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AN OVERVIEW OF HERBAL PLANTS IN RESPIRATORY DISEASE TREATMENT

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ABSTRACT

Upper and lower respiratory tract anatomically are divided into two parts which are separated from each other by the throat. Respiratory diseases can involve the respiratory tract, lungs or blood vessels and usually a combination of these abnormalities can be seen in many respiratory diseases. Respiratory diseases can generally classify into the following groups obstructive pulmonary disease, restrictive lung disease, pulmonary vascular disease and other diseases. Herbal medicine is simply the science of using plants to treat or prevent medical conditions. It is one of the main modalities in traditional as well as contemporary medicine and is increasingly acknowledged due to the extensive use of herbal remedies in public and societies. As respiratory tract infections (RTI) are highly prevalent and variable, especially lower respiratory infections are a leading cause of sickness and mortality both in children and adults. There is a growing need for new treatments for such infections, particularly in the setting of worsening antibacterial resistance. Since ancient times, people who have tried herbs to treat diseases have also used them to treat infectious respiratory diseases. Many plants and herbal medicine- derived natural products could be used as an alternative therapeutic potential for RTI since they have antibacterial, antiviral, and anti-inflammatory effects. Although there are some doubts about safety and efficacy, Chinese Herbal medicines may help treat symptoms of viral respiratory disease, including COVID-19. Natural products such as plant extracts and their active compounds, directly target the processes involved in RTI and could be suitable therapeutic options with fewer adverse effects. In the meantime, it should be kept in mind that there are many factors that affect the therapeutic potential of medicinal herbs and related products, including the collection and

development processing. This section aims to highlight the examples of herbal medicines that are effective against RTI and their properties and therapeutic mechanisms.

KEYWORDS: Respiratory tract infection, Herbal medicines, COVID-19, Therapeutic mechanisms.

INTRODUCTION

Traditional medicine has a long history of servingpeoples all over the world. In many countries and culturesof different nations, the use of medicinal plants to treatdiseases and maintain public health is highly prevalent.Natural products play an important role in the field ofnew drugs research and development. Recent studieshave also revealed promising results from using of plantsin the treatment or prevention of a wide variety of hardcurable diseases such, athrosclerosis, diabetes, cardiovascular diseases, neurological disorders, and cancer. The main proposed mechanism forbeneficial effects of traditional plant is alterations in redox state. Therefore, medicinal plants with antioxidantactivity have been shown to counteract these situationsand always been considered as a healthy source of healthpromotion. Extraction of medicinal plants, drug preparation, Therefore, the aims of this study wereto gather local knowledge and traditional medicine. Traditional systems of medicine have been invogue for treating various ailments in many countries. Respiratory diseases such as asthma and COPD are one of the major causes of human mortality. Moreover, existing drugs are not adequate and give rise to numerous side effects.Herbal medicines, which have formed the basis of health care throughout the world since the beginning of humankind, are still widely used and play an economically important role in human society. Despite the use of herbal or botanical medicines for many centuries, only a relatively small number of plant species have been studied for possible medical applications. For two decades, the interest in medicinal plants and their international market value has been increasing. Herbal medicine may be used in addition to pharmaceutical treatments. Many countries and some health organizations classify herbal alternatives as a dietary supplement.

Infectious diseases have posed a threat to human life since the dawn of human existence and continuous efforts are required to develop effective treatments. The respiratory tract involves the nose, sinuses, pharynx, larynx, and bronchial tubes, finally extending to the smallest bronchi branch and into very small tubules called bronchioles in the lungs. A variety of bacteria, viruses, and fungi can cause respiratory tract infections. Respiratory tract infections are a group of common infectious lung diseases, including bronchitis, bronchiolitis, common

