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THERAPEUTIC POTENTIAL OF MEDICINAL PLANT IN CHHATTISGARH REGION FOR THE TREATMENT OF RESPIRATORY DISORDERS

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ABSTRACT

Respiratory disorders are known to affect the airways including the nasal passages, bronchi and lungs causing blockages. The advent of COVID-19 has further aggravated the complications of the respiratory systems where conventional medicine is not reachable or affordable by the majority poor in India. Respiratory diseases have in the recent past become a health concern globally. More than 523 million cases of coronavirus disease (COVID19), a recent respiratory diseases have been reported, leaving more than 6 million deaths worldwide since the start of the pandemic. In India, respiratory infections have largely been managed using traditional (herbal) medicines, due to their low cost and ease of accessibility. This review highlights the plants' toxicological and pharmacological evaluation studies explored. It seeks to document plants that have been traditionally used in India to treat respiratory ailments within and beyond the past four decades. From the study, there were at least 58 plant families comprising 160 medicinal plants widely distributed throughout the country. The Fabaceae family had the highest number of medicinal plant species, with a total of 21 species. A total of 12 respiratory ailments were reportedly treatable using the identified plants. From a total of 160 plants, colds were reportedly treatable with 56, pneumonia 53, coughs 34, chest pain and related conditions 29, asthma 25, tuberculosis and spots in lungs 22, unspecified respiratory conditions 20, influenza 13, bronchial problems 12, dyspnoea 7, sore throat and infections 5 and sinus clearing 1 plant. The study identified potential medicinal plants that can be utilised in future to manage respiratory infections.

Keywords: *Medicinal plants; Causative organisms; Respiratory disorders; Herbal remedies; Molecular mechanism.*

INTRODUCTION

Respiratory diseases are known to affect the airways including the nasal passages, bronchi and lungs. It is very often difficult to classify them because they have different levels of severity and are closely dependent on the patient's age. They can be bronchitis, pneumonia, asthma, tuberculosis, sinusitis, and rhinitis representing the main factors of morbidity and mortality in both developed and developing nations of the world [1] Respiratory infections account for up to 38.6% of infectious diseases and are responsible for the death of around 14.9% of children in India. Coronaviruses are emerging and reemerging enveloped RNA viruses that are distributed broadly among humans, mammals and birds. Coronaviruses vary significantly in the pathogenicity, and include highly pathogenic species such as MERS-CoV and COVID-19, and relatively harmless species such as the common cold. Severe Acute Respiratory Syndrome Corona Virus (SARS-COV) is the causal agent of the outbreaks in 2002, 2003 in China. [2] In December 2019, a new epidemic of SARS-COV was detected in several local health facilities from patients with pneumonia in Wuhan, Hubei Province, China. [3] COVID-19 is a species of coronavirus (CoVs), an etiologic agent which can systemically cause disorder in the respiratory and digestive tract, resulting in severe infections in both humans and animals. [4] Currently, no specific therapies for COVID-19 are available and investigations regarding the treatment of COVID-19 are still limited to preventive and supportive therapies, designed to prevent further complications and organ damage. [5]

The main symptoms described for COVID-19 were those of malaria (fever, fatigue, body aches, etc.), accompanied by symptoms of respiratory disorders (dry cough, breathing difficulties, chest pain, sore throat, etc.) and flu. [6]. After the panic caused by the first cases of contamination in Cameroon in March 2020, the population in search of preventive and even curative measures for COVID-19, flocked the traditional pharmacopoeia [7] in search of traditional medicine which have properties against any of the symptoms. The plants most in demand were largely those with anti-influenza, antimalarial and immunomodulatory properties including those with reported effects on respiratory disorders. In another study, some plant-sourced antioxidant and immune-boosters, kaempferol, quercetin, luteolin-7-glucoside, demethoxycurcumin, naringenin, apigenin-7-glucoside, oleuropein, curcumin, catechin, epicatechin-gallate, zingerol, gingerol, and allicin were investigated as potential inhibitor candidates for COVID-19, in comparison to antiretroviral protease inhibitors. [8] It was found that these plant products could act as potential inhibitors, meaning the source plants could be exploited as potential candidates for the development of improved traditional medicines (ITMs) as inhibitors of COVID-19. The use of traditional medicine dates back to prehistoric times and remains the major accessible and affordable treatment for the population in African countries. Today medicinal plants which are the main component of traditional medicine have been transformed into conventional drugs that are sold in pharmacies worldwide. Many other plants are currently undergoing investigation to ascertain their therapeutic efficacies and safety. Medicinal plants have long been known for their curative or protective effects against a broad range of microorganisms, such as viruses, protozoa, bacteria and parasites. [9-11] There are reports stating the protective effect of plant extracts against viral diseases, such as HIV 1&2; Herpes simplex virus, Hepatitis B & C virus just to name a few. Considering that COVID-19 is a respiratory disorder, the present study systematically reviewed the plants used in India for the treatment of respiratory disorders. [12-14]

Types of Respiratory Disorders

The most common respiratory diseases are asthma, chronic obstructive pulmonary disease, cystic fibrosis, lung cancer, tuberculosis, bronchitis, pneumonia, and emphysema. Some respiratory diseases are acute, like an infection that will get better with treatment, while others are or become chronic and need to be managed. Many types of lung diseases can cause chronic respiratory conditions. Chronic respiratory disease affects millions of people in the United States alone. It can be difficult to say how many people have lung diseases overall because these diseases are grouped into specific conditions. Many genetic and environmental factors can lead to lung disease, but smoking is the top preventable cause of many respiratory conditions. This article will look at the eight most common respiratory diseases, their symptoms, and what causes them.

