



# OVERVIEW ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE ALONG WITH ITS HERBAL ADVANCEMENT

Suryansh Pandey <sup>1\*</sup>, Tejaswini Kothare <sup>2</sup>, Ankita Bankhele <sup>3</sup>, Dr. Rajesh Oswal  
Genba Sopanrao Moze College of Pharmacy-Wagholi

## ABSTRACT:

Chronic Obstructive Pulmonary Disease (COPD) is a very versatile heterogeneous disease burgeoning downside worldwide, which is an incurable and progressive disease. According to GOLD Indian reports, it has killed almost 9,58,000 persons alone in India in 2017 and data is increasing year by year. COPD is present with spectrum of clinical manifestation and symptoms. It is the disease which is primarily characterized by chronic inflammation in lungs which in respect causes airway obstruction or airway hyper responsiveness. Airway obstruction may cause airway remodeling or it can cause airway edema or positive/negative mucus plugging. However, airway hyper responsiveness can cause bronchospasm. COPD is classically consists of chronic bronchitis, obstructive bronchitis and emphysema majorly. Somehow Asthma is also sometimes co related with COPD. One thing which remains uniform among every disease is airflow limitation which is not fully reversible. Patient have dyspnea and may experience wheezing and coughing frequently. It is contemporary to say that along with ongoing uses of dominant Allopathic English culture of medicine, herbal drugs are being more popular because allopathic medicine only uses synthetic drug derivative or specific ingredient but in herbal procedure we use complete plant as in whole plant all the materials of plant give synergistic effect of all ingredient. In case of herbal advancement, herbal plants like ADHATODA (Adhatoda vasica Nees) have a lot of potential in their therapeutic agents like vasicine, vasicinine, vasicinone, tritriacontane, beta-sitosterol, but their complete knowledge has still not been extracted also they can be more useful than several allopathic substituents.

Keywords- COPD, GOLD, Adhatoda, Herbal

## INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. According to GOLD Indian reports, it has killed almost 9,58,000 persons alone in India in 2017. According to 'Sundeep Salvi', Director of Chest Research Foundation (CRF), in

Pune which he helped to establish also a member of Global Initiative for Obstructive Lung Disease made some important points regarding the issue. [1]

Why COPD Is Not Majorily Concerned Even Being Second Highest Killer In India After Heart Disease :

- ❖ As India have faced rampage of communicable diseases like AIDS, Malaria, Tuberculosis, with span of time we somehow conquered on them but we lack our attention on such devastating non communicable diseases like COPD and such negligence results in severely bad outcomes.
- ❖ levels of air pollution has increased drastically in last two to three decades leading to tremendous rise in COPD cases.
- ❖ smoking is considered as conventional cause for COPD but non smoking risk factors are major cause for the disease and thus 'less research on non smoking factors is the reason for less development in treatment and diagnosis of COPD.' [2]

The 2019 Lancet study on air pollution also said that the number one group of diseases caused by air pollution were lower respiratory tract infections, and second was COPD [3].

## Objective

As it is known that basic problem that exist with COPD is decrease in lung capacity, symptoms majorly concern damage to alveolar tissue due to varieties of major pollutants and cigarette smoke.

Now the major problem that arises with treatment of COPD is that allopathic treatment can certainly reduce the effect of COPD but it can not turn back the normal capacity thus the problem with respiratory syndromes remains as same.

So basic objective that remains intact is revival of original capacity of lungs and to restore the previous or near previous condition thus there is requirement of drug which can heal alveolar tissues properly and increase lung capacity.

Thus it is prescribed that only use of herbal drugs can cure the root cause of disease and can only recover the lung capacity simultaneously. Thus with help of this article we will ensure to understand the disease first and will list various herbal crude drugs and their active constituents which can help to decrease COPD effect and will certainly improve the lung capacity and will serve as better treatment option than allopathic drugs.

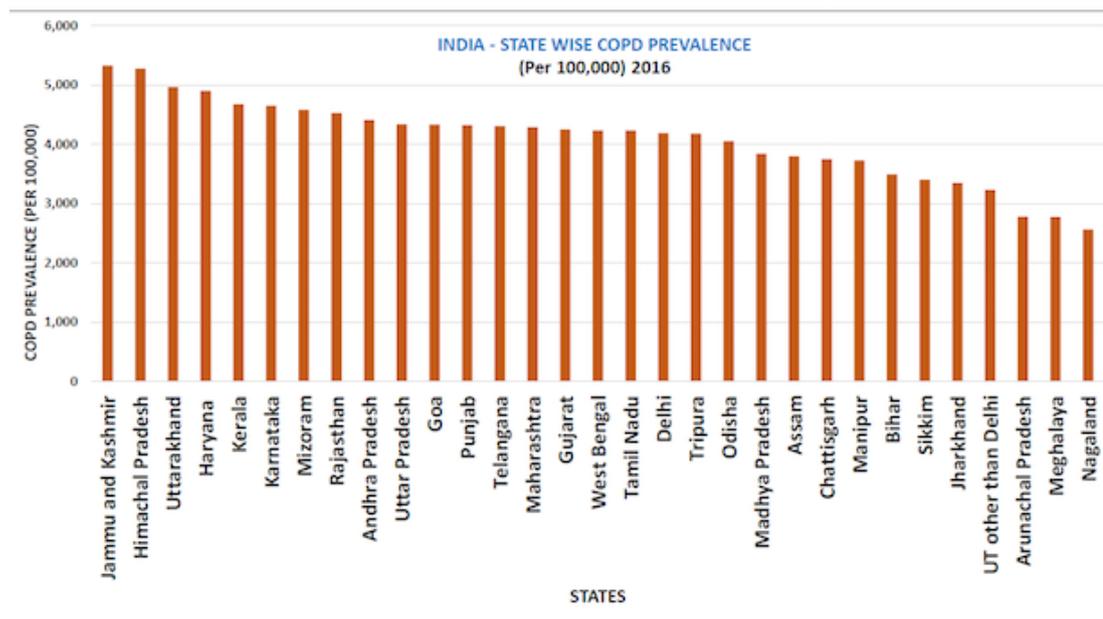
## Epidemology

COPD is the leading cause of death in world. Prevalence of COPD is derived mostly from industrial areas and the problem is not even concerned nor confirmed until it become clinically obvious. COPD is a huge social burden as its is among highly ranked diseases causing disability in living years and low life expectancy and high mortality rate. [4]

