A Systematic Review on Particulate Matter-Induced Diseases and Herbs Useful in Lung Tissue Damage

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ABSTRACT

Air pollution is the biggest challenge for environmental health and for human health as well. WHO cleared that if the air quality will not be controlled the range of death will be out of control in recent years. In this direction, we conducted a review study to evaluate the respiratory diseases and their pathogenesis which are induced due to ambient particulate matter (PM). Another aim of the present study is to examine the traditional herbal medicinal method to cure lung tissue damage due to respiratory diseases induced by PM. The investigation was conducted through the PRISMA method for a systematic review study. A total of 967 papers have been reviewed from Scopus search, PubMed, Google Scholar, Taylor & Francis, WHO online platform, and many classical texts for traditional medicines like Charaka Samhita, Sushruta Samhita, Bhavprakashetc. Eventually, 68 articles were included, and others were excluded according to the need of the study. After this deep review investigation, we observed that although there are many health issues induced by particulate matter, the major pathogenesis harm was revealed in lung tissue where the ultra-fine PM can deposit through inhalation even with short-term exposure. Particulate matter pollutant has the potent property of being oxidative and leaving a toxic effect on the lungs and respiratory system in the human body. There are many traditional methods and remedies available to cure lung tissue damage. We found some effective herbs such as *Dioscorea bulbifera*, *Angelica archangelica*, *Nasturtium offcinalea*, and *Perilla frutescens*, etc. which give more efficient effects in the remedies of cough, asthma, COPD, and lung tissue damage. These herbs are also being used in different combinations and formulations.

KEYWORDS: Particulate matter, Lung tissue damage, Herbal medicine, Respiratory disease.

INTRODUCTION

Air pollution is deleterious for human health because it is a mixture of gaseous and particulate matter (PM) constituents. The main components present in PM are carbonaceous material, reactive metal, nitrates, polycyclic hydrocarbons (aromatic), sulfates, endotoxin, and some metals like iron, copper, nickel, zinc, and vanadium. All of these depend on the amount and source of air pollution. The main source of PM is fossil fuel combustion. PM is again sub-classified into different categories according to the particle size. The first category is coarse called PM_{10} and the diameter of these particles is less

than 10μm, the second category is fine called $PM_{2.5}$ with a diameter of less than 2.5μm, and the third category is ultrafine called $PM_{0.1}$, and the diameter of these particles is less than 0.1μm[1]. These particles cause different variety of illnesses such as irritation of the eyes, nose, mouth and throat, skin, declining energy level, headache, and dizziness and after a long period, these symptoms can be converted into serious health problems. The death rates are higher in the areas with elevated pollution levels. The death of premature babies is more than two million in India and China because of particulate matter suspended in the air[2]. People who work in polluted environments can suffer from deadly diseases such as asthmatic attacks, and inflammatory diseases. The most common inflammatory disease is Chronic Obstructive Pulmonary Disease (COPD) while pulmonary cancer, liver cancer, and other types of cancers are caused by PM. All these diseases have an integrated pathogenesis and effects together with the symptom development. All lead to different biochemical processes for disease severity, inflammation, and dysfunction of organs. Although the bronchopulmonary tract has its own system for protecting the body like mucosal cilia and air-blood barrier inhaling the particulate matter surpasses the protective system of the body because these may deposit in lung tissues according to the size of pollutant particle[3]. Once PM penetrate lung tissues it starts to damage the lung tissue followed by degeneration of tissues and cell. To overcome those health issues, we found many herbal and traditional methods of medicine in literature. In this review study, some important herbs have been discussed to cure lung tissue damage due to most common diseases induced by particulate matter such as oxidative stress, cardiovascular diseases, autism, asthma, and chronic obstructive pulmonary disease (COPD).

METHODOLOGY

This review study was conducted to establish the correlation between particulate matter and lung tissue degeneration and the possible herbal remedies to cure lung and respiratory disease. We separated out different diseases that are induced by particulate matter followed by a deep investigation of the literature and selected the most extensive health defects. Another target of the search was mainly to evaluate the traditional medicine method for lung disease. The investigation was conducted through the PRISMA method for a systematic review study. All the papers were reviewed from Scopus search, PubMed, Google Scholar, Taylor & Francis, WHO online platform, and many classical texts for traditional medicines like Charaka Samhita, Sushruta Samhita, Bhavprakash, etc. We searched articles with a custom range of years from 2016 to 2022, language English with keywords such as air pollution, particulate matter, respiratory disease, cardiovascular disease, oxidative stress, and herbal medicine for lung disease. Eventually, 92 articles were included, and others were excluded according to the requirements of the study. The number of articles searched was shown through the PRISMA flow chart step by step (figure 1).