Asthma

Asthma affects 25 million people in the United States. People with a family history of asthma, respiratory allergies, or severe childhood respiratory illness are at a higher risk of developing asthma. Office of Disease Prevention and Health Promotion. Respiratory diseases. Asthma is a chronic inflammatory disease that causes breathing problems when the airways become narrowed by inflammation or blocked by mucus. The condition's severity varies from person to person, but most people take daily preventive medication to control their symptoms and prevent flare-ups.

Symptoms - Asthma can have several symptoms, including: Wheezing, Coughing, Tightness in the chest, Shortness of breath. [15]

Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) is an umbrella term used to describe two primary types of obstructive lung disease that used to be classified separately: emphysema and chronic bronchitis. Emphysema develops when the tiny air sacs in the lungs (alveoli) become damaged and less elastic. This reduces the ability of the sacs to move oxygen and other gases between the air that is breathed in and the blood. This can lead to a lack of oxygen in the blood (hypoxia) and a buildup of toxic waste products. Chronic bronchitis is a condition where the lining of the bronchial tubes becomes irritated and inflamed. The swelling can make it more difficult to breathe and cause an overproduction of mucus. Nearly 15 million people have been diagnosed with

COPD in the United States, and another 12 million are believed to have the disease but do not have an official diagnosis. COPD is the fourth leading cause of death in the United States. About eight in 10 cases are linked to exposure to cigarette smoke.

Symptoms

The symptoms of COPD vary based on which type you have. Common symptoms can include: A frequent or chronic cough, A cough that produces a lot of mucus, Wheezing, A squeaking or whistling sound when you breathe, Shortness of breath that is worse with activity, Tightness in your chest, Sensitivity to respiratory infections like colds or the flu, Weight loss, Weakness, Swelling in your legs and feet, A blue tinge to your lips or fingernails (cyanosis). [16]

Cystic Fibrosis

Cystic fibrosis (CF) is a genetic condition that affects about 35,000 people in the United States. It can cause both breathing and digestive problems because the disease makes the mucus in the body very thick. While the disease can involve several organs, it tends to cause specific problems in the lungs, such as blockages from thick mucus that trap harmful bacteria and lead to infections. A diagnosis of CF is usually made early in life because newborns in the United States are screened for the disease. If a diagnosis is not made at birth, symptoms that occur in childhood can lead to the diagnosis later on.

Symptoms

Since cystic fibrosis can affect many parts of the body, a wide range of symptoms can develop, such as: A cough that does not go away, A cough that produces thick mucus or blood, Wheezing, Shortness of breath, Frequent respiratory or sinus infections, Nasal polyps, Slow growth in childhood or poor weight gain, Constipation, Greasy or foul-smelling stools. [17]

Lung Cancer

Lung cancer is one of the most common types of cancer, ranking third in the United States with more than 218,000 people affected. It can develop as either small cell lung cancer or non-small cell lung cancer, which is the more common of the two.

Symptoms

Lung cancer can develop gradually and often with no symptoms. When it does appear, symptoms may include: Chest pain, Chronic cough, Difficulty breathing, Wheezing, Hoarseness, Weight loss, Fatigue or weakness, Difficulty swallowing, A cough that produces bloody mucus, Swelling in the face or neck.

Tuberculosis

Tuberculosis is a bacterial lung disease caused by *Mycobacterium tuberculosis*. More than 1.8 billion people around the world have tuberculosis, but the disease is only considered active in 10 million of them. People with strong immune systems sometimes carry an inactive form of the disease, called latent tuberculosis. In people with weaker immune systems, the bacteria attacks lung tissue. It can also spread and cause damage to other parts of the body.

Symptoms

Many respiratory diseases share symptoms, such as long-term cough. Certain symptoms are specific to one disease or another. For example, night sweats tend to occur in people with tuberculosis. Other tuberculosis symptoms include: A cough that lasts longer than three weeks, Weight loss, Poor appetite, A cough that brings up blood or mucus, Weakness, Fatigue, Fever, Night sweats. [18]

Bronchitis

Bronchitis is a condition that develops when the windpipe (bronchial tube) gets irritated or inflamed. In response to the inflammation, the lining of the bronchial tube may make too much mucus as it tries to coat the area. The mucus can make it difficult to breath. Inflammation can also cause swelling of the airway. This will cause it to narrow and makes it harder to breathe. Bronchitis can be acute or chronic. There are some key differences

between the two forms: In acute bronchitis, the inflammation is usually caused by an infection that will get better in a few days to several weeks. With chronic bronchitis, the inflammation is caused by repeated exposure to irritants like cigarette smoke or pollution. Chronic bronchitis does not go away. You may have periods of relief along with periods where it gets worse (exacerbations), especially if you get a cold or another respiratory infection.