COPD is major concern for individual economic crisis thus is a huge economic burden as it is very costly public health problem due to its high prevalence and serious clinical consequences. Direct costs of COPD

are due to hospital admissions and expensive treatments such as long-term oxygen, whereas indirect costs complies loss of working capacity and poor quality of life. [5]

Fig 1. [Burden of COPD in India] [6]



[Fig 2.] Classification of severity of COPD (GOLD 2021) update [7]

**Table 1**

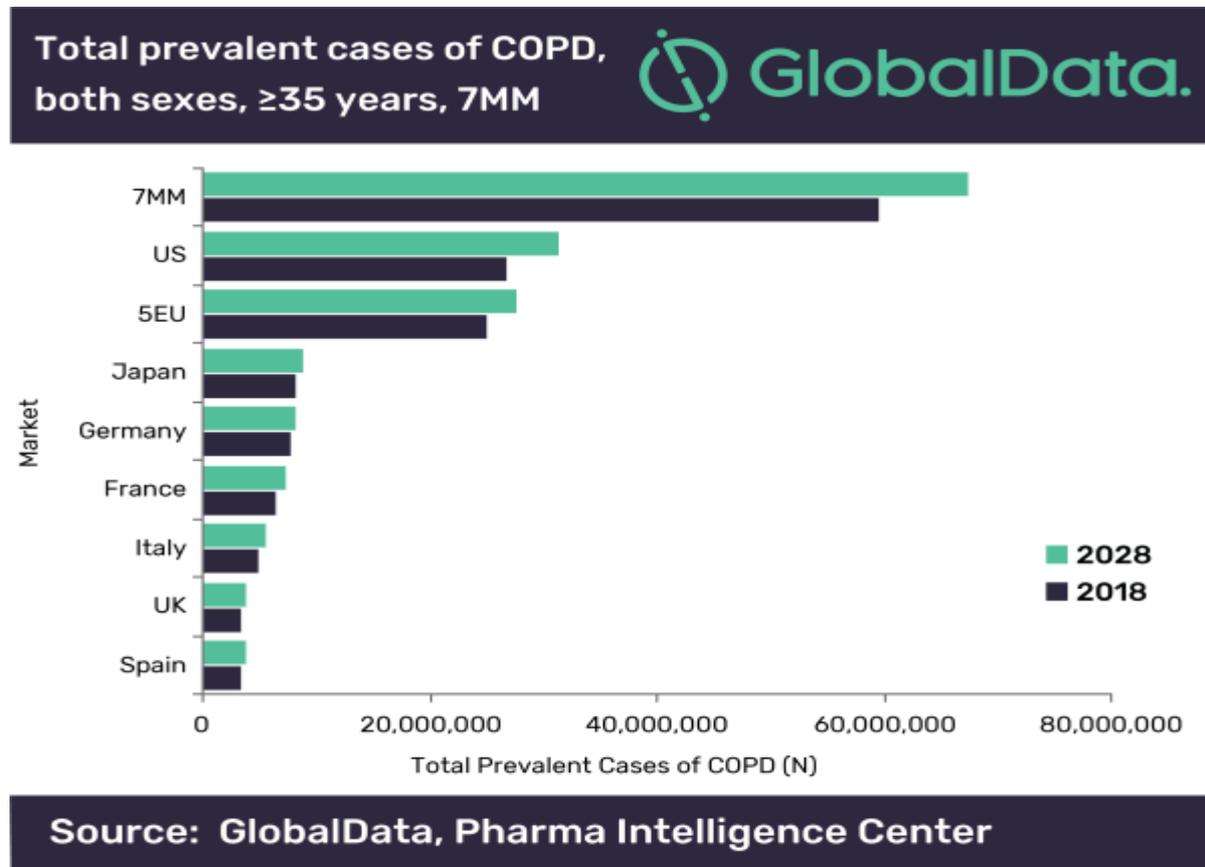
**CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV<sub>1</sub>)**

*In patients with FEV<sub>1</sub>/FVC < 0.70:*

<b>GOLD 1:</b>	Mild	FEV <sub>1</sub> ≥ 80% predicted
<b>GOLD 2:</b>	Moderate	50% ≤ FEV <sub>1</sub> < 80% predicted
<b>GOLD 3:</b>	Severe	30% ≤ FEV <sub>1</sub> < 50% predicted
<b>GOLD 4:</b>	Very Severe	FEV <sub>1</sub> < 30% predicted

COPD: chronic obstructive pulmonary disease; FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease. Source: Reference 1. Reprinted with permission.

Fig 3. [Global burden of COPD according to Global Data] [8]



## Causes of COPD

### [HOST FACTORS]-

#### (a) Genetic factors:

Complex genetic environment factors are involved in pathogenesis of COPD. Genetic factors contribute modestly to loss of lung function, with forced expiratory volume mostly influenced by locus on chromosome.

Siblings of patients with severe COPD have increased risk of airways obstruction, suggesting a recessive model of inheritance on whole. [9]

#### (b) Atropy and Airway hyper responsiveness:

COPD itself may result in increased airway responsiveness to histamine or methacholine due to geometric factors related to fixed airway narrowing. [10]

#### (c) Nutrition and lung growth:

Low dietary intake of antioxidant vitamins (A, C and E) has sometimes been found to be associated with increased risk of COPD, although a more recent study found vitamin C and magnesium to be important.