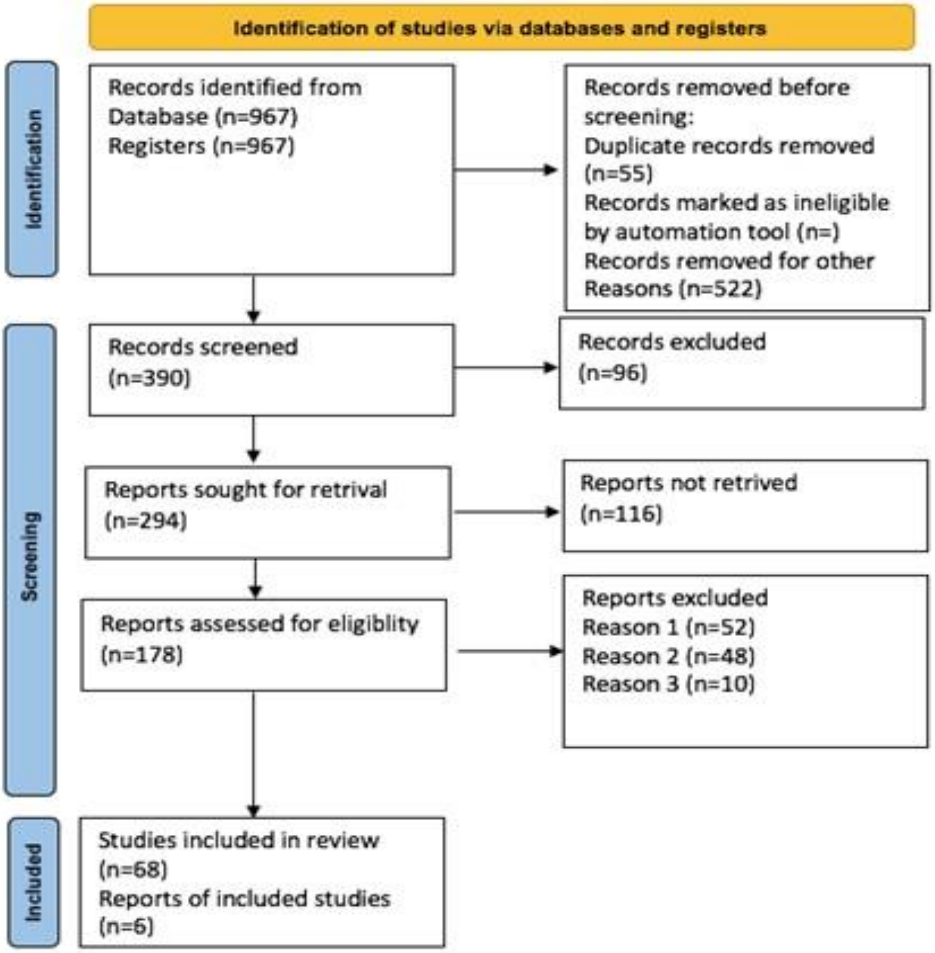

Figure 1 PRISMA flow diagram inclusion and exclusion of studies.

Particulate Matter (PM) induced diseases: The ultimate aim of this review study is to find out appropriate herbal substituents for lung tissue damage and find out the correlation between three key points, these are particulate matter, lung tissue damage by PM and botanical substituents to deal with that damage. The search strategy follows a systematic search from the Scopus database and from other sources discussed in the methodology section. According to the search plan, we reviewed all impacts of PM on health and mentioned a brief description of all health problems induced by PM in this section so that it will be evaluative to find out all mechanical aspects of pathogenesis.

Mortality attributed to PM in India: According to WHO, more than 90% Indian population lives in cities where exposure to $PM_{2.5}$ exceeds the limit concentration of 10 $\mu g/m^3$, annual average. In 2015 premature mortality in India induced by $PM_{2.5}$ was 1.1 million annually[4]. Devidet. al analyzed PM-induced premature mortality in India according to six main regions Northern India, Indo Gangetic Plain, Eastern India, Western India, Central India, and Southern India. They included ischemic heart disease (IHD), cerebrovascular disease (CeVD), chronic obstructive pulmonary disease (COPD), and Lung cancer (LC) in India for all ages for the year 2012. The highest rate of mortality found in Indo Gangetic Plain is 50% followed by Southern India and Central India, 21% and 12% respectively. Northern India, Eastern India, and Western India contributed with 17% altogether and less than 10%

individually. The disease burden imputed by PM was found to be highest by IHD approximately equal to 44% followed by CeVD 33% and the rest is from COPD and LC throughout India[5].

