

Lobelia inflata L. as an Alternative Medicine for Respiratory Problems Provoked by Covid- 19: A Review

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Abstract

Lobelia inflata (Indian tobacco, Campanulaceae) is an herbal remedy for many respiratory conditions such as asthma, bronchitis, pneumonia, and cough. The main objective of the current review is to document the potential use of *L. inflata* as respiratory stimulant in patients suffering from Covid-19 infection. Native Americans smoked the plant as a treatment for asthma and today, lobelia is sometimes suggested to help clear mucus from the respiratory tract, including the throat, lungs, and bronchial tubes. Although few studies have evaluated the safety and effectiveness of lobelia, some herbalists use lobelia as part of a comprehensive treatment plan for asthma. In the 19th century, American physicians prescribed the herb to induce vomiting in order to remove toxins from the body. However, because of its properties as a respiratory stimulant and expectorant, the plant should be used at the correct dose and together with herbs that are soothing to the throat and lungs, and it is often used in a synergistic herbal formula that includes *L. inflata* herb and seed, *Zingiber officinale*, and *Hyssopus officinalis*. The study species should not be used as a substitute for drug therapy during an asthma attack and its use is contraindicated during pregnancy. *Lobelia inflata* has no known adverse drug interactions and it is therefore a promising complementary therapy for the management of respiratory disorders, in particular in light of the recent increase in the prevalence of respiratory diseases associated with Covid-19. In conclusions, data of the current study has proven the possibility of using the plant in treating the respiratory disorders resulting from infection with Covid-19.

Keywords: Alternative medicine, Covid-19, Respiratory disorders, *Lobelia inflata*.

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INTRODUCTION

Lobelia is a genus of flowering plants that includes approximately 400 species and was popular in traditional Native American medicine as an emetic, expectorant and respiratory stimulant. It is an attractive annual or sometimes biennial herb that grows to a

height of about one meter. Its upright, hairy stem is angular, branching at the top, usually green with a tinge of violet (Li *et al.*, 2017). The pale green or yellowish leaves have a sharp taste and a slightly irritating odor. The sparse flowers are pale violet blue outside and pale yellow inside (Figure 1).



Figure 1: Morphology of *Lobelia inflata* shoots (A), flowers (B) and seeds (C)

Damaj *et al.* (1997) postulate that an active ingredient in the lobelia plant; lobeline, has similar effects to nicotine. For this reason, lobeline was once used as a nicotine substitute in many antismoking products and preparations designed to break the smoking habit. Researchers now think that lobeline may actually reduce the effects of nicotine in the body, particularly the release of dopamine. Dopamine is a brain chemical that plays a number of important roles in the brain. It is also involved in drug addiction, so researchers think that lobeline may have some potential in treating addiction. Lobelia is a potentially toxic herb. It can be safely used in small doses, but moderate-to-large doses may cause side effects ranging from dry mouth and nausea to convulsions and even coma. You should use lobelia only under the supervision of your health care provider. The above-ground portions of the lobelia plant are used for medicinal purposes. Few studies have examined at the effect of lobelia in either animals or people. It is sometimes suggested for the treatment of asthma, bronchitis and cough (Dwoskin and Crooks, 2002). Lobelia is also used alone or with other products for smoking cessation, muscle relaxation, nausea, vomiting, skin infections and various respiratory illnesses. Han *et al.* (2013) reported that Lobelia is available in liquid extracts, tinctures, and as a dried herb in capsules and for teas. It may also be put on the skin in the form of ointments, lotions, and plastics. Begin with low dosages and increase gradually, depending on response. Remember that even moderate doses can be toxic; herbal Lobelia should only be taken under the guidance of a knowledgeable herbal prescriber. For pediatric, there are no studies evaluating whether it is safe to give lobelia to a child. Avoid use in children unless under the supervision of your child's health care provider. For adult, Lobelia comes in dried form to be used as a tea, liquid extract, tincture, and even vinegar tincture.