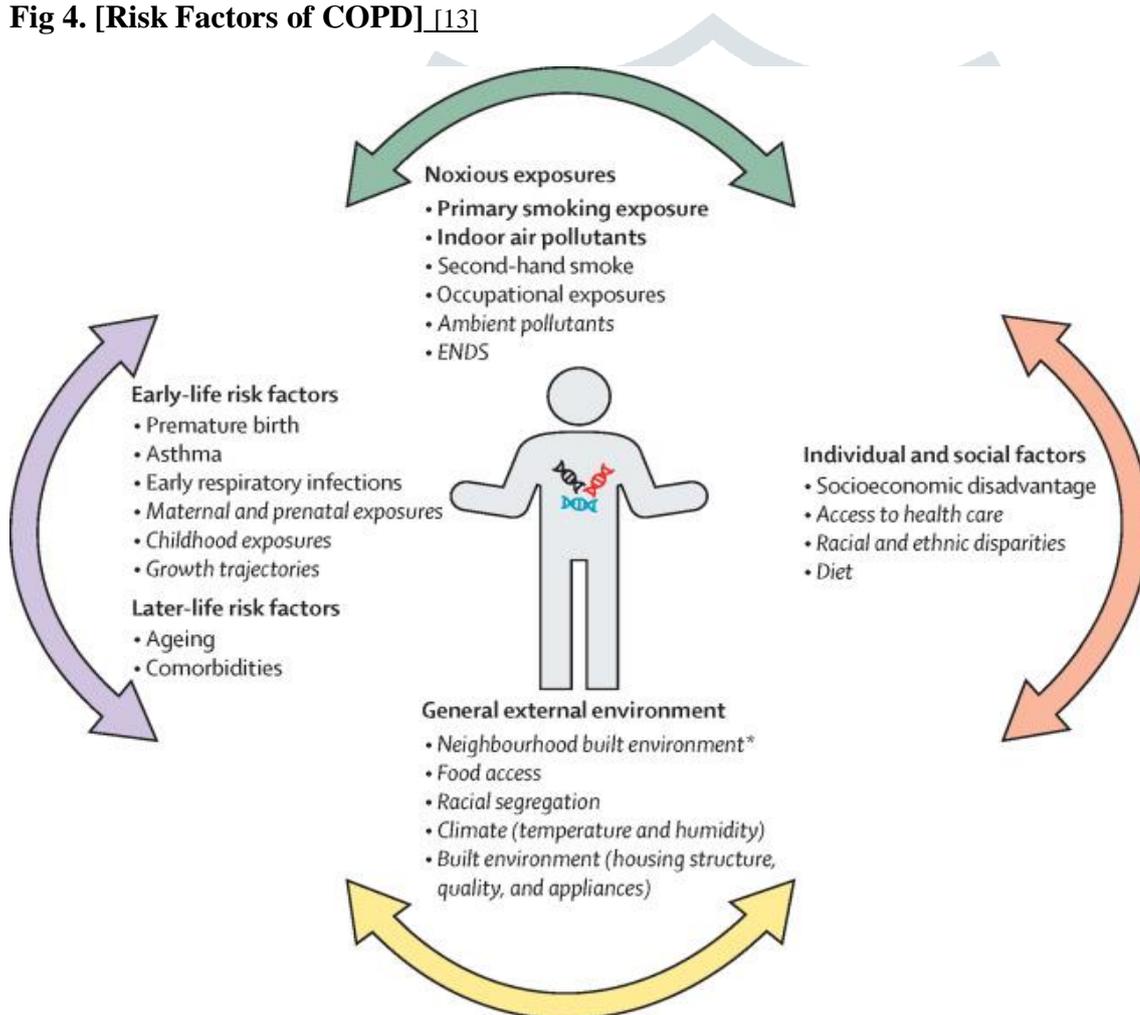
Patients with emphysema are more likely to have had a low birth weight and be underweight in adult life, and those with chronic bronchitis are more likely to be obese. [11]

(d) *Gender:*

It is controversial whether females are more susceptible to the effects of cigarette smoking, although a range of studies have found greater prevalence of COPD in women.

effects on females may be underestimated since males tend to smoke more, often start earlier, and have a greater degree of inhalation. [12]

Fig 4. [Risk Factors of COPD] [13]



Environmental factors -:

\*Cigarette smoking-:

Active smoking causes both mucus hypersecretion and chronic airflow obstruction. Cessation of smoking decreases respiratory symptoms and reduces the rate of decline in lung function. Pipe and Cigar cigarette can cause more risk of COPD than Non-smokers. Youth culture now leaning towards smoking of non tobacco smoke “ marijuana ” , but it is more

risky for causing COPD because it involves larger inhalation volume and longer holding capacity. Passive Smoking is cause of COPD. Smoking during pregnancy may cause COPD in child also. [14]

\*Air pollution (indoor or outdoor) :-

Air pollution, particularly sulfur dioxide and particulates (black smoke or particulate matter of  $\leq 10 \mu\text{m}$  [PM10]), is associated with chronic simple bronchitis.

Indoor pollution from burning biomass fuel in poorly ventilated homes are major risk factor for air pollution and majorly affect women.

While air pollution from exhaust and industries are major cause for external air pollution. [15] Occupational interaction with coal dust, silica in mines or industries can cause severe lung problems and major cause for COPD among workers.

### **Predominance of emphysema in COPD**

In accordance to physical examination of patients appear to be distressed and uses accessory sternal muscle for respiration to lift the sternum.