cold, epiglottitis, laryngotracheitis, pharyngitis, tuberculosis, pneumonia, and respiratory distress syndromes. Many of these diseases cause serious and even life-threatening health problems.[3-5] More than 50 million deaths worldwide are due to respiratory infections, which are the main cause of clinical visits and antibiotic prescriptions. Malnutrition and poor immunity are the main causes of the high incidence of respiratory infections. Although the discovery of antibiotics and antiviral agents has made the treatment of many infectious diseases possible, it has been observed that the emerging antibiotic-resistant strains and mutant microorganisms are stronger than existing ones. It is also known that microbial biofilms that cannot be treated with antibiotics can cause chronic infections. As infectious diseases continue to pose a threat to human health and antibiotic-resistant bacteria remain a challenging public health problem worldwide, continuous efforts are required to develop effective treatments. Natural products derived from many herbs and herbal remedies have been used as an alternative therapy for infectious respiratory diseases. For example, standardized Myrtol essentially consists of three mono- terpenes, namely (+)-alpha-pinene, d-limonene, and 1,8-cineole, which are used as a distilled phytotherapeutic extract.[9] The aim of this section is to draw attention to the herbal medicines used in the treatment of respiratory tract infections and to evaluate their efficacy by discussing their therapeutic effects. The antibacterial, antiviral, and anti-inflammatory effects of medicinal plants and other related natural compounds and brief mechanism of action will also be discussed. Asthma and chronic obstructive pulmonary disease (COPD) are common inflammatory obstructive lung diseases which affect many millions of people worldwide. While advances in basic and clinical research have led to important advances in drug therapy and improvements in care, both conditions are increasing in prevalence and are associated with considerable morbidity and mortality. Although mortality rates for asthma are relatively low, representing only 1 % of all deaths, it is recognised that in many cases that death could have been avoided with better routine care; COPD, however, is the 4th leading cause of death and is projected to rise to the second most common cause of death worldwide by 2020. Both conditions cause a significant impairment in quality of life due to impacts on patients' physical and psychological well-being. In addition, the social and economic effects are striking; among the most important are the escalating costs associated with unscheduled medical care, hospitalisations and loss of productivity. Oral and inhaled anti-inflammatory and bronchodilator medications have formed the basis of treatment recommendations for both conditions for the last three decades and despite proven efficacy there is a recognition that therapeutic options are limited and not

without adverse effects. Thus there is a need to consider other therapeutic options including phytomedicines which could be used to complement existing treatments.

OVERVIEW OF RESPIRATORY DISEASE

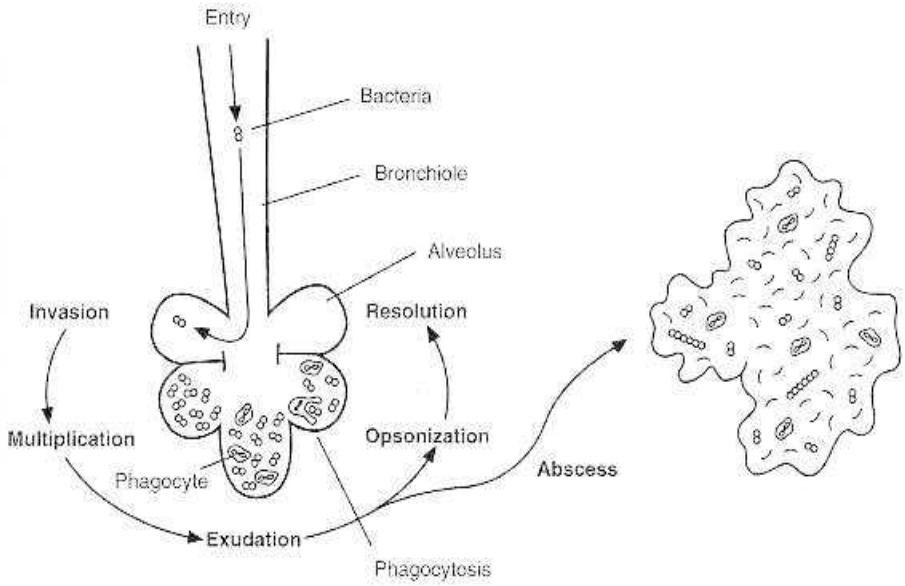
Even though research in respiratory medicineand related technology is in an advanced stage, respiratory diseases are still one of the perpetrators of the global health and are extending their vicious domain with each passingay. There are several respiratory diseases suchas asthma, chronic obstructive pulmonary disease (COPD), sarcoidosis and pulmonary fibrosis. Among these, asthma and COPD are the major ones, which adversely affect a huge number of human populations. A brief description of COPD and asthma is given below.