Oxidative stress: Oxidative stress is a misbalance between the production of reactive oxygen species, these are free radicals called ROS and antioxidants, which can further lead to elevation of cells and issue injury because oxidants are extremely reactive molecules[6]. The biochemical process generates free radicals in massive amounts and these radicals act as by-products of these biochemical processes. In the presence of environmental electromagnetic radiation, the body may respond by producing free radicals. The toxic effect and health inadequacy of PM and gas pollutants cause adverse impacts on the cardiopulmonary system of human[7]. Individual pollutants show a particular property of being oxidant and toxicity developers in the respiratory system as well as in the cardiovascular systems of the human body. These pollutants are part of the relative characteristic property of potent oxidants. They can directly affect lipids and proteins and show secondary effects in intracellular oxidant routes[8,9,10].

Chronic Obstructive Pulmonary Disease (COPD): COPD is an inflammatory lung disease that causes changes in the structure of the lungs. It is a series wise progressive and predominantly irreversible airflow obstruction, including emphysema and small airway remodeling that is also called chronic obstructive bronchiolitis. It causes air trapping and shortness of breath[11]. Many environmental and industrial exposures generate pathology. There are two comprehensive sources of air pollution, which have been focused on in recent research. Primarily biomass fuel (BMF), a carbon-based material originating from living organisms, and another source is the emission of motor vehicle exhaust (MVE)[3] which causes massive amounts of pollutants such as CO, NO, and small amounts of SO_2. Smoke generated from BMF is now acknowledged as a substantial cause of initiation of COPD pathogenesis in rural areas of developing countries particularly among women due to burning the BMF. The use of inefficient stoves causes household pollution due to BMFs-induced smoke. MVE has also negative effects on the respiratory system and lung health due to the emission of different pollutants from it[12,13]. Inhalable particulate matter (PM) plays a pernicious role in the induction and pathogenesis of COPD. As the size of PM decreases, its capacity to penetrate most distal airway units increases and increases the potential to insert into the systemic circulation as well[14].

Asthma: The main reason for air pollution in metro cities and urban areas is uncontrolled traffic and industrial emissions. Different kinds of air pollutants can be a reason behind the aggravation of pre-existing asthma and develop new-onset asthma. However, in developing countries like India asthma is an important concern because domestic cooking is executed with the less efficient stoves with solid fuel[15]. According to the WHO report on asthma 2020, it is the most common and persistent disease found in children worldwide. More than 262 million population are affected by asthma worldwide. In low to middle-income countries that are underdeveloped, the ratio of asthmatic death is over 80% as they do not have efficient work processing[16,17]. Some recent research focuses on epigenetic mechanisms. This mechanism is helpful in the development and perseverance of asthma caused by traffic pollution exposure. Traffic-related air pollution (TRAP) and several gas particles which act like pollutants (ozone, nitrogen dioxide, and sulphur dioxide), diesel exhaust particles (DEP) becoming hazardous to asthma patients[18]. 90% contribution in particulate matter (PM) derivation in the form of ultra-fine particle size (<100 nm) is generated from DEP. This ultra-fine PM is potent enough to be retained in the nasal and peripheral airways, and induction of oxidative stress and airway

hyper-responsiveness can be possible, further that will enhance allergic responses and airway inflammation[19,20]. Nowadays some herbs like *Adhatoda vasica* are in demand to cure asthmatic conditions efficiently[21].

