patient presented at urgent care for treatment of an upper respiratory tract infect with sinusitis. She was prescribed an antitussive and received a cortisone shot and also self-prescribed an over-the-counter decongestant and expectorant. Her infection lasted about 14 days. She succumbed to another infection shortly after in January. Over-the-counter decongestants and expectorants alleviated her symptoms in about 14 days.

Upon examination, her throat was mildly erythematous with a thin layer of clear mucous. The nasal mucosa was red and inflamed with clear mucous in the nasal passages. Percussion on her frontal and maxillary sinuses revealed tenderness and pain. The sinuses did not transilluminate, which is consistent with inflammation of the mucosa and obstruction owing to mucus.

Working Diagnosis and Treatment Plan

Based upon the history and physical examination, she was diagnosed with a case of acute sinusitis. A tincture of G glabra was the only treatment prescribed to the patient at a

Table 2. Severily of Symptoms Second Infection October 201	Table 2. Severity of Symptoms Set	cond Infection October 201
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Symptom	Numeric Scale G glabra Day 1	Numeric Scale G glabra Day 2	Numeric Scale G glabra Day 3
Cough	1	3	0
Fatigue	1	2	0
Rhinorrhea	1	3	0

dosage of 12 to 15 drops of the tincture twice a day for 14 days. The dosage of G glabra in the tincture was 2 000 mg for 12 to 15 drops.

Results

The patient subjectively reported feeling about 50% better after the first day of treatment with *G glabra*. Her symptom scores were reduced to 7, 4, 6, and 4 of 10 for her cough, fatigue, rhinorrhea, and facial tenderness and pressure, respectively. Her overall rating of the illness was a 5 of 10. After the second day of treatment, she subjectively reported that she felt about 90% better and that her rhinorrhea, nasal congestion, fever, myalgias, and pharyngitis had resolved. The symptom scores had reduced to 3, 1, and 1 of 10 for her cough, fatigue, and facial pressure and tenderness, respectively. Her overall rating of the level of illness was a 2 of 10 (Table 1). By day 3, resolution of symptoms had occurred. However, to prevent remission she continued to ingest the tincture of *G glabra* twice a day for 11 more days.

A follow-up was performed on October 18, 2017. At the beginning of October, she experienced a dry cough with fatigue and rhinorrhea. The first day she noticed symptoms, she administered 12 to 15 drops of her 2 000-mg tincture of *G glabra*. She described her symptoms on day 1 as a 1, 1, and 1, respectively, on a numeric scale from 1 to 10 for her cough, fatigue, and rhinorrhea, respectively. Her symptoms intensified to a 3, 2, and 3 for her cough, fatigue, and rhinorrhea, respectively day 3, all of her subsequent symptoms were reduced and alleviated by the end of the day (Table 2). The patient was instructed to

Table I. Severity of Symptoms Before and After G glabra Administration

Symptom	Numeric Scale Days 1-10	Numeric Scale G glabra Day 1	Numeric Scale G glabra Day 2	Numeric Scale G glabra Day 3
Cough	10	7	3	0
Fatigue	7	4	1	0
Rhinorrhea	9	6	0	0
Facial pain and pressure	7	4	1	0
Severity of illness	8	5	2	0

continue the dosage for 11 more days even though she was symptom free. A subsequent follow-up was performed on January 16, 2018. The patient has not succumbed to an illness since her last episode in October. The patient gave consent for this case study to be published.

Discussion

From the clinical presentation, it cannot be determined the exact extent of the positive effect of G glabra on the patient. However, it would appear as if G glabra may have attenuated her symptoms after 3 days of administration. She received acupuncture twice the week before being administered G glabra and she had supplemented with zinc, Emergen-C, and A sativum and O vulgare oil for 3 to 6 days. All of these treatment strategies may have had a therapeutic effect that cannot be discounted. Acupuncture, zinc, A sativum, and O vulgare all have the potential to enhance immune function.²⁵⁻²⁷ In addition, zinc, A sativum, and O vulgare possess antioxidant agents and the active ingredients in Emergen-C may have some mild immuneenhancing effects, but has great antioxidant potential. A sativum and O vulgare are also antimicrobial.²⁸⁻³³ However, only research exists that demonstrates that A sativum is antiviral while the antiviral effects of O vulgare in the research is largely unknown.^{18,26,33} Consequently, the combined immunostimulatory and antioxidant functions of zinc, Emergen-C, O vulgare, and A sativum in conjunction with the antiviral activity of A sativum should have reduced the severity of her illness and her symptoms. However, their effects were marginal. The most probable explanation for her minimal improvement is that the herbs and supplements were not used for a long enough period of time, they may not have been administered frequently enough, and they were not used on a consistent basis.