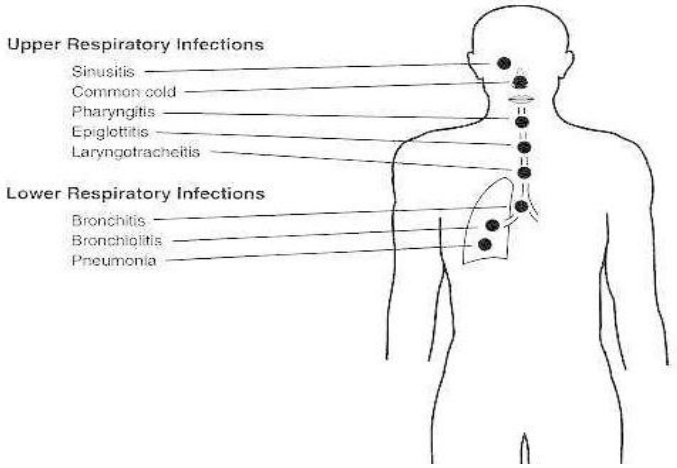
RESPIRATORY INFECTION

Organisms gain entry to the respiratory tract by inhalation of droplets and invade the mucosa. Epithelial destruction may ensue, along with redness, edema, hemorrhage and sometimes an exudate. Initial symptoms of a cold are runny, stuffy nose and sneezing, usually without fever. Other upper respiratory infections may have fever. Children with epiglottitis may have difficulty in breathing, muffled speech, drooling and stridor. Children with serious laryngotracheitis (croup) may also have tachypnea, stridor and cyanosis. Common colds can usually be recognized clinically. Bacterial and viral cultures of throat swab specimens are used for pharyngitis, epiglottitis and laryngotracheitis. Blood cultures are also obtained in cases of epiglottitis. Causative agents of lower respiratory infections are viral or bacterial. Viruses cause most cases of bronchitis and bronchiolitis. In community-acquired pneumonias, the most common bacterial agent is *Streptococcus pneumoniae*. Atypical pneumonias are cause by such agents as *Mycoplasma pneumoniae, Chlamydia spp, Legionella, Coxiella burnetti* and viruses. Nosocomial pneumonias and pneumonias in immunosuppressed patients have protean etiology with gram-negative organisms and staphylococci as predominant organisms. Organisms enter the distal airway by inhalation, aspiration or by hematogenous seeding. The pathogen multiplies in or on the epithelium, causing inflammation, increased mucus secretion, and impaired mucociliary function; other lung functions may also be affected. In severe bronchiolitis, inflammation and necrosis of the epithelium may block small airways leading to airway obstruction. Symptoms include cough, fever, chest pain, tachypnea and sputum production. Patients with pneumonia may also exhibit non-respiratory symptoms such as confusion, headache, myalgia, abdominal pain, nausea, vomiting and diarrhea. Sputum specimens are cultured for bacteria, fungi and viruses.

Culture of nasal washings is usually sufficient in infants with bronchiolitis. Fluorescent staining technic can be used for legionellosis. Blood cultures and/or serologic methods are used for viruses, rickettsiae, fungi and many bacteria. Enzyme-linked immunoassay methods can be used for detections of microbial antigens as well as antibodies. Detection of nucleotide fragments specific for the microbial antigen in question by DNA probe or polymerase chain reaction can offer a rapid diagnosis. Common colds are the most prevalent entity of all respiratory infections and are the leading cause of patient visits to the physician, as well as work and school absenteeism. Most colds are caused by viruses. Rhinoviruses with more than 100 serotypes are the most common pathogens, causing at least 25% of colds in adults. Coronaviruses may be responsible for more than 10% of cases. Parainfluenza viruses, respiratory syncytial virus, adenoviruses and influenza viruses have all been linked to the common cold syndrome. All of these organisms show seasonal variations in incidence. The cause of 30% to 40% of cold syndromes has not been determined. After an incubation period of 48–72 hours, classic symptoms of nasal discharge and obstruction, sneezing, sore throat and cough occur in both adults and children. Myalgia and headache may also be present. Fever is rare. The duration of symptoms and of viral shedding varies with the pathogen and the age of the patient. Complications are usually rare, but sinusitis and otitis media may follow.