Autism: ASD (autism spectrum disorder) is a disease where a cluster of neurodevelopmental disorders (leading to abnormal brain function) takes place[22]. Core identification and symptoms of the disease are impairment in social communication and interaction. Autistic people repeat their patterned behavior and their activities and interest are restricted[23]. Autism is an escalating problem all over the world and it creates a huge economic and healthcare burden in developing nations like India. Research has come into the light recently on understanding different aspects of autism and finding out the pathophysiology, epidemiology, etc. of this condition[24]. Although there is no specific data available regarding what range of environmental factors forced the elevation in the number of ASD and how much environmental elements contributed to the recent elevation in this disease. Some previous studies suggested that genetic factors are responsible for ASD, but environmental factors are also enforcing the condition of ASD[25]. According to the US Clean Air Act introduced in 1970, exposure to air pollution acts as an environmental factor for increasing ASD. Some researchers in the US and many other countries have reported ambient air pollution is correlated with ASD, at the time of pregnancy if a female is exposed to air pollution the child can have the symptoms of ASD at the later stage of growth[26,27]. Epidemiologic studies showed the relationship between pregnant females' exposure to a polluted environment and ASD, however, the mechanism regarding this relationship between pollution and ASD is still not clearly understood or accepted. In some recent animal experiments on mice, it was found that during the period of pregnancy, air pollution could cause changes in the structure and anatomy of the cerebrum of the brain (the cerebral cortex). These changes take place in the outer layer of neural tissue and these changes are ultra-fine, which is the similar position of the brains of autistic patients[28]. In some research, it is found that the central nervous system of an embryo who has parental exposure to air pollution during his developmental stage can show a systemic inflammatory response that can cause neural injury and that injury can cause autism-like symptoms[29,30]. Particulate matter obtained from diesel which can be included in traffic-related air mixture, has been associated with ASD[31]. Although the etiologic study of autism spectrum disorder (ASD) is not well understood, some studies advocate associations between airborne pollutants and ASD.

Cardiovascular Diseases: According to WHO, CVDs, are the number one cause of death globally basically this disease is associated with heart dis-functioning and blood vessel disorders. The blood vessels that supply the heart muscle, and the brain, supplying arms and legs are called coronary heart disease, cerebrovascular disease, and peripheral arterial disease respectively. Other than this rheumatic heart disease, congenital heart disease is related to damage to the heart muscle and malformations of heart structure. When blood clots in the leg vein, it is called deep vein thrombosis and pulmonary embolism, which can knock over and move to the heart and lungs[32]. Exposure to particulate matter and its effects has been correlated with cardiovascular events and episodes. The major cause of cardiovascular disease is active cigarette smoking[33,34]. However, the risk of active cigarette smoke is much higher than that of air pollution and second-hand cigarette smoke which anyone can inhale. Even if anyone smokes very lightly, it has more bad effects and more risk than ambient air pollution. Here the point is that inhaled PM is eventually a risk for CVD whether in terms of smoking or in terms of any other kind of air pollution[35]. When a blood clot blocks the vein, it is

venous and if the clot blocks the artery, it is arterial thrombosis so both have common risk factors. Recently epidemiologists started exploring arterial and venous thrombotic events related to air pollution and their risk factor correlation with the environment[36]. The connection between chronic patient exposure to the increasing number of pollutants in the air and deep vein thrombosis (DVT) has been studied and investigated for the first time in 2008 by Baccarelli et al. The mechanism of the venous and arterial circulatory system or vasculature is easy to understand if the functioning of pro-hemostatic as well as anti-hemostatic is a complex mechanism taken into consideration with protagonist variants.

The cardiovascular system in the human being is functional and consists of a continuously functioning vascular system that distributes blood through the body, this vascular network consists of two core subsystems called the systemic and pulmonary circulatory systems. The cardiovascular system transports the blood having a large portion of oxygen called oxygenated blood from the left heart to organs through the arteries and returns the oxygen-depleted blood or oxygen-poor blood to the lungs through the veins. Pulmonary circulation is a very important aspect of blood circulation in the body. It subsequently works and transports the oxygen-depleted blood from the heart through the vein to the lungs, where it is oxygenated and returns to the heart. Now it is a phenomenon to be understood how air pollution initiates the malfunctioning of this whole system[37]. After a deep investigation, it was clear that PM can cause different health problems, but lung damage, lung disease, and respiratory disease can be induced in a very short-term exposure and can show symptoms easily. The pathogenesis of PM in the lungs has been deeply investigated to fulfill the aim of the study.