In this case, although G glabra may have been effective for resolving her acute sinusitis, the causative factor of the infection was not known. The pathogen responsible for her illness may have been a virus, which is more prevalent, or a bacterium. Unfortunately, there is no information demonstrating the effects of G glabra for the treatment of acute sinusitis regardless of its source. In addition, the evidence pertaining to the effectiveness of G glabra against the pathogens that cause acute sinusitis is limited. Of the 3 viruses affiliated with the onset of acute sinusitis, only one in vitro study performed by Grienke et al revealed that several of the components of G glabra inhibited neuraminidase activity, which could prevent the replication of influenza. Other data show that G glabra is an effective antibacterial agent. However, no information is available as to its activity or inactivity against *H influenzae*, which is the bacterium associated with sinusitis. Nevertheless, G glabra may have been responsible for the eradication of her infection.

The other consideration is that the patient typically would experience an episode of acute sinusitis every 2 to 3 months. In this case, after using G glabra for 2 weeks she did not succumb to an infection until 4 months later, which is a slight improvement. However, upon the administration of G glabra, she experienced a low-grade infection that was resolved on day 3 and was not afflicted by another infectious agent from November to January. This may indicate that G glabra was administered appropriately to prevent a severe infection from ensuing. However, this is impossible to determine becuase the cause of the infection is unknown. She may have come in contact with a less virulent strain of an analogous virus or a different, less severe strain of a virus than the first infection.

Although the contagion responsible for her disease is not known and the antiviral and antibacterial data are minimal, *G* glabra possesses other properties that make it appropriate for the treatment of acute sinusitis. The main effect of this herb that has been shown in research is the inhibition of 11- β -hydroxysteroid dehydrogenase and 5- β reductase in the liver, which metabolize cortisol into cortisone.^{20,34} Cortisone is the inactive form. Down-regulating the activity of these enzymes increases the circulating levels of cortisol.^{20,34} Additional evidence has demonstrated that glycyrrhizic acid and glycyrrhetinic acid interact with glucocorticoid receptors and may have a regulatory effect.^{20,34} However, the regulatory effect is weak.³⁴

There are 2 studies that exemplify the potential modulatory effects of *G glabra*. The first study was performed by Methlie et al using *G glabra* in patients with Addison's disease.³⁵ *G glabra* increased serum cortisol levels for 2.6 hours after consumption,³⁵ whereas in a study conducted by Armanini et al, glycyrrhetinic acid was administered topically onto the thighs of 18 healthy women.³⁶ The application of glycyrrhetinic acid decreased the activity of cortisol in the adipocytes.³⁶ This demonstrates the ability of *G glabra* to potentially regulate cortisol activity.

Raising cortisol levels seems counterintuitive for the treatment of an infection because of its immunosuppressant and pro-oxidant effects. Cortisol acts an immunosuppressant agent and accelerates cellular metabolism, increasing oxidative stress-generating reactive oxygen species (ROS).³⁷ The greater the level of ROS produced, the more stress that is placed on the body, which secretes more cortisol to compensate. The higher amounts of cortisol release compounds its immunosuppressive effect.

The level of oxidative stress is exacerbated further by the immune response in the form of phagocytes facilitating respiratory burst during an infection. Respiratory burst uses ROS to eradicate pathogens. The combination of glucocorticoid release and respiratory burst promoting the synthesis of ROS increases the level of oxidative stress and can impair the antioxidant defense system.³⁷ Using antioxidant supplements has been shown to prevent dysfunction of the

antioxidant defense system, diminish ROS, and reduce serum cortisol, mitigating the immunosuppressant effect.³⁸

However, the effects of *G* glabra on cortisol are considered to be analogous to that of the administration of oral corticosteroids for the treatment of acute sinusitis, but to a lesser extent. The practice of prescribing oral corticosteroids for certain infections is becoming more prevalent. The reason is that inflammation occurs parallel to the infection. Administering a cortisol agonist can dissipate the inflammatory response, which can alleviate symptoms at least temporarily.³⁹ Although cortisol has an immunosuppressive effective, the down-regulation of inflammation could lower cortisol levels over the long-term. Higher levels of cortisol release.⁴⁰ Consequently, the effect of *G* glabra may attenuate the release of cortisol over time by a similar mechanism.