MECHANISM OF RESPIRATORY INFECTION

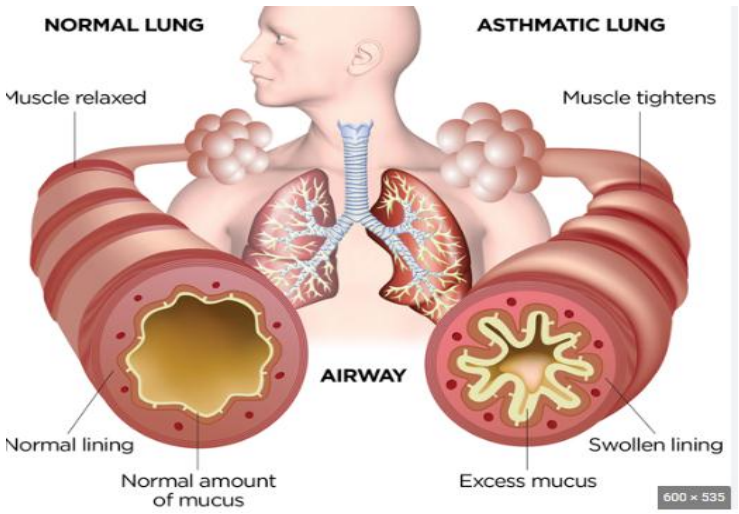




Asthma

Asthma is characterized by reversible airway obstruction, airway hyperresponsiveness and airway inflammation. The pathological features include infiltration of lymphocytes and eosinophilsinto airways, damage and loss of bronchial epithelium, mast cell degranulation, hyperplasiaand collagen deposition in the epithelium sub-basement membrane area. Asthma pathology is associated with the release of numerous pro-inflammatory agents including lipid mediators, inflammatory peptides, chemokines, cytokines and growth factors. The structural cells of the airways like smooth muscle cells, endothelial cells, fibroblast and airway epithelial cells are also important sources for causing asthma .Allergic asthma exhibits an allergen-induced immediate or early phase response with the abrupt onset of bronchoconstriction, and a secondary obstructive response, late phase response is associated with inflammation of the airways and airway hyperresponsiveness, which occurs 8 to 24 hrs after allergen exposure.[5]