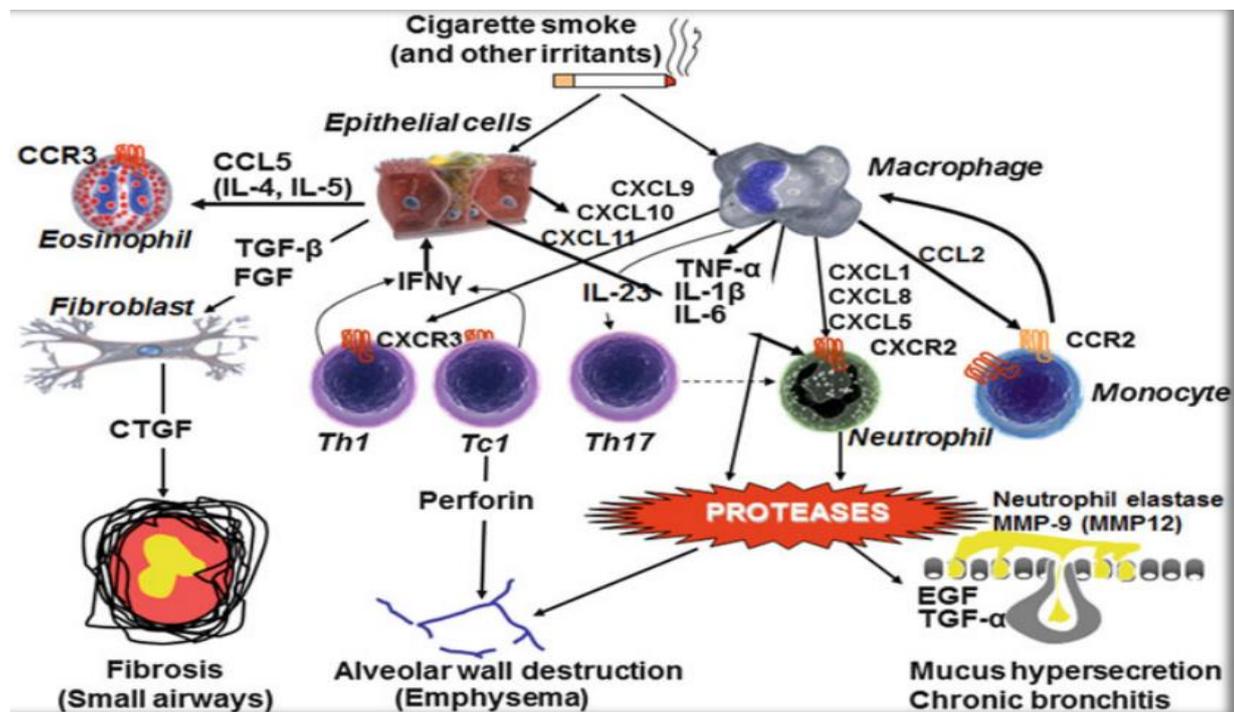
Patient experiences tachypnea and expiration starts with grunting sound.

Flattened diaphragm causes the lateral ribcage to move inward with each breath. Patients leans forward extending arms to brace him and attain tripod like position. Faint, high pitched crackles observed in early respiration and wheezes in expiration. [16]

Minute ventilation is maintained, the arterial  $\text{Po}_2$  is often maintained above 60 mm Hg,  $\text{pCo}_2$  is low to normal. Pulmonary function testing demonstrates increased total lung capacity and residual volume and decreased vital capacity. Diffusing capacity for carbon monoxide i.e. (DLco) demonstrating destruction of alveolar septa showing decrease in reduction in capillary surface area.

“When (DLco) decreases below 50% predicted, the patients with emphysema have arterial oxygen desaturation with exercise.” [17]

[Fig 5] Pathogenesis of COPD [18]



### Predominance of chronic bronchitis in COPD:

Patients with predominance of chronic bronchitis have a history of chronic cough and sputum production for many years along with heavy cigarette smoking. Cough may be present only in winter months, but with course of time patient illness increases. Patient seek medical attention only when condition of purulent bronchitis become worse with increased frequency, duration and severity of illness. [19]

Patients report nocturnal snoring and daytime hypersomnolence and demonstrate sleep apnea syndrome, predominance of bronchitis are often overweight and cyanotic. [20] Because of irregular chemosensitivity, such patients do not compensate properly and permit hypercapnia to develop with  $Paco_2$  levels above 45 mm Hg. The low  $Pao_2$  produces desaturation of hemoglobin, which causes hypoxic pulmonary vasoconstriction and eventually irreversible pulmonary hypertension. Desaturation may lead to visible cyanosis, and hypoxic pulmonary vasoconstriction may cause right sided heart failure. [21]

The TLC is often normal and the residual volume is moderately elevated.

The vital capacity (VC), is moderately deviated. Maximal expiratory flow rates are invariably low. Lung elastic recoil property may be normal or impaired slightly, the (DLco) is normal or might be decreased. [22]

## Diagnosis and assessment of COPD

A clinical diagnosis of COPD is considered in patients over age of 40 years having dyspnea, chronic cough or sputum production.

Spirometry is a fundamental for COPD diagnosis and the presence of a post-bronchodilator  $FEV_1/FVC < 0.70$  confirms the presence of persistent airflow limitation. The spirometric criteria for airflow limitation remains a post-bronchodilator fixed ratio of  $FEV_1/FVC < 0.70$ . [23]

## Physical Examination

As we all know that physical findings of chronic bronchitis usually appear only when case becomes severe. Patients shows various symptoms including barrel shaped chest, pursed lip breathing and debility. It may be suspected with a loud pulmonary component of the second heart sound and heart sounds may be displaced to the midline due to hyperinflation. [24]

## Pulmonary Testing

Pulmonary testing has three basic component :- (a) Spirometry (b) lung volume (c) diffusing capacity of lung for carbon monoxide (DLco).

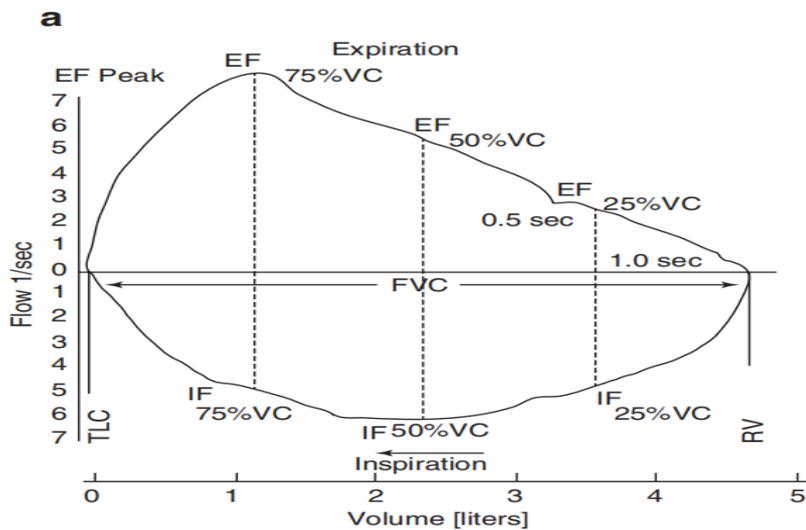
Each of these component is affected by COPD. The most important and useful test is through is Spirometry. [25]