Symptoms

Chronic bronchitis falls under the umbrella of COPD. Acute bronchitis is not considered COPD, but it shares symptoms with the chronic form of the disease. These symptoms include: A frequent cough that produces mucus, Wheezing, A whistling or squeaking sound when you breathe, Shortness of breath (especially with activity), Tightness in your chest, Fever (acute bronchitis only). [19]

Pneumonia

Pneumonia is a generic diagnosis. Even though there are different types of pneumonia, the way that the condition affects the lungs is similar in each one. With pneumonia, a virus, bacteria, or another infectious agent causes the tiny air sacs in the lungs (alveoli) to fill with fluid or pus. These air sacs are what help exchange oxygen and other gases between the air that is breathed in and the blood. When these sacs are filled with fluid, the body's ability to exchange gases is reduced. The several types of pneumonia are: Viral, Bacterial, Mycoplasma (also called "walking pneumonia"), Fungal, Aspiration.

Symptoms

In some types of pneumonia, such as walking pneumonia, the symptoms can be mild and not affect daily activities. However, the symptoms of pneumonia can be severe and, in some cases, will require hospitalization. Common symptoms of pneumonia are: Fever, Chills, A cough that produces phlegm, Shortness of breath, Chest pain when you cough or breathe, Nausea, Vomiting, Diarrhea.

Emphysema

Emphysema is a type of COPD that occurs when the tiny air sacs (alveoli) in the lungs lose their elasticity. These sacs are made to inflate and shrink and stretch with each breath, which allows air to move in and out of them. If you have emphysema, these sacs have been damaged and cannot stretch when you breathe. As these air sacs become damaged and die off, your lungs have fewer working parts to move oxygen from the air you breathe into your blood. Smoking is a leading contributor to emphysema, but exposure to other pollutants and chemicals can also cause it. Age and obesity are also risk factors for emphysema.

Symptoms

With early emphysema, you may not notice any symptoms. As the disease progresses, the symptoms can become more severe and may include: Frequent coughing, A cough that produces a lot of mucus, Wheezing, Shortness of breath that gets worse with activity, A whistling or squeaking sound when you breathe, Tightness in your chest. [20]

Infectious Conditions

Infectious lung conditions are usually temporary, although some respiratory infections can become chronic or frequently recur. For decades, acute lower respiratory tract infections have been among the top three causes of death and disability among both children and adults. Pulmonary infections are common and are caused by a wide range of organisms. Causes include: Pulmonary viral infection, Pulmonary bacterial infection: bacterial pneumonia, Pulmonary mycobacterial infection: pulmonary tuberculosis; pulmonary non-tuberculous mycobacterial infection, Pulmonary fungal infection: pulmonary aspergillosis. [21]

Causes of Respiratory Diseases

The most common respiratory disease causes are as follows –

Smoking and Air Pollution:
Smoking's toxins and air pollution cause damage to the lungs' alveoli (alveolar membrane). Therefore, it cannot properly immerse gaseous oxygen into the blood. As a result, the patients experience discomfort and shortness of breath.

Allergies:
Some people's immune systems react poorly to specific chemicals, such as pollen, dust, or animal dander. When allergic people are exposed to these allergens, they experience breathing difficulties.

Viral Infection:
One of the main causes of respiratory disorders is viral infection. Some viruses enter alveoli and produce inflammation, such as influenza viruses, respiratory adenoviruses, and respiratory syncytial viruses. [22]

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One of the main causes of respiratory disorders is **viral infection**. Some viruses enter alveoli and produce inflammation, such as influenza viruses, respiratory adenoviruses, and respiratory syncytial viruses.

Bacterial Infection:
Respiratory diseases can also be brought on by some bacteria, including otitis, sinusitis, and pneumonia. Some additional respiratory disease causes are as follows – Chest trauma and consequent bleeding, Abdominal and chest infection, Inflammatory or autoimmune diseases, Tuberculosis. [23]