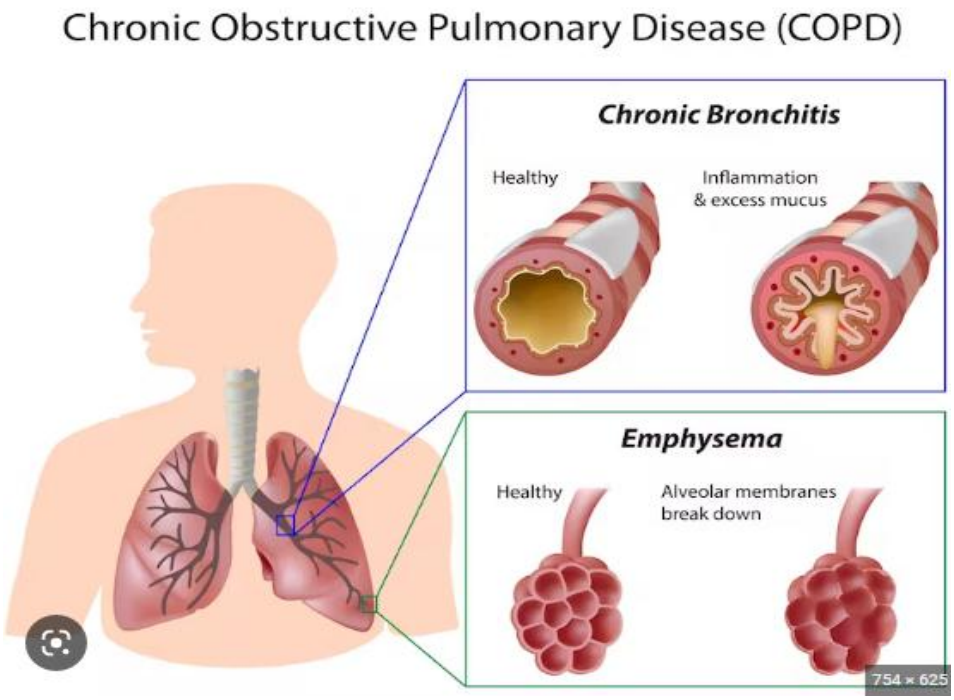
ROUTE CAUSE IMAGE



Chronic obstructive pulmonary disease (COPD)

COPD iscaused by a prolonged inhalation of irritants and toxins (e.g., cigarette smoke) into the airwaysband can directly injure lung structures leading tochronic inflammation in the airways and alveolar structures of the lung.[6] COPD includes chronic bronchitis, chronic bronchiolitis and emphysema. Chronic bronchitis is associated with hyperplasia and hypertrophy of mucus secreting glands within the large airways, submucosal inflammatory cell infiltration, edema, peribronchiolar fibrosis and increased smooth muscle contraction.[7] Chronic cough is a common symptom of COPD patients.[8] Chronic bronchiolitis refers to the presence of an inflammatory response in the respiratory bronchioles and is difficult to be defined clinically but may be recognized by the tests of small airway function (i.e., in airways of 2 mm diameters or less). Emphysema involves destruction of the alveolar wall, enlargement of airspaces and loss of elastic recoil.[7]

ROUTE CAUSE IMAGE



Current therapies, their adverse effects and need of new therapy

Despite increased understanding of pathogenesisof the respiratory diseases such as asthma and COPD, their incidence is increasing rapidly all over the world.[9][10] Several drugs are available which may give a temporary good relief, but they are mainly symptomatic and transient. Almost all currently available drugs such as steroids, β2-agonists, anticholinergics and phosphodiesterase (PDE) inhibitors have numerous adverse effects. For example, longer

use of corticosteroids produces deficiency in bone mineral density, cardiovascular effects , osteoporosis and osteonecrosis risk of cataract, panniculitis, migraine or migraine-like headache, pharyngitis and sore throat and renal deterioration. Most recently, it has been reported to cause serious pneumonia also. The long acting 2-adrenoreceptor agonists produce myocardial ischaemia and osteoporosis. Anticholinergics cause papillary dialation, blurred vision and acute glaucoma.[28] PDE inhibitors like theophyline cause gastrointestinal symptoms to palpitations, arrhythmias, hypocalcaemia, nausea, diarrheaand headache.[29,30] Hence continuous efforts are going on worldwide to search effective and safer remedies for these respiratory diseases preferably of natural origin, to obtain negligible or no adverse effects for treating these epidemic diseases.

Traditional System of Medicine

First one is "Ayurveda", which flourished in north India and became popular all over the country and also in abroad, and the second one is "Siddha", which originated from Tamil Nadu, a south-east state of India and practiced mostly in and around areas of its origin. The common specific features of these two systems are: tridosha siddhantam; wind (vatham), bile (pittam) and phlegm (siletuman), pancha bhuta theory; space (aakasam), air(vayu), fire (thee), water (neer) earth (munn), three gunas; subtle (sattva), activity (rajas), gross (tamas), and six kinds of tastes (arusuvai).[11] [12]

Medicnal Plants from Traditional System of Medicine Used for Treating Respiratory Diseases