## Spirometry

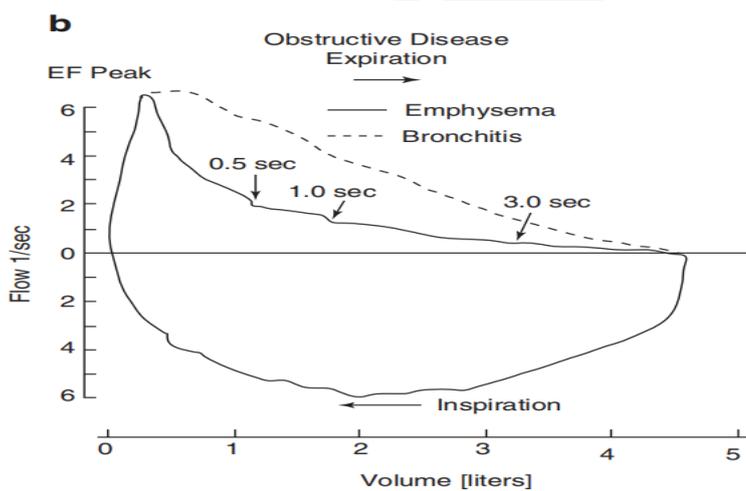
In Spirometry, a flow volume is typically generated. A flow volume loop plots flow on Y-axis while volume on X-axis.

A normal flow-volume loop has a characteristic shape (Fig. a). In obstructive lung disease such as COPD, the expiratory limb takes on a curved shape (Fig. b). [26]

\*[Flow-volume curve for healthy person (a)] (Fig. 6) [27]



\*[Flow - volume for patients with airflow obstruction (b)] (Fig. 7) [27]



### Lung Volume:

Lung volume typically consist of TLC (total lung capacity), FRC (fixed residual volume), RC (residual volume). TLC is the total volume that can be accompanied in lungs after full inhalation. RV is the volume left in lungs after full exhalation and FRC is the volume of gas left in lungs after tidal breath. [28]

Most commonly used method is Plethysmography. Destruction of lung tissue lead loss of elastic recoil of lungs and loss of elastic recoil of lungs results in increased TLC. RV and FRC might also get increased.

Air trapping can lead to hyperinflation. With each breath, the patient becomes more hyper inflated and this leads to insufficient respiratory muscle function and increase the work of breathing. [29]

**[Fig.7] Table demonstrating the air flow limitation severity in COPD: [30]**

<b>Classification of severity of airflow limitation in COPD (post-bronchodilator FEV1 in patient with FEV1/FVC&lt;0.70)</b>	
GOLD 1: Mild	FEV1 $\geq$ 80% Predicted
GOLD 2: Moderate	50% $\leq$ FEV1 <80% Predicted
GOLD 3: Severe	30% $\leq$ FEV1 <50% Predicted
GOLD 4: Very severe	FEV1 <30% Predicted

### **Effect of Diffusing Capacity of Lungs for carbon Monoxide:**

The diffusing capacity of lungs for carbon monoxide is a measure how easily carbon monoxide (CO) molecules transfer from the alveolar gas to the hemoglobin of the red cells the pulmonary circulation.

A person inhales small amount of CO for around 10 sec. and then exhales the breath, exhaled breath is then analyzed for CO. [31]

The change in concentration of the CO is then multiplied by single breath TLC to calculate (DLCO) and DLco is reduced in COPD because of loss of alveolar and capillary bed. [32]

### **Assessment of the Disease:**

Being a heterogeneous disease, no single measure can provide an adequate assessment of the severity of disease.

Global initiative for Chronic Obstructive Lung Disease (GOLD) gives aspects of disease which are following-:

- Current levels of patient's symptoms.
- Severity of spirometric abnormality.
- Exacerbation risk.
- Presence of comorbidity. [33]

### **Problems with existing therapy of COPD and need of new therapy:**

In COPD, however, both bronchodilator and anti-inflammatory therapy is less effective, and there are currently no therapies that reduce the of the progression disease. Driven by the

urgent need for new therapies, a shift in resources from discovery of drugs for asthma to COPD is taking place.

As we all are aware that Allopathic approach for various disease results in development of various side effects and complication. Corticosteroids have adverse effects because being steroidal in nature, particularly dysphonia. A recent community shows linear relationship between dose intake and risk of fracture. [34]

Effect of bronchodilator in COPD is not that much beneficial as in Asthma and high doses are required for optimal effects. Also bronchodilator do not reduce the the accelerated decline in lung efficiency and natural history of COPD. Apart from quitting smoking and preventing external risk factors, there is nothing to reduce the severity of disease. [35]

Several studies have shown that long term use of corticosteroids are ineffective in suppressing the inflammation of COPD so new anti-inflammatory drugs are needed to be introduced in market to improvise current COPD treatment and better option for treatment. [36]

### **Herbal crude drugs for COPD treatment**

Several herbs and herbal medicines are proved to be beneficial for chronic and obstructive pulmonary disease.

We all are aware that use of allopathic medicine or English medicine consist use of synthetic drugs that show targeted action on body organs and show effects accordingly to suppress cause of disease, where as traditional medicine system like Indian medicine system 'Ayurveda' or Chinese medicine system use medicinal plants or herbs to treat the disease which act in root cause of disease and thus remove the disease completely from the body.

Also, in course of medication our allopathic medicine act on targeted body action but with span of time body become resistant of the medicine and after which that particular drug becomes resistant to body.

English medicine have adverse effects on body i.e. due to altering mechanism of body it can cause any other problem to be generated in body.

So, to eliminate all these complication it is required that we should rely on use of herbal crude drugs. Although herbal drugs take time to show their proper effect but they do not cause any side effect and eliminate root cause of the disease.

There are several drugs that are intended to use for COPD and works very well for cure of the disease. Herbs and medicinal plants which are usually confined under traditional medicine system of China and India.

*Some prescription according Chinese traditional medicine system-:[37]*

1. **Lack of sweating:** Use Ephedra Combination for bronchial asthma and emphysema, especially combined with Aster, Apricot seed, Farfarae, Trichosanthes fruit and Stemona.
2. **For External Wind Cold with Internal Phlegm:** Use Minor Blue Dragon.
3. **For chronic asthma:** Use Minor Bupleurum Combination, which should also be used inter currently between the use of any of the previous Ephedra formulas.
4. **Heat:** Use and Ginkgo Combination or Decoction for Asthma for asthma with associated symptoms of heat including thick, yellow phlegm, increased thirst, red complexion.