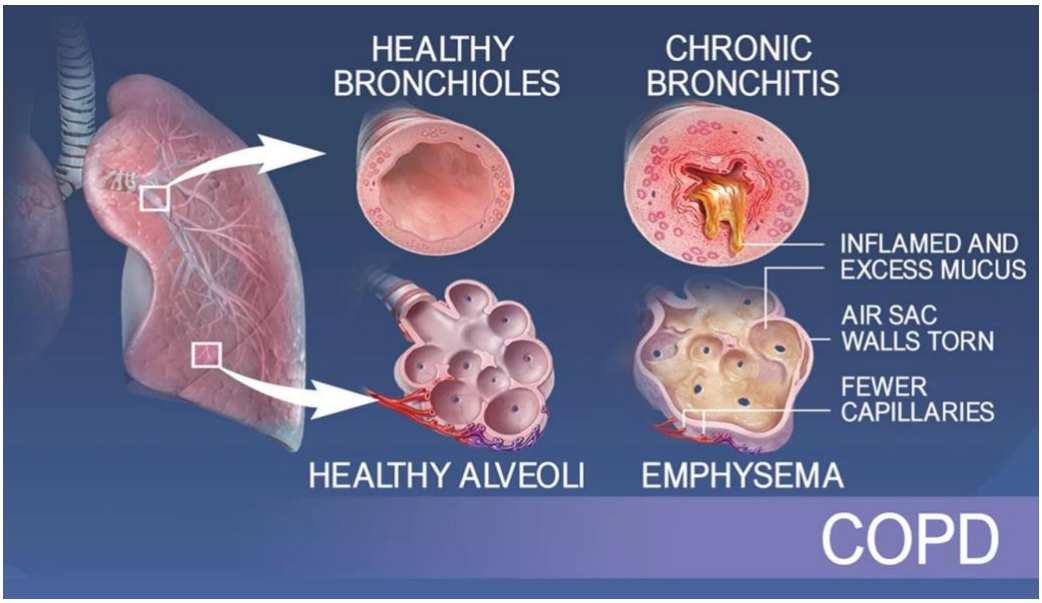

Fig. 1 – Respiratory disorder – COPD

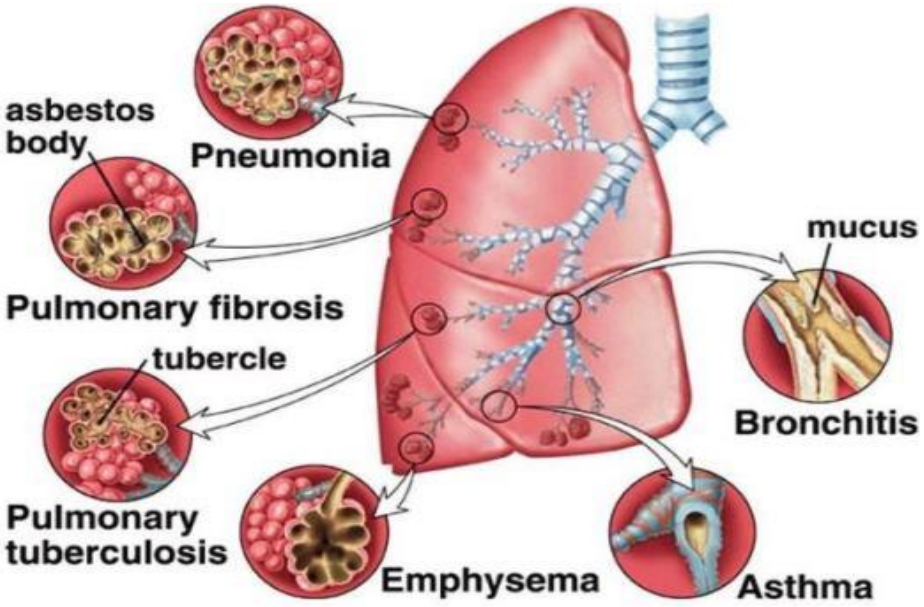

Fig. 2 – Different types of respiratory disorders.

Table 1: Herbal remedies for the treatment of different respiratory disorders.

S. No	Botanical Name	Family	Synonyms	Parts Used	Diseases Cured
1.	*Eugenia caryophyllus*	Myrtaceae	Laung	Dried flower buds	Anti-inflammatory, antimicrobial
2.	*Tinospora cordifolia*	Menispermaceae	Guduchi, Amrita	Stem	Anti-inflammatory, Hepato-protective, Immuno-modulatory, Antipyretic
3.	*Piper longum*	Piperaceae	Long pepper, Thippali	Roots and fruits	Anti-inflammatory and analgesic
4.	Honey comb by the hive bee Apis millifera	Apidae	Madhu	Flowers and flower buds	*Bronchial Asthma, Throat Infections, Tuberculosis*
5.	*Picorrhiza kurroa*	Plantaginaceae	Yellow gentian, Picroliv	Roots, stems, and leaves	Anti-inflammatory, Broncho-dilatory, Pain-relieving, Anti-microbial
6.	*Abrus precatorius L*	Fabaceae	*Gundumani*	Leaf extract	Bronchitis, Cough
7.	*Acalypha indica L*	Euphorbiaceae	*Kuppaimeni*	Whole plant extract	Asthma
8.	*Achyranthes aspera L*	Amaranthaceae	*Nayuruvi*	Whole plant Extract dry ash	Cold and cough
9.	*Allium cepa L*	Liliaceae	*Vengayam*	Bulb extract	Asthma
10.	*Allium sativumL*	Liliaceae	*Vellaippoondu*	Garlic gloves	Cough
11.	*Azadirachta indica A. Juss*	Meliaceae	*Vembu*	Leaf extract	Bronchitis
12.	*Boswellia serrata Rox.*	Burseraceae	*Parankisambirani*	Gum-Resin	Asthma
13.	*Calotropis gigantea (L) R.Br Ex Ait*	Asclepiadaceae	*Erukku*	Root bark	Cough, Cold
14.	*Carica papaya*	Caricaceae	*Pappali*	Fruits	Emphysema
15.	*Cassia occidentalis*	Caesalpinaceae	*Peyavarai*	Leaves, Flowers	Asthma, Chronic Respiratory disorder, Cough and Cold