G glabra can reduce inflammation through other actions besides elevating cortisol. Glycyrrhizic acid further potentiates the anti-inflammatory activity of *G* glabra by downregulating the expression of nuclear factor- κ B, which is a transcription factor associated with inflammation.²⁰ Another component known as glabridin acts directly on cyclooxygenase, inhibiting the synthesis of inflammatory prostaglandins and thromboxanes associated with inflammation.¹⁸ *G* glabra has the ability to reduce inflammatory mediators, such as inducible nitric oxide synthase, tumor necrosis factor- α , interleukin 1 β , and interleukin 6.⁴¹ All of these effects could reduce inflammation and suppress cortisol secretion.

Concurrently, agents with antioxidant properties can reduce cortisol secretion. G glabra possesses 7 active constituents with antioxidant properties. It has the capacity to lower ROS by 48.5%.⁴² There are several mechanisms that can explain this potent reduction in ROS. One study by Hejazi et al demonstrated that G glabra enhanced the ROS scavenging effects of superoxide dismutase, catalase, glutathione peroxidase and glutathione S-transferase.⁴³ In addition, G glabra reduced nitrogen radicals and enhanced mitochondrial function during cellular metabolism abating the initial production of free radicals.^{20,44} Because of its ability to lower ROS, G glabra can decrease the total level of oxidative stress, which indirectly impedes cortisol release. Therefore, although G glabra has been shown to increase the release of cortisol, which is an immunosuppressant, and only has weak cortisol modulatory activity, the anti-inflammatory and antioxidant potential of G glabra may hinder cortisol release, lessening the immunosuppressive effect of cortisol.

However, *G glabra* may attenuate the immunosuppressive activity of cortisol by another mechanism. *G glabra* has a stimulatory effect on the immune system. *G glabra* can increase the production of T-lymphocytes, especially CD4 T cells.^{18,20} It also potentiates the activation of T-lymphocytes and natural killer cells.¹⁸ *G glabra* increases the expression of the CD40 and CD86 ligands expressed on T

cells.⁴⁵ CD40 ligands promote the differentiation of B cells and activate monocytes and macrophages enhancing the immune response.⁴⁶ The CD86 ligand is an immunoglobulin, which is involved with the activation of T cells.^{47,48}

In addition, *G glabra* increases the transcription of major histocompatibility complex (MHC) II.⁴⁹ Major histocompatibility complex II is synthesized in dendritic cells, macrophages and B cells.^{21,49} These cells are phagocytes that are capable of engulfing pathogens, which then are metabolized and attached to MHC II.⁵⁰ The phagocytic cells then travel to the lymphoid tissue and present the antigen attached to the MHC II to CD4 T cells, which stimulate an immune response.⁴⁹

The combination of immune-enhancing and potential immunosuppressive effects from cortisol release cause G glabra to be classified as an immunomodulatory agent. Consequently, the exact extent of activity of G glabra that has a positive effect toward the alleviation of an infection is difficult to distinguish. However, because it augments antiinflammatory and antioxidant activity in the body and possesses immunostimulatory properties, in theory it could negate some of the negative immunosuppressant effects of cortisol.

In addition, *G* glabra is used as an expectorant and antitussive agent.^{18,20} As an expectorant, *G* glabra may enhance the excretion of mucus from the pulmonary system. There is limited information on the expectorant effect of *G* glabra, so the mechanism is poorly understood. As an antitussive agent, it may reduce the severity of a cough.^{18,20} *G* glabra has been shown to do this by acting as a calcium channel blocker in the smooth muscle of the respiratory tract.¹⁸ Its antitussive effects were demonstrated in a study by Agarwal et al. In this study, a tincture of *G* glabra was administered to patients before surgery. After surgery, it was found that individuals prescribed the tincture of *G* glabra had a less pronounced cough.⁵⁰ Another study by Liu et al found that the isoliquiritigenin component of *G* glabra had the ability to act as a spasmolytic in the trachea of guinea pigs.⁵¹

Limitations

The exact cause of acute sinusitis was not known for this patient. Without knowing the exact cause, it is difficult to determine the reason that *A sativum* and *O vulgare* produced minimal therapeutic effects while *G glabra* potentially eliminated the infection. The patient had the infection for 11 days and had self-prescribed antioxidant and immune stimulating supplements and received acupuncture. It is not possible to know the effects these therapeutic modalities had on her immune function and possibly alleviating her infection. Each may have had positive effects on her immune system, allowing for the resolution of her symptoms, and the administration of *G glabra* may have been purely coincidental. However, this seems unlikely as the patient inconsistently took the supplements for the first 6 days of the infection and received

acupuncture twice. She did not supplement for 5 days or receive acupuncture for 2 days before receiving *G glabra*.