*Herbs prescribed according to Indian herbal medicine system:*

[INULA] (*Inula racemosa* Hook. F)

- It is majorly found in Temperate and Alpine Himalayas from Chitral to Nepal at 1500-4200 m.
- According to Ayurveda 'Inula' is known as Pushkaramuula, Pushkara, Paushkara, Padmapatra, Kaashmira.
- Root of the plant is commonly used for medicinal purposes. [38]

### *Classical use*

According to Charaka, Pushkaramuula is a specific remedy for cough, **asthma**, hiccough, chest pain. The powder of Pushkaramuula was prescribed with honey for alleviating cough, hiccough, **dyspnoea**, chest pain. [39]

### *Active Ingredients and pharmacology*

Essential oil and extracts from roots contained inulin, alantolactone, iso-alantolactone, and dihydroisosalantolactone, himichalol, viridiflorol etc.

Specific studies for bronchodilator properties on isolated trachea were performed and found it a potent bronchodilator.

The extract also protected guinea-pigs against various experimental asthma, plant pollen etc. It possessed antihistaminic as well as anti-5-HT activity, suggesting its use in bronchial asthma. [40]

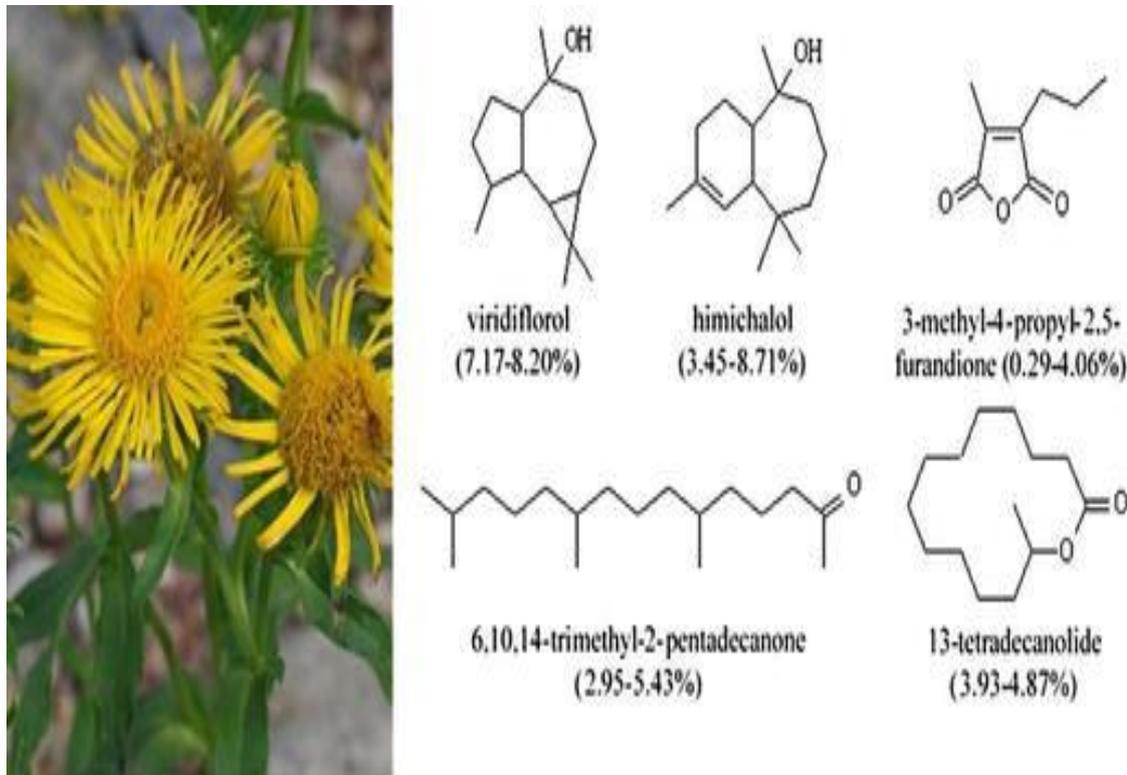


Fig. 8 [41] Therapeutically active agents of INULA

(MALVA) *Malva sylvestris* Linn.

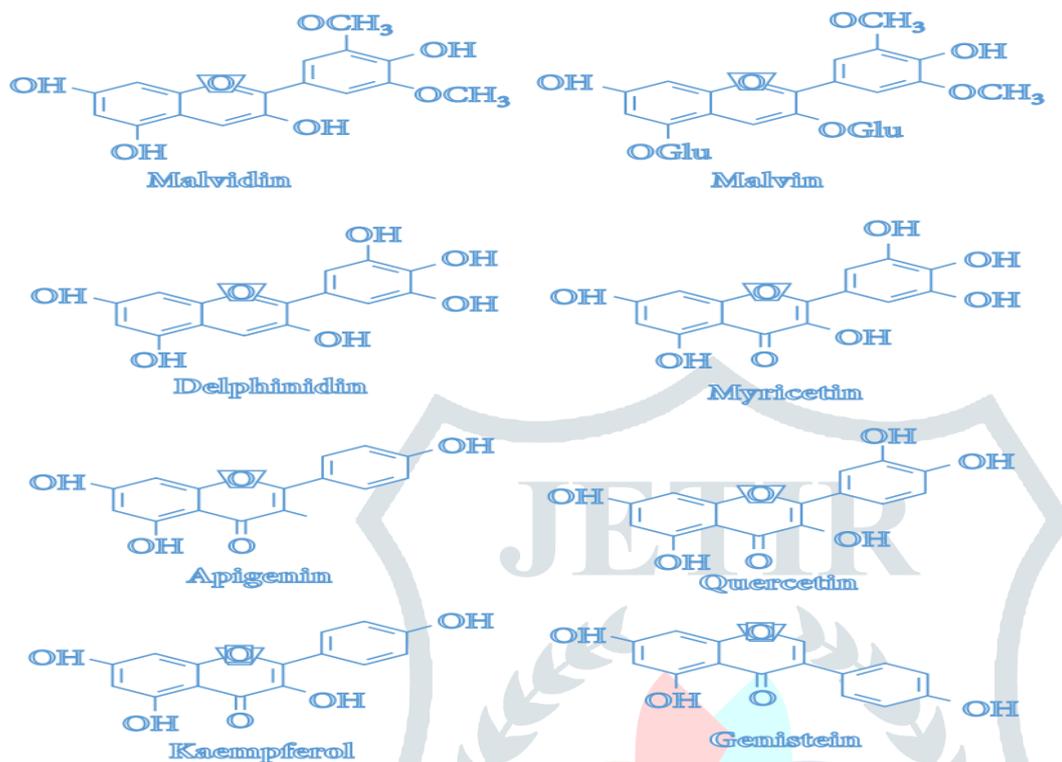
- It is majorly found in areas of Temperate Himalayas from Kashmir to Kumaon up to 2400 m, Bihar and Peninsular India.
- It is commonly termed in Unani as: Khubhaaji, Bhubbaaji Bustaani, Gul-Khair.
- Fruits and seeds of plant are commonly used for medicinal purpose.[38]