Particulate matter impact on lung health: Air pollution adversely affects overall human health, but the lungs show its deleterious impacts even in early pathogenesis. The most common lung diseases are chronic obstructive pulmonary disease (COPD), asthma, lung cancer, and respiratory infection[38]. A study reported that FEV1(forced expiratory volume) and FVC (forced vital capacity) were found variable according to the amount of particulate matter exposed. Elevated concentrations of PM lower the FEV1 and FVC in adults or children and vice versa[39]. An experiment on mice proved that even a low dose of PM can induce pulmonary inflammation and affect the antioxidant functionalities in the lungs. The most obvious question arises what happens to lung tissues after PM incubation inside the respiratory tract and which activity induces disease in the lungs? It is very clear in animal models that after exposure to PM many pro-inflammatory cytokines produce oxidative stress in lung tissue and lung epithelial cells because PM is a strong oxidant and it increases the circulation of IL-1β, IL-6, and TNF-α markers in lung tissues[40]. The pathogenesis of PM to induce lung disease is shown in figure 2. In recent years, pulmonary drugs have been used along with medication through nebulizers, metered-dose inhalers, and dry powder inhalers[41]. Through this review study, we tried to find out different medications for lung tissue degeneration and correlate these medications with PM-induced lung tissue degeneration or lung tissue injury.

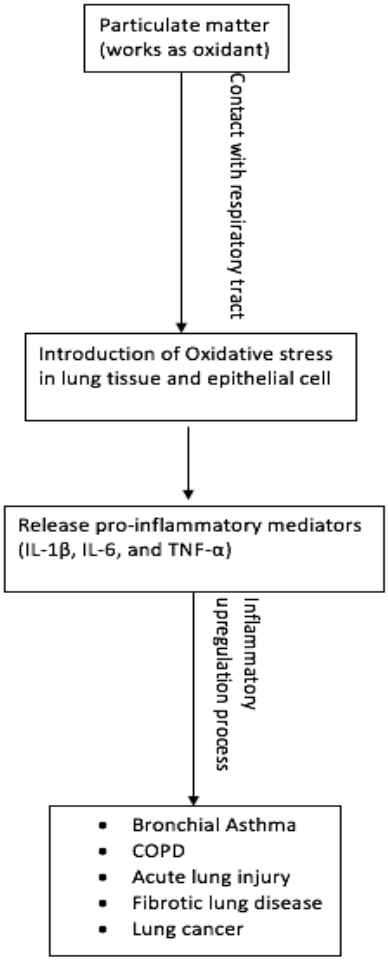

Figure 2 Pathogenesis of PM to induce lung disease.

Beneficial herbs for the treatment of lung tissue damage: Plants have been proven very effective in medical treatments since the long human history of the Paleolithic age and widely practiced till now[42]. After a deep literature study, it has been found that there are many herbal or botanical substituents that are useful in dealing with lung disease and lung infection. That may effectively suppress the production of pro-inflammatory cytokines such as IL-6, IL-1β, and ROS[43]. Many herbs' phytochemicals such as cinnamaldehyde, eugenol, and piperine are used as potent antioxidants that can suppress oxidative stress[44]. It is investigated in a study that *Dioscorea bulbifera* shows anti-inflammatory activity of saponin[45]. The use of many herbs is mentioned in classical Ayurvedic texts like Charaka Samhita, Sushruta Samhita, Bhavprakash, etc. We have identified some potential herbs that have been found useful in the treatment of lung disease and lung injury (table 1).

Table 1: Useful herbs in the treatment of lung disease and lung injury

Herb profile (Botanical name/ Family/ Common name/ usable part)	Phytoconstituents	Medicinal uses	References
• *Cinnamomum camphora* (L.) Presl. (Lauraceae) • Camphor • Essential oil	• Caryophyllene • 1,8-Cineole • α-terpinene • Borneol • Kaempferol • Carvacrol • Eugenol • Limonene • Vanillin • p-cymene • Safrole • Camphor • Citronellol • Geraniol	• Bronchitis, • Arthritis • Cardiovascular • Colds • Congestion • Bruises • IBS • Sprains • Lupus • Insomnia • Cough • Sleep • Aromatherapy	[46]
• *Dioscorea bulbifera* (Dioscoreaceae) • Air Yam • Rhizomes	• Diosgenin • Sapogenin • Saponin • Cyanidin • Flavonoids • Allantoin • Dioscorine • Ohenoliccompounds	• Gastrointestinal disorders, • Sour throat from struma, • Diarrhea, • Irritability, • Abdominal pain, • Wounds, • Burns • Anemia, • Lung cancer, • Piles, • Chronic liver pain disease	[47]
• *Fagopyrum dibotrys* (Polygonaceae) • Buckwheat • Rhizome	• flavonoids • phenolics • triterpenoids tannins • steroids • fatty acid • 3-Methylquercetin, • Hyperin • Diboside A • Procyanidine B-2,	• lung diseases, • Swelling, • Anti-inflammatory • Anti-cancer • Anti-oxidant • Anti-viral • Anti-diabetic • Anti-bacterial	[48]