The use of herbs is a time-honored approach to strengthening the body and treating disease. Herbs, however, contain substances that can trigger side effects and interact with other herbs, supplements, or medications. For these reasons, you should take herbs with care, under the supervision of a health care provider. *Lobelia inflata* is considered a potentially toxic herb. It can cause serious side effects, such as profuse sweating, nausea, vomiting, diarrhea, tremors, rapid heartbeat, mental confusion, convulsions, hypothermia, coma, and possibly even death (Cupp,

2000). Check with your provider to determine the right dose for you, and do not exceed your provider's recommended dose. People with high blood pressure, heart disease, liver disease, kidney disease, tobacco sensitivity, paralysis, seizure disorder, and shortness of breath, and those recovering from shock should not take lobelia. Lobelia can irritate the GI tract and may make symptoms worse for people with ulcers, chronic disease, inflammatory bowel disease (IBD), or intestinal infections. Pregnant and breastfeeding women should also avoid this herb. Few studies have looked at the effects of lobelia, so scientists are not clear about which medications might interact with this herb (Singh *et al.*, 2012).

COVID-19 and Respiratory System

COVID-19 is a respiratory disease, once that especially reaches into the respiratory tract, which includes lungs it can cause a range of systemic and breathing problems, from mild to critical (Figure 2). Older adults and people who have other health conditions like heart disease, cancer, and diabetes may have more serious symptoms (El-Darier and Nasser, 2021). When the virus gets in the body, it comes into contact with the mucous membranes that line nose, mouth, and eyes. The virus enters a healthy cell and uses the cell to make new virus parts. It multiplies, and the new viruses infect nearby cells. Think of the respiratory tract as an upside-down tree. The trunk is the trachea, or windpipe, it splits into smaller and smaller branches in the lungs. At the end of each branch are tiny air sacs called alveoli. This is where oxygen goes into your blood and carbon dioxide comes out (El-Darier *et al.*, 2021). The new coronavirus can infect the upper or lower part of the respiratory tract. It travels down the airways. The lining can become irritated and inflamed and in some cases, the infection can reach all the way down into the alveoli. As the infection travels the respiratory tract the immune system fights back. Lungs and airways swell and become inflamed. This can start in one part of the lung and spread (Orhan and Senol Deniz (2020). About 80% of people who have COVID-19 get mild to moderate symptoms. You may have a dry cough or a sore throat. Some people have pneumonia, a lung infection in which the alveoli are inflamed. Doctors can see signs of respiratory inflammation on a chest X-ray or CT scan. On a chest CT, they may see something they call "ground-glass opacity" because it looks like the frosted glass on a shower door (Biscardi, 2020).

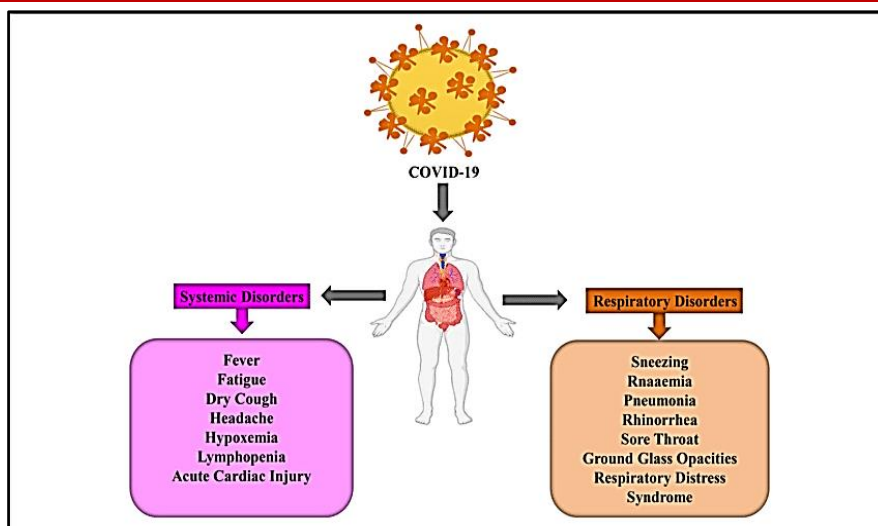


Figure 2: The systemic and respiratory disorders caused by COVID-19 infection

Clinical Insinuations

Severe asthma is on the rise and is often managed with corticosteroids and other pharmaceuticals known to be immune suppressive. Such pharmaceutical management typically must be continued long-term, if not for life, and is often associated with side effects (Oray *et al.*, 2016). Complementary Alternative Medicine (CAM) therapies, including herbs, may reduce allergic phenomena and airway reactivity such that drug therapies can be reduced or possibly eliminated altogether. *Lobelia inflata* is a mainstay of botanical therapy for asthma among practitioners of the previous century up to the present time. The active