Numerous plants seem to be used in this system; but there is no adequate data because of multiple reasons. The top two of them are as follows; 1) it is only in ancestral use and inherited by disciple to disciple and generation to generation and 2) it was documented in

scholarly Tamil language with numerous cryptic references which differs from the today's common Tamil language and is difficult to understand even by native Tamil people also.[13] After a long time, some of them were translated into common Tamil language, and thereafter, few of these texts were translated into English. Several organizations such as department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (AYUSH), Government of India; Central Council for Research in Ayurveda and Siddha, New Delhi; and Gandeepam, a non government organization (NGO)) have been established. These organizations have an important role in maintaining and reviving the ancient Indian systems of medicine. In addition, they encourage the scientific studies on these systems. Alongside, some ethnomedicinal studies were also done by some groups of workers in south India[14-16] by gathering the valuable information's from the practitioners of rural area near forest region where the people depend mostly on the herbs and have a discreet knowledge of herbal medicines. Based on these literatures numerous plants have been observed for treating various human ailments. Many of these plants, which are used for multiple diseases but mainly used for respiratory diseases.

Acalypha indica L. (Euphorbiaceae); Siddha name: Kuppaimeni

The Leaves, roots, stalk and flowers of Acalypha indica are used in SSM for its medicinal properties. The leaf powder cures respiratory diseases. Its other actions include cathartic, anthelmintic, expectorant, emetic, anodyne, hypnotic, antimicrobial and wound healing properties.[17] Recently, the ethanolic leaf extract of this plant has been shown a potent snake venom neutralizing property in the experimental animals[18] which indicates its detoxification effect. There is no specific study on its toxicological aspect; however, one clinical report indicated its hemolytic effect in glucose-6-phosphate dehydrogenase deficient individuals.[19]

Adhatoda vasica Nees (Acanthaceae); Siddha name: Adathodai

The leaf extract of Adhatoda vasica is used to cure bronchial asthma, eosinophilia[20] and cough.[21,22] In some areas the traditional healers use the leaves of this plant orally along with the flowers of Hibiscus rosa-sinensis to treat asthma.[23] The relief of bronchial obstruction by its leaf extracts may be attributed even if partially, to the presence of alkaloids.[24,25] The plant also consists of antiinflammatory , antiulcer , hepatoprotective and antitussive properties.

Apium graveolens L. (Umbelliferae); Siddha name: Celery-keerai

The seeds and leaves of Apium graveolens are used in the treatment of asthma and bronchitis as well as liver and spleen diseases. Seeds are also used in the treatment of chronic skin disorders including psoriasis. One of its compound apigenin (flavonoid) has been proven to possess vasodilatory action in thoracic aorta of rat.[26] The another compound apiin (flavonoid) showed significant inhibitory activity on nitric oxide production in-vitro and reduces inducible nitric oxide synthase expression in-vivo.[27] The seeds and leaf extracts have been shown to reduce the drug induced toxicity[28,29] in rats. Its root has been reported for some side effects such as allergy and irritation.[30,31]

Boerhavia diffusa L. (Nyctaginaceae); Siddha name: Mukaratee

The roots of B. diffusa are used in SSM for the treatment of asthma and also in other diseases such as dropsy, ascities, heart disease, kidney stone and colitis.[22] Recent molecular studies have shown that the ethanolic extract of B. diffusa has immunosuppressive effect including reduction of nitric oxide and superoxide in vitro which are associated with asthma and COPD. It has also been demonstrated to have spasmolytic, anti-bacterial anti-microbia, antidiabetic[32] and antifungal[33] activities. There is no toxic report on this plant; rather it has been shown to have chemopreventive activity in mice.[34]

Caesalpinia bonduc L. (Caesalpiniaceae); Siddha name: Kaliccikkai

The seeds of Caesalpinia are used in the treatment of asthma and also in intermittent and chronic fevers, colic, acute arthritis, palsy, painful and swollen testicles.[22] There is no scientific investigation of this plant on any respiratory diseases.