### Classical use

Fruits and seeds are imported into India from Persia and used in Unani medicine for their mucilaginous and demulcent properties in coughs, affections of mucous membranes of the pulmonary tract. The drug is employed as expectorant.[42]

### Active Ingredients and pharmacology

Leaves gave the flavonol glycosides gossypetin-8- O-beta-D-glucoside-3-sulphate and gossypetin-8- O-beta-D-glucuronide-3-sulphate; mucilage and tannins. Flowers contain malvin (an anthocyanin), malvidin. It also contains delphinidin, Genistein.[43] Flowers and leaves show expectorant effect and show bronchodilator effect with soothing effect.



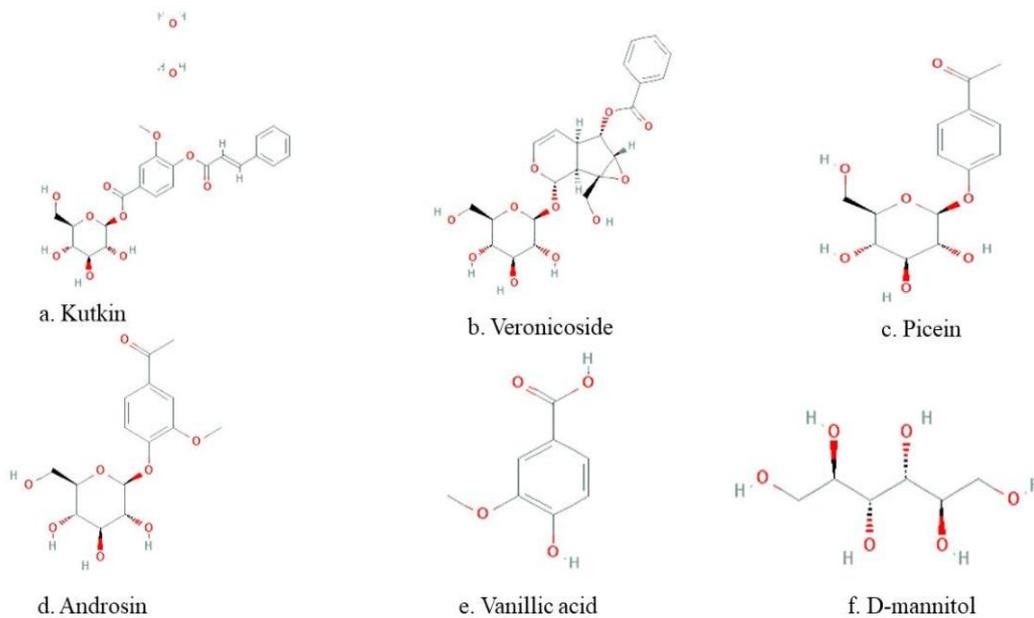
**Fig. 9** [44] Therapeutically active agents of MALVA

### [PICRORHIZA] (*Picrorhiza kurroa* Royle ex Benth)

- It is Primarily Alpine Himalayas from Kashmir to Sikkim at an altitude 2700-4500 m.
- It is commonly termed in Ayurvedic as: Katukaa, Katurhini, Kattarohini, Katuki, Katukikaa, Shatparvaa.
- Roots and Tuber plants are used for medical purpose.[45]

#### **Active uses and pharmacology:**

*Picrorhiza kurroa* has also been claimed to have led to beneficial results in the management of bronchial asthma. In a study on 20 patients of bronchial asthma, a preparation containing the crude extract *P. kurroa* roots gave encouraging results in 10 patients. Patients with mild to moderate asthma responded with clinical relief, reduction in the need to use of bronchodilators and by better performance in pulmonary function tests.[46]



[Fig. 10] [47] Therapeutically active agents of MALVA

## [VIOLA] (odorata Linn.)

- It is basically Found in Kashmir and other parts of the western Himalayan regions at altitudes of 1500-1800 m; frequently cultivated in gardens.
- It is commonly termed in Unani as : Banafshaa, Banafsaj, Kakosh, Fareer.
- Flowers are commonly used for pharmacological purposes. [48]

### *Classical use:*

The herb (mature flowers) are used in Unani medicine as expectorant, diaphoretic, antipyretic and diuretic; alone or in prescriptions, for catarrhal and *pulmonary affections*.