16.	*Cassia tora Linn*	Caesalpinaceae	*Tagarai*	Shoot and leaves	Cough, Asthma and Bronchitis
17.	*Centella asiatica* (L)	Apiaceae	*Vallarai*	Leaves	Asthma
18.	*Coccinia indica*	Cucurbitaceae	*Kovai*	Leaves	Asthma
19.	*Coleus aromaticus Benth*	Lamiaceae	*Karpura valli*	Leaves	Whooping cough, Breathlessness and Influenza
20.	*Curcuma longa Sal.*	Zingiberaceae	*Kasthuri Manjal*	Rhizome Powder	Cough
21.	*Cymbopogan citrates Stapf.*	Poaceae	*Lemon grass*	Leaves	Cough
22.	*Cyanodon dactylon L*	Poaceae	*Arugam pul*	Leaves	Asthma
23.	*Drypetes roxburghii wall.*	Euphorbiaceae	*Puttira-civi*	Bark	Cough
24.	*Euphorbia hirta L*	Euphorbiaceae	*Amman pacharisi*	Whole plant extract	Asthma
25.	*Ficus racemosa L*	Moraceae	*Athi*	Fruits	Asthma
26.	*Grewia hirsute Korth.*	Tiliaceae	*Tavuttai*	Root, Fruit	Tuberculosis, Chronic respiratory disease
27.	*Gymnema sylvestris (Retz). Shult.*	Asclepiadaceae	*Sakkarai Kolli*	Leaves	Cough
28.	*Hemidesmus indicus (L)*	Asclepiadaceae	*Nannari*	Root	Cough, Cold and Asthma
29.	*Holorrhena pubescens*	Apocyanaceae	*Paambu Kaalachchedi*	Root, Bark	Cough
30.	*Justicia Adhatoda L*	Acanthaceae	*Vasambu*	Leaves	Cold and Cough
31.	*Kalanchoe pinnata (LamK)Pers.*	Crassulaceae	*Rana Kalli*	Leaves	Tuberculosis
32.	*Lantana camera L.*	Verbinaceae	*Arisimalar*	Leaves	Asthma
33.	*Leptadenia reticulate W&A*	Asclepidaceae	*Palaikkodi*	Root and leaf decoction	Asthma, Tuberculosis and cough
34.	*Leucas aspera Spreng*	Lamiaceae	*Thumbai*	Leaves and flowers	Asthma, other respiratory disease can also be cured with inhalation of thumbai leaves
35.	*Myrstica dactyloides Gaert.*	Myrtaceae	*Kattu Jatikkai*	Leaf and Fruit	Cough, bronchitis
36.	*Ocimum sanctum L.*	Lamiaceae	*Tulsi*	Leaves	Asthma, Bronchitis,
37.	*Piper betle L.*	Piperaceae	*Vetrilai*	Leaves	Bronchitis, Cough
38.	*Plectranthus amboinicus (Lour)*	Lamiaceae	*omavalli*	Leaves	Cough and Asthma
39.	*Psidium guajava L.*	Myrtaceae	*Koyya*	Leaves	Pneumonia
40.	*Punica granatum L.*	Punicaceae	*Madhulai*	Juice of fruit	Asthma, Bronchitis
41.	*Elettaria cardamomum*	Zingiberaceae	**Elaichi**, **Ela**	Seeds and fruits	Asthma, Teeth and gum infections, Cardiac, Kidney disorders
42.	*Shorea Robusta*	Dipterocarpaceae	Sal, sakhua and sarai	**Bark, Leaves and** Resin	**Anti-inflammatory, Antimicrobial, Analgesic** and **Wound healing**
43.	*Fagonia indica*	Zygophyllaceae	*Dhamasa, Dhama, and Chittigara.*	**Leaves, Aerial parts and Twigs**	Anti-inflammatory, Anti-pyretic, Laxative, Anti-diabetic, Anti-cancer
44.	*Fumaria Officinalis*	Papaveraceae	• Earth-	**Bark and Leaves**	Laxative, Diuretic and

			smoke, Drug fumitory, and Wax-dolls		Eczema
45.	*Picrorhiza kurroa*	Plantaginaceae	Kutki, Rohini, Kaur and Kadu	Leaves, Bark and Rhizomes	Anti-inflammatory, **Asthma,** Jaundice, Vitiligo, Constipation and Diarrhea