Another limiting factor is that the resolution of her signs and symptoms was subjective based on a numerical scale. Because no instrumentation was used, the true improvement observed is an estimate and not an exact value. The addition of objective outcome measures would have increased the understanding of the effects of G glabra. Lastly, her previous cases of acute sinusitis typically resolved around 2 weeks. Because the administration of Gglabra was on days 11, 12, and 13 of her infection, her immune system may have overcome the infection anyway. However, her symptoms improved very quickly after administration of G glabra, which usually is not seen with her pattern of sinusitis. Also, the fact that she has reoccurring infections every 2 to 3 months and she did not have another infection until 4 months later may indicate that it improved her immune function. In addition, the infection that occurred in October was low grade, and that she did not succumbed to another infection between November and January may indicate that G glabra was effective at alleviating her second infection. Further research is required to determine the efficiency of G glabra for the treatment of acute sinusitis and other viral infections.

Conclusion

After 11 days of an infection with acute sinusitis and receiving other therapies intermittently and experiencing minimal improvements, *G glabra* may have helped alleviate the symptoms of the patient within 3 days. We hypothesized that *G glabra* may have resolved her symptoms by reducing inflammation and acting as an antioxidant or by acting as a cortisol regulator through its interactions with cortisol receptors. *G glabra* acts as an immunostimulant, expectorant, and antitussive agent, which also may have helped resolve the patient's symptoms. *G glabra* may be an effective therapeutic agent for the treatment of an acute case of viral or bacterial sinusitis either alone or in combination with other antiviral or mucolytic agents.

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No funding sources or conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): B.R.M., G.R., M.S.

Design (planned the methods to generate the results): B.R.M., G.R., M.S.

Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): B.R.M., G.R., M.S. Data collection/processing (responsible for experiments, patient management, organization, or reporting data): B.R.M., G.R., M.S.

Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): B.R.M., G.R., M.S.

Literature search (performed the literature search): B.R.M., G.R., M.S.

Writing (responsible for writing a substantive part of the manuscript): B.R.M., G.R., M.S.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): B.R.M., G.R., M.S.

Practical Applications

- *G* glabra is utilized as an expectorant and antitussive agent.
- *G* glabra may be a natural therapeutic remedy for the treatment of acute sinusitis.

References

- 1. Lucas JW, Benson V. Summary health statistics for U.S. adults: National Health Interview Survey, 2001. *Vital Health Stat.* 2004;218:1-134.
- 2. Worrall G. Acute sinusitis. *Can Fam Physician*. 2011;57(5): 565-567.
- 3. Fleming DM, Cross KW, Barley MA. Recent changes in the prevalence of diseases presenting for health care. *Br J General Pract.* 2005;55(517):589-595.
- 4. Falagas ME, Mourtzoukou EG, Vardakas KZ. Sex differences in the incidence and severity of respiratory tract infections. *Respir Med.* 2007;101(9):1845-1863.
- 5. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg.* 2015;152(2):S1-S39.
- 6. Gwaltney JM, Scheld WM, Sande MA. The microbial aetiology and antimicrobial therapy of adults with acute community-acquired sinusitis: a fifteen-year experience at the University of Virginia and review of other selected studies. *J Allergy Clin Immunol.* 1992;90(3):457-461.
- Masood A, Moumoulidis I, Panesar J. Acute rhinosinusitis in adults: an update on current management. *Postgrad Med J.* 2007;83(980):402-408.
- Aring A, Chan M. Acute rhinosinusitis in adults. Am Family Physician. 2011;83(9):1057-1063.
- 9. Brook I. Microbiology of sinusitis. *Proc Am Thorac Soc.* 2011;8(1):90-100.
- 10. Bahtouee M, Monavarsadegh G, Ahmadipour M. Acetylcysteine in the treatment of subacute sinusitis: a double-blind placebocontrolled clinical trial. *Ear Nose Throat J.* 2017;96(1):E7-E11.
- 11. Togrul S, Dogan R, Eren SB. The use of large volume low pressure nasal saline with fluticasone proprionate for the

treatment of pediatric acute rhinosinusitis. Int J Pediatr Otorhinolaryngol. 2014;78(8):1393-1399.