Calotropis gigantea L. (Asclepiadaceae); Siddha name: Erukku

The flowers of Calotropis gigantea are used in cough, asthma, catarrh and loss of appetite. The powdered root bark is soaked in its own milky juice from which bougies are prepared

and their fumes are inhaled to treat cough in SSM. The flowering tops pounded and boiled with molasses are given every morning for treating asthma.[35]

Crocus sativus L. (Iridaceae); Siddha name: Kungumapu

The dried stigma and tops of styles are used in treating asthma and cough.[22]

Euphorbia hirta L. (Euphorbiaceae); Siddha name: Amman pachharisi

Euphorbia hirta is also popularly called as “asthma weed” the whole plant is used in treating asthma and bronchitis.

Ocimum sanctum L. (Lamiaceae); Siddha name: Thulasi

The leaves of Ocimum sanctum are used in bronchitis, asthma, eosinophilia and chronic cough.[22]

Piper longum L. (Piperaceae); Siddha name: Thippili

In natural system of medicine, Piper longum fruits are usually dried for using in cough, cold and asthma.[20]

Piper nigrum L. (Piperaceae); Siddha name: Milagu

In natural system of medicine, the dry unripe fruit powder of Piper nigrum along with the honey is given to treat asthma and bronchitis.[20]

Solanum nigrum L. (Solanaceae); Siddha name: Manathakkali

The leaves and fruits of Solanum nigrum are used in asthma and bronchitis.[20]

Solanum trilobatum L. (Solanaceae); Siddha name: Thuthuvalai

The whole plant is used to treat asthma, bronchitis and eosinophilia.[20]

Solanum xanthocarpum (Solanaceae); Siddha name: Kandankatthiri

The fruits of Solanum xanthocarpum are used tocure bronchial asthma, eosinophilia[20] and cough.[21]

Source:https://www.researchgate.net/figure/The-plant-fruits-of-Solanum-xanthocarpum-a-b_fig1_230612036

Terminalia bellirica Roxb (Combretaceae); Siddha name: Thandrikkai

The fruits of Terminalia bellirica are effective in asthma, cough, hoarseness, sore-throat, and also for other conditions such as dropsy, dysentery and diarrhea.[22]

Source:https://www.iafaforallergy.com/dravya-herbs-part-a/bibhitaki-vibhitaki-terminalia-bellirica-roxb/

Tylophora indica Merrill (Asclepiadaceae); Siddha name: Kurinjan

The root and leaves of Tylophora indica are used as medicine in SSM for its effectiveness in asthma. These parts are also used in diarrhea, dysentery and syphilitic rheumatism.[22]

Source: http://pharmaveda.com/kb/Aantmool.html

LIMITATIONS

- Minimal scientific research. When it comes to scientific proof, evidence is still limited. Many people are skeptical about the reliability of alternative medicine for back pain. Methods that have worked for some people don't work for others. It's not 100 percent proven to cure every problem or every person.
- Longer term treatment. Traditional medical procedures can be quick and easy. With alternative medicine, it's a marathon, not a sprint. Alternative medicine is largely based

on natural products and how they interact with and heal your body. Alternative medicines entail a longer treatment and healing time as they heal the problem at its root. They also require you to have an active role in the healing process.

- Not useful in emergency cases. In case of an emergency, alternative medicines won't do you much good. Traditional medicine is made to work fast. Should you be in an emergency situation, turn to the traditional medical professions.
- No Regulation. Much of alternative medicine isn't approved by the U.S. Food and Drug Administration. So, as with anything, do your research. Make sure you become informed about different forms of alternative medicines and trustworthy practices. Ask for referrals and references before taking chances with your health.

CONCLUSION

The present approach to manage the both asthma and COPD is predominately based on the use of inhaled bronchodilators and corticosteroids. For a large number of patients these treatments are effective at improving lung function. Furthermore there is growing recognition of subgroups of patients that appear refractory to current therapy and who are considered 'difficult to treat'. At present, novel and expensive biologic therapies are being developed to address this unmet need. Alternative approaches to address the issue of adverse effects and reduced efficacy include the use of phytomedicines. Therefore there is a need for properly conducted scientific research into the effects of safe, plant-based medicines in asthma and COPD. The articles included in this review the vast majority of various medicinal plants which used to cure the respiratory disease based on natural medicine system since its the permanent remedy for respiratory disorders this says that, "traditional opinion of most of the modern world".

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