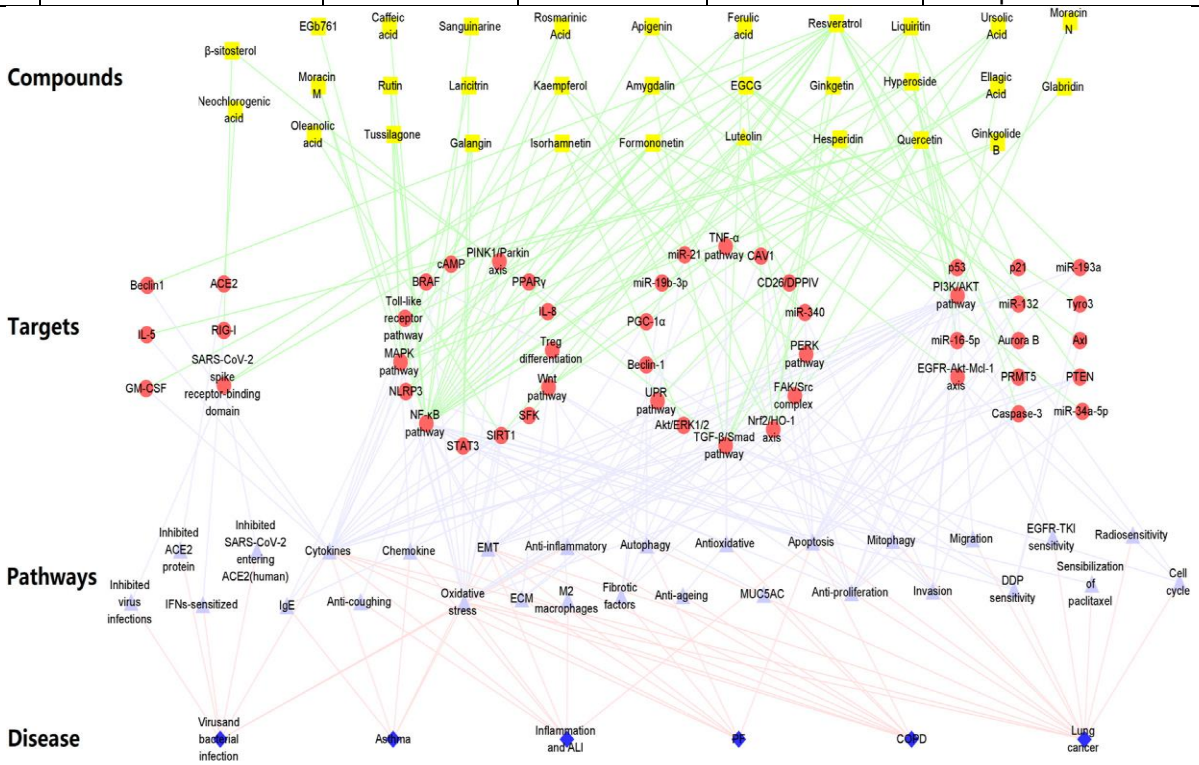

Fig. 3 - Network of bioactive compounds, targets, pathways, and six main respiratory diseases.

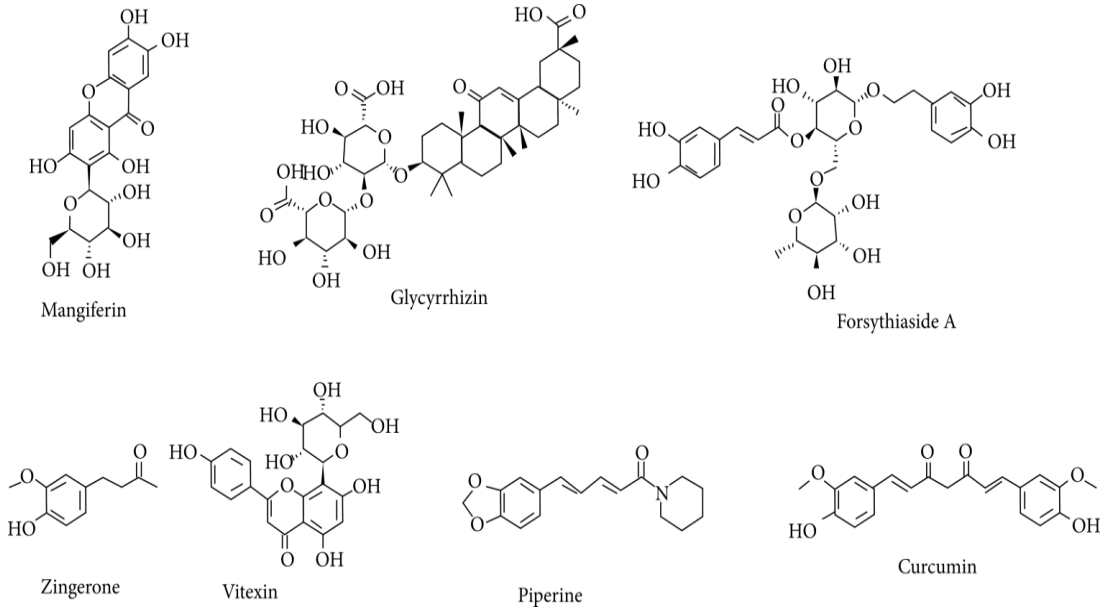

Fig. 4 - Some promising bioactive compounds for respiratory disease.