- Gelardi M, Mezzoli A, Fiorella ML. Nasal irrigation with lavonase as ancillary treatment of acute rhinosinusitis: a pilot study. J Biol Regul Homeost Agents. 2009;23(2):79-84.
- Ragab A, Farahat T, Al-Hendawy G. Nasal saline irrigation with or without systemic antibiotics in treatment of children with acute rhinosinusitis. *Int J Pediatr Otorhinolaryngol.* 2015;79(12):2178-2186.
- King D, Mitchell B, Williams CP. Saline nasal irrigation for acute upper respiratory tract infections. *Cochrane Database Syst Rev.* 2015;20(4)CD006821.
- Chistiakova VR, Miasnikov LL. The efficacy of rinopront for the treatment of acute and chronic rhinitis in children. *Vestn Otorinolaringol.* 2012;3:88-91.
- Venekamp RP, Thompson MJ, Hayward G. Systemic corticosteroids for acute sinusitis. *Cochrane Database Syst Rev.* 2014;25(3):CD008115.
- 17. Oxford L, McClay J. Complications of acute sinusitis in children. *Otolaryngol Head Neck Surg.* 2005;133:32-37.
- 18. PDR for Herbal Medicines. 4th ed. Montvale, NJ: Thomson; 2007.
- Ghannad MS, Mohammadi A, Safiallahy S. The effect of aqueous extract of *Glycyrrhiza glabra* on Herpes Simplex Virus 1. *Jundishapur J Microbiol*. 2014;7(7):e11616.
- Braun L, Cohen M. Herbs and Natural Supplements: An Evidence-Based Guide. 3rd ed. Chatswood, New South Wales: Elsevier Australia; 2010.
- Marieb EN, Hoehn K. *Human Anatomy and Physiology*. 10th ed. Boston, MA: Pearson; 2016.
- Grienke U, Braun H, Seidel N. Computer-guided approach to access the anti-influenza activity of licorice constituents. J Nat Prod. 2013;77(3):563-570.
- Chakotiya AS, Tanwar A, Srivastava P. Effect of aquo-alcoholic extract of Glycyrrhiza glabra against Pseudomonas aeruginosa in mice lung infection model. *Biomed Pharmacother*. 2017;90: 171-178.
- Rohinishree YS, Negi PS. Effect of licorice extract on cell viability, biofilm formation and exotoxin production by staphylococcus aureus. *J Food Sci Technol.* 2017;53(2):1092-1100.
- Pais I, Correia N, Pimentel I. Effects of acupuncture on leucopenia, neutropenia, NK and B cells in cancer patients: a randomized pilot study. *Evid Based Complement Alternat Med.* 2014;2014;217397.
- 26. Nantz MP, Rowe CA, Muller CE. Supplementation with aged garlic extract improves both NK and $\gamma\delta$ -T cell function and reduces the severity of cold and flu symptoms: a randomized, double-blind, placebo-controlled nutrition intervention. *Clin Nutr.* 2012;31(3):337-344.
- Walter BM, Bilkei G. Immunostimulatory effect of dietary oregano etheric oils on lymphocytes from growth-retarded, low-weight growing-finishing pigs and productivity. *Tijdschr Diergeneeskd*. 2004;129(6):178-181.
- Burt SA, Reinders RD. Antibacterial activity of selected plant essential oils against Escherichia coli O157:H7. *Lett Appl Microbiol.* 2003;36(3):162-167.
- 29. Gilling DH, Kitajima M, Torrey JR. Antiviral efficacy and mechanisms of action of oregano essential oil and its primary component carvacrol against murine norovirus. *J Appl Microbiol*. 2014;116(5):1149-1163.
- Iwalokun BA, Ogunledun A, Ogbolu DO. In vitro antimicrobial properties of aqueous garlic extract against multidrugresistant bacteria and Candida species from Nigeria. *J Med Food*. 2004;7(3):327-333.
- Liang CH, Chan LP, Ding HY. Free radical scavenging activity of 4-(3,4-Dihydroxybenzoyloxymethyl)phenyl-*O*-β-D-glucopyranoside from *Origanum vulgare* and its protection

against oxidative damage. J Agricultural. Food Chem. 2012; 60(31):7690-7696.