	• Glutinone • β-Sitosterol		
• *Myrtus communis Linn* (Myrtaceae) • Baragasha and true myrtle • leaves and fruit	• Tannins • Flavonoids • Coumarin • Galloylglucosides • Ellagitannins • Caffeic acid • Gallic acid • Ellagic acids • Myricetin 3 • 3-di-ogalactoside • Myricetin-3-(600-O-galloyl galactoside).	• Skin disorders • Haemorrhoid • BV • Chronic rhinosinusitis • Abnormal uterine bleeding • HSV-1 infection • Vaginal lavage • Enemas • Respiratory diseases • Aphthous stomatitis	[49]
• *Nasturtium offcinalea* (Brassicaceae) • Watercress • leaves	• Proanthocynidin B1 • P-coumaric acid derivative • Apigenin • Phydroxybenzoic acid • Sinapic acid • P-coumaric acid • Caftaric acid • Indole-3-acetonitrile-4-methoxy-2-S-β-dglucopyranoside • 8-(methylsulfonyl) octanonitrile	• Scurvy • Tuberculosis • Bronchitis • Influenza and asthma • Pulmonary diseases • Hypertension • Cardiovascular diseases	[50]
• *Perilla frutescens* (Lamiaceae) • Chines basil • leaves	• Phenolic acids • Apigenin • Tormentic acid • Isoegomaketone • Perillaldehyde • Tocopherols • Triterpenes • Rosmarinic acid • Phytosterols • Flavonoids • Policosanols • Fatty acids	• Depression-related disease • Coughs and colds, flus • Anxiety • Tumours • Allergies • Fever and headache with stuffy nose • Indigestion • Asthma	[51]

	• Essential oils • Carotenoids • Luteolin	• Analgesic, • Anti-abortive agent and sedative • Phlegm • Chest stuffiness • Vomiting • Intoxication • Constipation • Abdominal pain	
• *Catharanthus roseus* (Apocynaceae) • Sadabahar and Red periwinkle • Leaves	• Catharoseumine • 14′,15′-didehydrocyclovinblastine • 17-deacetoxycyclovinblastine • 17-deacetoxyvinamidine • Vindoline • Vindolidine • Vindolicine • Vindolinine	• Cell ageing • Cardiovascular disease • Brain disease, • Mutagenic changes • Cancerous tumor growth (testicular, breast and lung)	[52]
• *Solanum xanthocarpum* (Solonaceae) • Kantkari and Wild Eggs Plant • Juice of berries and roots	• Alkaloids • Sterols • Phenolic compounds • Glycosides • Saponin	• Asthma • Cough • Dyspnea • Dropsy • Chest pain • Fever, • Asthma • Inflammation • Common cold • Antipyretic • Diuretic and antiemetic • Respiratory tract infection	[53]
• *Angelica archangelica* (Apiaceae) • garden angelica	• Essential oils • Bitter principles • Coumarin compounds	• Bronchial ailments • Coughs • Colds	[54]

• Roots and rhizomes	• Urinary antiseptic • Chronic fatigue • Menstrual and obstetric complaints • Anorexia • Migraine • Carminative • Stomachic • Digestive • Antispasmodic disorders

CONCLUSION

Air pollution with different ranges of particulate matter has become a very challenging issue in recent scenarios especially in middle-income and developing countries due to unawareness and maximum use of inefficient processes of working in industries and household works. In urban lifestyle, the elevated amount of vehicle emissions and industrial emissions leads the higher and uncontrollable air pollution. PM causes deadly diseases in human beings such as asthma, cardiovascular disease, cancer, lung diseases, COPD, and respiratory disease. It is evidenced that lung tissue damage and related diseases are extensively caused by PM exposure due to the oxidant activity of PM and elevated circulation of pro-inflammatory cytokines. To overcome this there are many medications available in allopathy, homeopathy, and ayurveda. It has been proven that herbal remedies are quite powerful for lungs. Many herbs have been found out during research which indicate future scope to develop more effective formulation with combination and variety of herbs with proper quality, efficacy, and toxicity study.

CONFLICT OF INTEREST:

There is no conflict of interest.

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