Mechanism of Action of Plant-Based Natural Product

The lung inflammation involves the activation of inflammatory cells such as eosinophils, lymphocytes, macrophages, and neutrophils, which serve as the source of different inflammatory mediators such as tumor necrosis factor (TNF-α), interleukins (IL-4, IL-1β, IL-6, and IL-5), histamine, prostaglandins, nitric oxide, and leukotriene. The release of these inflammatory mediators causes several abnormalities in the lungs and their function. [24] Natural products target the epithelial-mesenchymal transition (EMT), oxidative stress, fibroblast activation, inflammatory injury, metabolic regulation, and extracellular matrix accumulation. The basic mechanisms involved are the NF-κB, TGF-β1/Smad, PI3K/Akt, p38 MAPK, Nrf2-Nox4, and AMPK signaling pathways. [25] The plant flavonoid such as eriodictyol was reported to serve as the anti-inflammatory agent in the lungs which regulates the Nrf2 pathway and inhibited the expression of inflammatory cytokines IL-6, TNF-α, IL-1β, etc. [26] The flavonoids kaempferol and luteolin reduced the LPS-induced activation of the MAPK and NF-κB pathways and also reported to inhibit the ICAM-1, TNF-α, SOD, KC, and neutrophil inflammation. This compound was also found to involve in the reduction of the activity of superoxide dismutase and catalase and further reduces the lipid peroxidation and oxidative damage in the lung tissue. [27] A natural product such as sakuranetin was also reported to reduce the TNF-α, eosinophils, M-CSF, RANTES, IL-5, and IL-1β and inhibited the NF-κB, MMP-12-positive, and MMP-9-positive cells and also increased the TIMP-1 expression to serve as anti-inflammatory activities in the lungs of the elastase-treated animals. [28] Several compounds such as epigallocatechin, gallocatechin gallate, berberine, berbamine, coptisine, and dicentrine were reported to involve in the inhibition of viral replication, by inhibiting the viral life cycle in the host and act against the viral-induced respiratory inflammations. The 1, 8-cineol isolated from the essential oil of Eucalyptus globulus leaves was studied for its ability to reduce the expression of NF-κB target gene MUC2. The 3-methoxy-catalposide had been studied for its ability to inhibit the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2 in RAW264.7 cells stimulated by LPS. This compound also suppressed the release of nitric oxide (NO) and prostaglandin E2 (PGE2). This compound significantly reduced the activation of inflammatory genes such as interleukins IL-1β, IL-6, and TNF-α and inhibited the activation of nuclear translocation of NF-κB and AP-1. [29] Nepitrin, matte flavonoside G, rutin, etc. were reported to inhibit the influenza virus by damaging the viral membrane, by blocking the viral penetration into the cells, and by suppressing neuraminidase in both bacterial and viral infections. Thus, the possible mechanism of action of natural products to reduce the inflammation and diseases in the respiratory system could be by the inhibition of bacteria and viruses and also by the protease-antiprotease balance, NF-κB activation, oxidative stress, and MAPK pathways. [30]

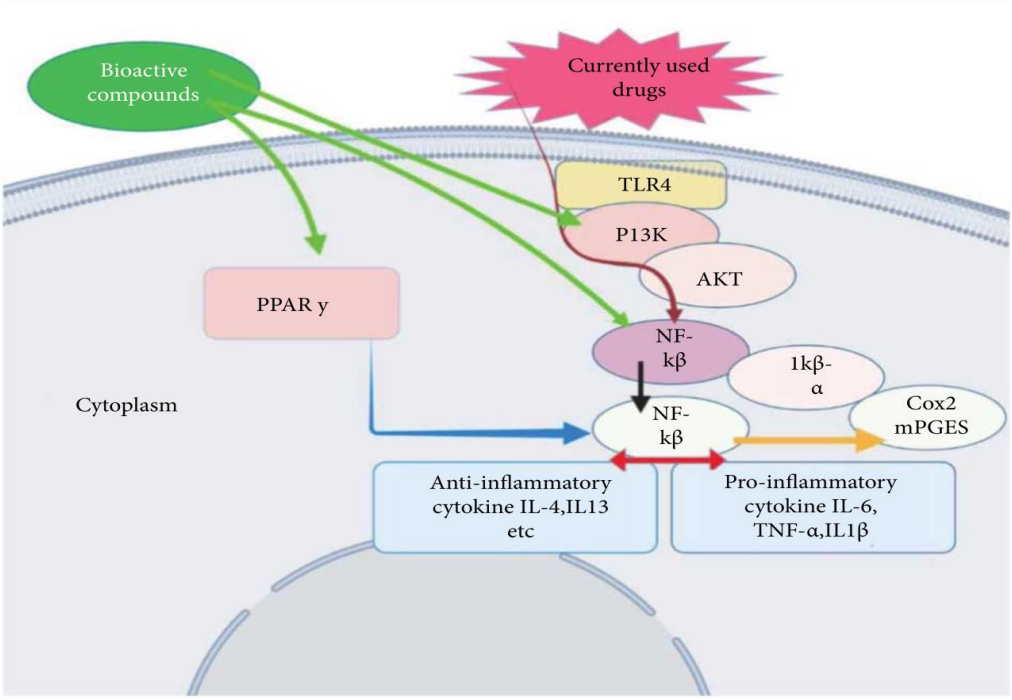

Fig. 5 - Mechanism of action of a natural product in respiratory inflammation.