constituents of *Lobelia* are alkaloids, including lobeline (Krochmal *et al.*, 1970). The highest amount of *Lobelia* alkaloids is found in the seeds and flowers, but not in the leaf (Grieve, 1931). Therefore, for most effective results it is important to administer *Lobelia* that has been picked in seed and/or at the flowering stage. Lobeline is reported to inhibit the release of catecholamines from adrenal glands (Figure 3). Specifically, it inhibits the flow of calcium ions into chromaffin cells of rat adrenal glands but does not affect the calcium ion release from the cytoplasmic calcium store (Lim *et al.*, 2004).

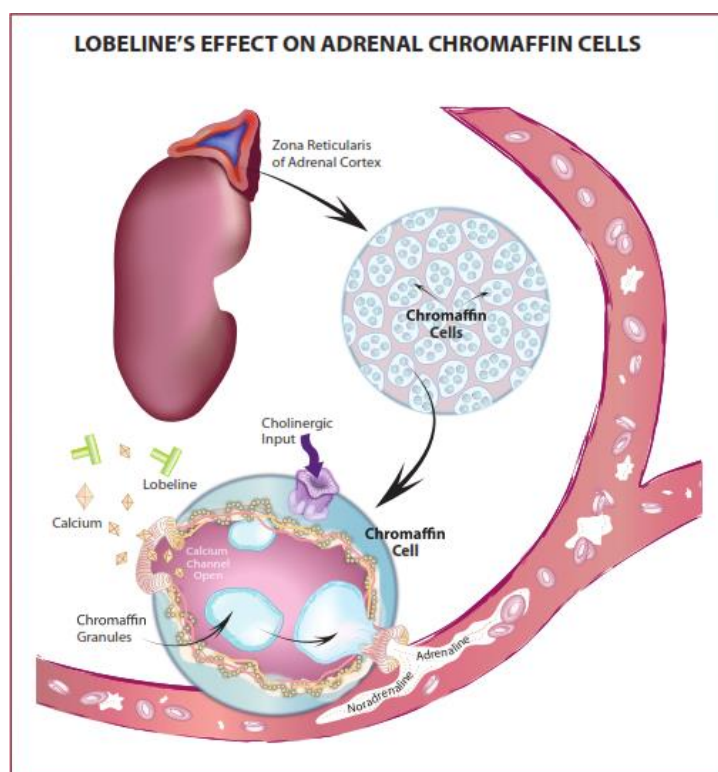


Figure 3: Lobeline effect on adrenal chromaffin cells

DISCUSSION

Lobelia Constituents

The physiologically most potent constituents of Lobelia are the piperidine alkaloids, including lobeline, lobelanine, and lobelanidine. *L. inflata* also contains beta-amyrin palmitate, lobelic acid, gums, resin fixed oils and mineral salts including calcium, potassium and ferric oxide (Felpin and Lebreton, 2004). The highest amount of lobeline is found in the seeds. Lobeline is a lipophilic molecule which has been reported to act as both an agonist and antagonist to beta nicotinic receptors (Kesting *et al.*, 2009). Animal studies have suggested that piperidine alkaloids, such as lobeline, are able to cross the blood-brain barrier, and (similar to nicotine) promote the release of the neurotransmitters dopamine and norepinephrine (Dwoskin and Crooks, 2002) On the other hand, in animal studies, beta-amyrin palmitate has been shown to reduce the effects of amphetamines and exert a mildly sedative effect (Santha *et al.*, 2000).

Lobelia Against Attention Deficit Hyperactivity Disorder (ADHD)

ADHD is a behavioral and neurocognitive disorder associated with abnormalities in central nervous system dopamine (DA) and norepinephrine (NE) neurotransmission (Sonuga-Barke, 2003), and nicotinic receptor dysfunction (Levin, 1992). It is characterized by inattention, hyperactivity, and impulsivity (American Psychiatric Association, 1994). ADHD is common in adults with prevalence rates estimated at 4.4% (Kessler *et al.*, 2006). Studies indicate that lobeline, its main active compound, may protect against depression, help treat drug addiction, and improve memory and concentration. Martin *et al.* (2018) demonstrated modest evidence that lobeline improves working memory in adults with ADHD.