- 32. Nasiri A, Ziamajidi N, Abbasalipourkabir R. Beneficial effect of aqueous garlic extract on inflammation and oxidative stress status in the kidneys of type 1 diabetic rats. *Indian J Clin Biochem.* 2017;32(3):328-336.
- Chavan RD, Shinde P, Girkar K. Assessment of anti-influenza activity and hemagglutination inhibition of Plumbago indica and Allium sativum extracts. *Pharmacognosy Res.* 2016;8(2):105-111.
- Mills S, Bone K. Principles and Practice of Phytotherapy: Modern Herbal Medicine. Austin, TX: Churchill Livingstone; 2013.
- Methlie P, Husebye EE, Hustad S. Grapefruit juice and licorice increase cortisol availability in patients with Addison's disease. *Eur J Endocrinol.* 2011;165(5):761-769.
- Armanini D, Nacamulli D, Francini-Presenti F. Glycyrrhetinic acid, the active principle of licorice, can reduce the thickness of subcutaneous thigh fat through topical application. *Steroids*. 2005;70(8):538-542.
- Spiers JG, Cortina Chen SJ, Sernia C. Activation of the hypothalamic-pituitary-adrenal stress axis induces cellular oxidative stress. *Front Neurosci.* 2014;8:456.
- Atsumi T, Tonosaki K. Smelling lavender and rosemary increases free radical scavenging activity and decreases cortisol level in saliva. *Psychiatry Res.* 2007;150(1):89-96.
- Venekamp RP, Thompson MJ, Hayward G. Systemic corticosteroids for acute sinusitis. *Cochrane Database Syst Rev.* 2011;7(12):CD008115.
- 40. Wolkow A, Aisbett B, Reynolds J. Relationships between inflammatory cytokine and cortisol responses in firefighters exposed to simulated wildfire suppression work and sleep restriction. *Physiol Rep.* 2015;3(11):e12604.
- Li C, Eom T, Jeong Y. Glycyrrhiza glabra L. extract inhibits LPS-induced inflammation in RAW macrophages. *J Nutr Sci Vitaminol (Tokyo).* 2015;61(5):375-381.
- Rahimifard M, Navaei-Nigjeh M, Mahroui N. Improvement in the function of isolated rat pancreatic islets through reduction of oxidative stress using traditional Iranian medicine. *Cell J.* 2014;16(2):147-163.
- 43. Hejazi II, Khanam R, Mehdi SH. New insights into the antioxidant and apoptotic potential of Glycyrrhiza glabra L. during hydrogen peroxide mediated oxidative stress: an in vitro and in silico evaluation. *Biomed Pharmacother*. 2017;94:265-279.
- 44. Singh P, Singh D, Goel RK. Protective effect on phenytoininduced cognition deficit in pentylenetetrazol kindled mice: a repertoire of Glycyrrhiza glabra flavonoid antioxidants. *Pharm Biol.* 2016;54(7):1209-1218.
- Bordbar N, Karimi MH, Amirghofran Z. The effect of glycyrrhizin on maturation and T cell stimulating activity of dendritic cells. *Cellular Immunol.* 2012;280(1):44-49.
- Grewal IS, Flavell RA. The role of CD40 ligand in costimulation and T-cell activation. *Immunol Rev.* 1996;153:85-108.
- 47. Chen L, Flies DB. Molecular mechanisms of T cell co-stimulation and co-inhibition. *Nat Rev Immunol.* 2013;13(4):227-242.
- Bajorath J, Peach RJ, Linsley PS. Immunoglobulin fold characteristics of B7-1 (CD80) and B7-2 (CD86). *Protein Sci.* 1994;3(11):2148-2150.
- Broeke TT, Wubbolts R, Stoorvogel W. MHC class II antigen presentation by dendritic cells regulated through endosomal sorting. *Cold Spring Harb Perspect Biol.* 2013;5(12):a016873.
- Agarwal A, Gupta D, Yadav G. An evaluation of the efficacy of licorice gargle for attenuating postoperative sore throat: a prospective, randomized, single-blind study. *Anesth Analg.* 2009;109(1):77-81.
- Liu B. Isoliquiritigenin, a flavonoid from licorice, relaxes guineapig tracheal smooth muscle in vitro and in vivo: role of cGMP/ PKG pathway. *Eur J Pharmacol.* 2008;587(1-3):257-266.