Current Clinical Practice and Approved Drugs for Respiratory Disorders

Respiratory inflammatory diseases like asthma and chronic obstructive pulmonary disease (COPD) are usually treated with effective modern medicines of different classes. Nonsteroidal anti-inflammatory drugs (NSAIDs) is a class of drug that has been used efficiently and commonly in the inhibition of the cyclooxygenase enzyme. The past study showed the prescription of triple therapy for the treatment of pulmonary diseases [31] which suggested the use of a long-acting beta-agonist (LABA) and long-acting muscarinic antagonist (LAMA) in combination with inhaled corticosteroid (ICS). There is a major development in treating COPD and asthma by the ICS-LABA-LAMA therapy. The most common prescriptions nowadays are LABA and ICS discovered by the physician in Europe. The common uses of 22% ICS and 39% bronchodilators are for lower symptoms and 46% ICS and 67% bronchodilators are for greater symptoms. Due to the limited effect of this medication, a trial for triple therapy is tried in every patient. [32] NSAIDs, bronchodilators (β2-adrenoreceptor (AR) agonists, muscarinic receptor antagonists, and xanthines) and corticosteroids are a highly recommended initial therapy for most patients individually or in combination with one of the other classes. Nonselective COX inhibitors for reducing respiratory inflammation include aspirin, ibuprofen, naproxen, and diclofenac, and selective COX inhibitors include celecoxib, lumiracoxib, etoricoxib, valdecoxib, and rofecoxib. Among different bronchodilators, fast-acting and short-acting albuterol, terbutaline, and fenoterol are efficiently used, yet long-acting agonists salmeterol and formoterol are best for therapy. Some drugs of class ultra-long-acting β2 agents indacaterol, olodaterol, vilanterol, carmoterol, PF-610355, LAS100977, AZD3199, etc. had been prescribed for achieving one dose daily. [33] The use of a combination of drugs using β2 long-acting and antimuscarinic controls the transforming growth factor (TGF)-β1-mediated inflammation in COPD. The novel antimuscarinic agents such as QAT370, glycopyrronium (NVA237), aclidinium, GSK573719, CHF5407, BEA2180BR, TD4208, PF452297, RBx343E48F0, trospium, and dexpirronium are generally used at a high dose for a prolonged duration of action. Anti-inflammatory and bronchodilator action of xanthines such as bamiphylline, enprofylline, isbufylline, and doxophylline is reported to be used in the treatment of asthma and COPD. The safer use of xanthines inhibits the family of phosphodiesterase (PDE3 and 4) enzymes for long-term improvement in lung function. [34] Different NSAIDs like ibuprofen are used in COVID-19 infection, but there is a lack of studies that shows the association between the use of NSAID

and COVID-19 severity. Currently, known antiviral agents like lopinavir/ritonavir and remdesivir have a high affinity to the viral enzyme and could inhibit the synthesis of the nitrogenous base resulting in the inhibition of RNA replication through premature termination of the virus. Anti-inflammatory drugs like corticosteroids had a role in the significant reduction of in-hospital mortality by COVID-19. During this pandemic of COVID-19, several pulmonary complications from this disease were reported such as mucormycosis and pulmonary aspergillosis. [35] These are life-threatening fungal infections and have a role in complicating pulmonary conditions like asthma, bronchiectasis, and COPD. These pulmonary infections are found to attack patients with low immunity. Many researchers and health personnel assumed it was due to the excessive use of corticosteroids. Corticosteroids are used for the treatment of COVID-19 patients which in turn reduces immunity due to which the patients are prone to be infected by mucormycosis and aspergillosis. [36] Losmapimod, p38, a subfamily of mitogen-activated protein kinase (MAPK) inhibitor, is widely studied and used safely as a single IV infusion of 1 to 3 mg doses. There are no severe effects reported except headache, nausea, and fatigue. Various reports suggested that this can be appropriate in treating COVID-19 patients. The recent trial in the mouse model supported a similar result. [37] Besides this, p38 was able to cause a pathogenic role in asthma and COPD. The adverse factors causing these diseases activate the p38 which in turn amplifies lung inflammation. The clinically trialed anti-interleukins like benralizumab, daclizumab, reslizumab, MEDI-528, mepolizumab, and lebrikizumab showed improvement in patients by decreasing eosinophils and other exacerbations. [38] The clinical trial of benralizumab revealed the effects in reducing eosinophil and improved lung function but with some headache and nausea effects. [39] Number of trials had been conducted for treating upper airway disorders such as allergic rhinitis, nasal polyps, and chronic rhinosinusitis for which several therapeutics such as omalizumab, mepolizumab, dupilumab, a monoclonal antibody targeted toward IgE, an anti-IL-5 agent, anti-IL-4, and IL-3 had been used. The outcomes of the trials were positive. [40]

CONCLUSION AND FUTURE PERSPECTIVE

The findings of the present investigation mainly focused on the role of Use of Medicinal plants which are closely associated with Rural, Tribal community, and also Traditional healers. The investigation will assist in making information available on how these drugs obtained from medicinal plants are prepared and administered. Further Pharmacological and clinical studies on these plants may provide effective natural medicines for various respiratory disorders. In this review, the drawbacks and limitations of currently adopted treatment procedures and available drugs have been highlighted. This study also reported the several plant species that are being used in the treatment of respiratory complications in the traditional medicinal system based on traditional knowledge and indigenous knowledge. The reported bioactive compounds and their mechanism of action have been critically analyzed for possible therapeutic compounds. Some of the plant products are promising against respiratory diseases and can be the best source of alternative medicine. Although, some clinical shreds of evidence have been reported for some of the compounds, there needs to be an extensive study on the toxicological aspect and interaction with other therapeutics. The detail studies on the formulations, forms of doses, evaluation of pharmacokinetic parameter, and safety are necessary. The future study should focus on the identification and isolation of more effective compounds, their mechanism of action, and formulations. This study can facilitate the newly discovered compounds to enter a clinical trial. Therefore, it is concluded that further research on the traditionally used plants and plant-derived products could lead to the discovery of a new kind of therapeutic drug of high potential and interest.

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