Lobelia versus Asthma, Cough and Bronchitis

Lobelia has been used traditionally to treat coughs and spasms in the lungs from all kinds of causes. Doctors in North America who used herbs as their main medicine, considered lobelia to be one of the most important plant medicines. Traditionally, it was used by physicians to treat coughs and spasms in the lungs from all sorts of causes. A plant that originates in Africa, khella, is also considered an anti-spasmodic like lobelia. Though it is not strong enough to stop acute asthma attacks, khella has been recommended by German physicians practicing herbal medicine as possibly helpful for chronic asthma symptoms (Prasad *et al.*, 2009). Szeleny and Brune (2002) stated that, very small amounts of this herb are considered helpful in suppressing or easing coughs. The herb has also shown anti-inflammatory properties. Lobelia contains many active alkaloids, of which lobeline is considered the most active. Very small amounts of this herb are considered helpful as an antispasmodic and antitussive agent (a substance that helps suppress or ease coughs). Anti-inflammatory properties of the herb have been

demonstrated, which may be useful, since bronchitis is associated with inflammation in the bronchi. Lobelia should be used cautiously, as it may cause nausea and vomiting.

Lobelia has a long history of use for relieving coughs. The mucilage of slippery elm gives it a soothing effect for coughs. Usnea also contains mucilage, which may be helpful in easing irritating coughs. There is a long tradition of using wild cherry syrups to treat coughs. Other traditional remedies to relieve coughs include bloodroot, catnip, comfrey (the above-ground parts, not the root), horehound, elecampane, mullein, lobelia, hyssop, licorice, mallow (*Malvia sylvestris*), red clover, ivy leaf, pennyroyal (*Hedeoma pulegioides*, *Mentha pulegium*), onion (*Allium cepa*), and plantain (*Plantago lanceolata*, *P. major*). None of these has been investigated in human trials, so their true efficacy for relieving coughs is unknown (Capasso *et al.*, 2003). Even though, Lobelia is a classic herb for cough and lung symptoms, Lobelia itself is known to induce a cough and pressure sensations in the chest if injected intravenously or administered orally, especially in large doses (Lim *et al.*, 2004) The sensation of fumes or pressure in the throat and upper chest may occur within seconds of oral dosing with Lobelia extracts; if dosing is continued, choking sensations and emesis may follow. With smaller, physiologically appropriate dosages, Lobelia is a rapid-acting expectorant. Lobelia supports the cough reflex by a variety of mechanisms including acting on juxtapulmonary capillary receptors (J-receptors) (Jaju *et al.*, 1998). The smooth muscles of the upper airways receive input from peripheral chemoreceptors and pressure receptors including J-receptors. Lobeline's stimulation of breathing has been shown in animal studies to be abolished by carotid sinus denervation, suggesting that lobeline may act on pressure receptors in the carotids and other blood vessels.14 Lobeline stimulates carotid body chemoreceptors via an adrenergic mechanism and promotes neural firing of the phrenic nerve (Deep *et al.*, 2001).

Lobeline may affect the cough reflex, expectoration, vascular tone, and bronchial smooth muscle tone via effects on lung cells and innervation. The larynx and trachea are the most common locations of eliciting the cough reflex where nerve fibres associated with "rapidly adapting receptors", and laryngeal J receptors can be stimulated and trigger a cough. J-receptors are known to be activated by capsaicin, lobeline, bradykinin, Sulphur gases, and mechanical manipulation (Raj *et al.*, 1995) Research has demonstrated that the throat and chest symptoms produced by Lobelia occur due to binding and activation of the J-receptors by lobeline, which in turn may trigger brief pulmonary congestion J-receptors are bound and activated by lobeline. Lobeline may trigger brief pulmonary congestion due to effects on J-receptors (Raj *et al.*, 2005). Theoretically, in patients

suffering from excessive secretions in the bronchial passages, Lobelia may act like an internal “counter-irritant”, but this has not been proven. If true, Lobelia may alleviate pressure and congestion in the lungs which are triggering a cough reflex. Therapeutically, Lobelia should be formulated with herbs that are soothing to the throat and lungs and have an antispasmodic effect to complement the stimulating effects of Lobelia (Jill Stansbury, 2013).