Khamira-e-Banafshaa and Sharbat-e-Banafshaa (Bayaz-e-Kabir) are prescribed for catarrh of the respiratory tract, *bronchitis*, fever. [49]

### *Active Ingredients and pharmacological uses:*

Flowers contain an emetic principle called violin (present in all parts of the plant), which is acrid and bitter, a volatile oil, rutin (2% ), cyanin (5-3%) > a colourless chromogen, a glycoside of methyl salicylate and sugar. In experiments conducted on rats, an extract of the herb (containing an emetine-like alkaloid) was found to be effective against induced inflammation. [50]

**(Fig. 11) [51] Therapeutically active agents of VIOLA**

Ingredients	Value (%)	Retention time (min.)
1 2-(2-methoxypropoxy)propan-1-ol	46.88	15.220
2 3-(3-hydroxybutan-2-yloxy)butan-2-ol	3.60	15.432
3 $\beta$ -Citronellol	0.29	16.749
4 Linalyl acetate	0.22	17.016
6 Citronellyl formate	0.46	17.356
9 Isobornyl acetate	0.20	17.665
10 p-Menth-6-en-2-one	0.49	18.376
11 1,4-cineole	0.61	18.445
12 p-Cymene	0.76	19.367
13 6-Methyl gamma ionone	2.29	21.225
14 $\beta$ -ionone	5.04	21.331
15 $\beta$ -linalool	1.16	21.925
16 Dihydro-alpha-terpineol	0.69	22.437
17 p-Menth-3-en-9-ol	0.65	23.512
18 $\alpha$ -hexyl cinnamaldehyde	2.93	25.86
19 Benzyl benzoate	8.00	26.316
20 O-Trifluoroacetyl dihydrocinnamyl alcohol	0.35	27.779
Total ingredients	74.62	

**ADHATODA (Adhatoda vasica Nees)**

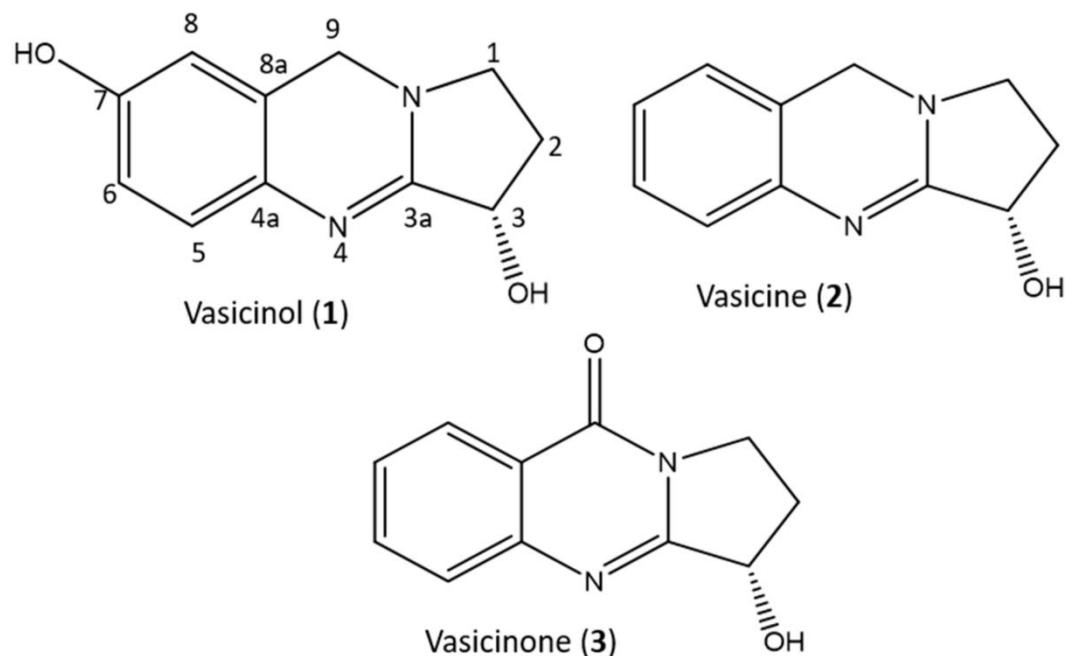
- It is mostly distributed through out India up to an altitude of 1300m.
- In Ayurvedic terms it is commonly known as Vaasaa, Vaasaka, Vaasikaa, Simhaasya.
- In Unani terms it is commonly known as Arusaa, Baansaa, Basauntaa.
- Flowers and whole plant is commonly used. [52]

**Classical use:**

Vasicinone showed bronchodilatory activity in vitro but bronchoconstrictory activity in vivo. Vasicine and vasicinone in combination (1:1) showed pronounced bronchodilatory activity in vitro and in vivo. [52]

**Active Ingredients and pharmacological uses:**

Chemical analysis show that the main alkaloid vasicine is the primary alkaloid content of Adhatoda. The chemical extract is primarily made by fresh and dry Adhatoda leaves. The leaves, root and flowers contain vasicine, vasicinine, vasicinone, tritriacontane, beta-sitosterol, which impart a marked therapeutic property to the drug. [52]

**(Fig. 12)** [53] Therapeutically active agents of ADHATODA

## Research Gap-

Although a lot has been achieved in last 5-10 years but still what we know is just tip of an iceberg and there is scope of a lot to be discovered.

Researches regarding more accurate assessment of the disease and better drug delivery system are in process. We are unaware of several aspects about disease which can lead to more proper evaluation of results and analysis. There are still a lot of variety of medicinal herbs which need more attention and work as they are proven to be useful for using as expectorant, bronchodilator and can detoxify lungs to increase respiratory capacity.

Other plants with relaxing, bronchodilatory, antitussive, anticholinergic, mucociliary clearance, and antispasmodic characteristics might be explored in addition to these. In the future, other cellular pathways will need to be studied to determine the efficacy of natural compounds. Sirtuins, have recently been identified as target molecules in COPD diseases. MMPs i.e. (metallic metalloproteins) are also involved in the regulation of lung elasticity. With continued research, several plant extracts and components may be produced as new disease-modifying drugs for lung inflammatory diseases. In addition to the aforementioned points of view, several safety concerns should be thoroughly explored and investigated.

## CONCLUSION

In this article I have tried to compile every useful data relating to the topic which I thought of and also which was necessary to be mentioned to serve the purpose of review and make this article to create an impact on the topic.

Initially I have tried to cover introduction of disease and various concern related to it. Later on I have discussed Clinical stages, assessment, symptoms and versatility of the disease. I have discussed various methods of diagnosis as well as various method of treatment based on English medicine system 'allopathy' using synthetic drugs and Indian medicine system 'ayurveda' and Chinese medicine system using herbal crude drugs and medicinal plants and herbs.

Various methodology to examine the disease and rectify the problem, cure of disease has been discussed but still that is very less to cope up with the severity of disease and to properly handle the disease we need to work more aggressively on research and clinical trial of herbal drugs and medicine. It is only possible by herbal medicine that we can control and cure the disease and even possibly reduce the chances of disease happening by strengthening our body to work against disease causing factors.

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