Chronic Obstructive Pulmonary Disease

Lobelia is used traditionally to promote mucus discharge. Mullein is classified in the herbal literature as both an expectorant, to promote the discharge of mucus, and a demulcent, to soothe and protect mucous membranes. Historically, mullein has been used as a remedy for the respiratory tract, particularly in cases of irritating coughs with bronchial congestion. Other herbs commonly used as expectorants in traditional medicine

include elecampane, lobelia, yerba santa (*Eriodictyon californicum*), wild cherry bark, gumweed (*Grindelia robusta*), anise (*Pimpinella anisum*), and eucalyptus (Jill Stansbury, 2013). Animal studies have suggested that some of these herbs increase discharge of mucus. However, none have been studied for efficacy in humans.

Lobeline and Lung Prostacyclin

Prostacyclin is produced by vascular endothelial cells. The production of prostacyclin by the lungs may help protect the coronary and cerebral arteries against thrombosis and atherosclerosis (Anand *et al.*, 2009) (Figure 4). In the lungs, it decreases vascular tone (Gryglewski, 1980) and may be beneficial against respiratory diseases. Prostacyclin levels are decreased in patients with pulmonary hypertension, and prostaglandin analogues are now widely used in the treatment of pulmonary hypertension (Mubarak, 2010).

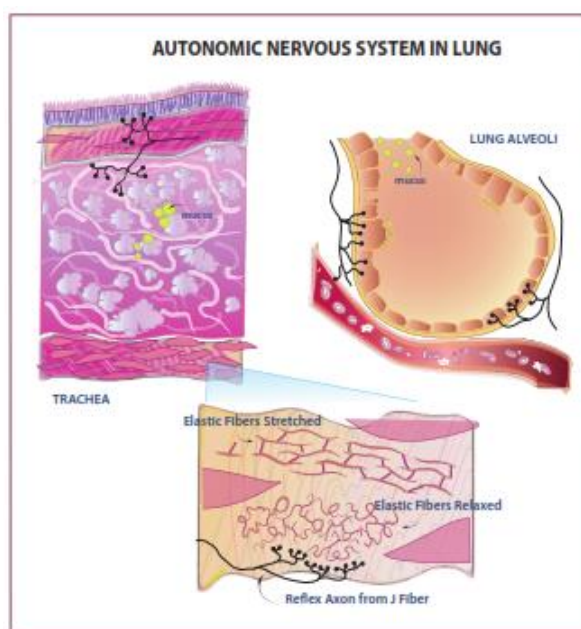


Figure 4: Autonomic Nervous System in Lung

Prostacyclin production in the lungs is promoted by angiotensin II, bradykinin, and the presence of arachidonic acid (its metabolic precursor). Prostacyclin production is also stimulated by abnormally high oxygen levels associated with pulmonary air emboli and hyperventilation. Interestingly, lobeline has also been shown to stimulate the release of prostacyclin from the lungs (Safdar, 2011) suggesting that Lobelia may constitute a new manner of treating pulmonary vascular inflammation as well as wheezing and other asthma-related symptoms.

Smoking Cessation

Lobeline has been used for over 50 years as a smoking cessation agent (Ejrup, 1960; Kalyuzhny, 1968). While more recent evidence indicates lobeline is ineffective as a smoking cessation aid (Stead & Hughes,

2000), its extensive use in humans over the years, together with the successful completion of Phase I Clinical Trials, provides substantial safety and tolerability data for lobeline. Research suggests that lobelia herb, which contains a substance with a similar effect on the nervous system as nicotine, could be useful in supporting smoking cessation. Lobelia also known as Indian tobacco, contains a substance (lobeline) that has some effects on the nervous system that are similar to the effects of nicotine, and preliminary reports suggested that pure lobeline or lobelia herb could be used to support smoking cessation (Tamboli *et al.*, 2011).

CONCLUSIONS

1. Lobelia is indicated for asthma and other respiratory ailments.

2. It influences several mechanisms involved in proper functioning of the respiratory tract including stimulating breathing, supporting the cough reflex, promoting expectoration, and improving vascular tone.
3. Therapeutically, Lobelia should be formulated with herbs that are soothing to the throat and lungs and have antispasmodic effect to complement the stimulating effects of Lobelia.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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