

## Efficacy of Pippali Rasayana as an adjuvant therapy on pulmonary function in patients of Chronic Obstructive Pulmonary Disease.

### Abstract:

**Background:** Chronic Obstructive Pulmonary Disease (COPD) is a chronic, recurrent condition, prevalent in the general population. In modern medicine, treatment modalities are aimed to diminish the incidence and extreme aggravation of clinical features. Nowadays, *pippali rasayana* being considered as a promising treatment approach for COPD. However, due to methodological limitations, there is no strong evidence to support *pippali rasayana*. **Aim:** The goal of the study is to evaluate the efficacy of *Pippali Rasayana* on pulmonary function in COPD patients. **Material and methods:** It is double arm randomized placebo controlled single blind clinical trial. Total 60 patients of COPD will be randomly divided into two groups (each group contain 30). In both groups, standard treatment of modern medicine will be continued. With this, in Group A (Intervention), *pippali rasayana* 5gm ( 25 gm twice a day after meal ) with honey will be given for 45 days and Group B (placebo group) will be given placebo ( 250 mg twice a day after meal ) with water for 45 days. Assessment will be done on 15<sup>th</sup>, 30<sup>th</sup> and 45<sup>st</sup> day. **Result** –Result will be declared on the basis of effect of *pippali rasayana* with pulmonary function test as well as frequency of Dyspnea, Chronic cough, Excessive sputum production. **Conclusion** - This trial may provide evidence on the efficacy of *pippali rasayana* on pulmonary function in COPD.

**Keywords:** COPD, *Pippali Rasayana*, Standard modern medicine treatment, pulmonary function test

### Background:

Chronic Obstructive Pulmonary Disease ( COPD ) is defined as preventable and curable lung infection with major additional pulmonary effect that may confer the rigourousness in particular patients. Chronic Obstructive Pulmonary Disease (COPD) is an inadequacy of airflow caused due to lessening of small bronchioles and damage of lung alveoli which is caused due to chronic inflammatory reaction in the lungs to the foreign particles. The most common respiratory features include cough, dyspnea and/ or intermittent production of sputum.<sup>(1,2)</sup> Chronic Obstructive Pulmonary Disease( COPD ) is highest in patient who smoke or have history of tobacco use, those older than 40 years. It is observed that 70–80% exacerbation of COPD is elicited by bacterial or viral respiratory contagions. More than 3 million people died of COPD in 2012 accounting for 6% of all deaths worldwide. In coming decades due to constant contact to COPD risk factors and aging of the population COPD problem is probably increase<sup>(1,2)</sup>.

**Comment [IKK1]:** The abstract should reflect that the research has been done, and the whole abstract should be written in past tense to indicate that the research has been done

**Comment [IKK2]:** The result of the abstract should tell the outcome of the finding(s)???

**Comment [IKK3]:** The conclusion should project the benefit of *pippali rasayana*

In Ayurveda the features like cough, breathing difficulties are caused due to *dushti*(vitiation) of *Pranavaha Srotas*. Though it is difficult to correlate with any particular disorder of *Pranavaha Sroto Dushti*, but advanced condition of *Doshika Kasa* and *Tamaka Shvasa* may result into COPD<sup>(3,4,5)</sup>. In modern medicine, management procedure is targeted to diminish the incidence and severity of intensification of the clinical features. The classes of medications commonly used are Bronchodilators, Anti-inflammatory agents, Inhaled corticosteroids, Oral glucocorticoids etc. Other treatments are Pulmonary rehabilitation, Oxygen therapy, Ventilatory support, Lung volume reduction surgery, Bullectomy, Lung transplantation, Bronchoscopic interventions<sup>(6,7)</sup>.

In *Samhitas*, *rasayanais* described for rejuvenation. *Naimittik Rasayana* is specially mentioned for chronic illnesses. *Naimittika rasayana* is a type of Rasayana therapy advised for particular curative purpose. It quickens the recovery from prevalent illnesses. The main motive of Naimittika Rasayana is to treat particular illnesses in addition to restoring the health of individual.<sup>(8)</sup> In view of above facts this study is planned to assess the efficacy of the ayurvedic formulation *Pippali rasayana* is specially suggested in *charaksamhita* for disorders of *Pranavaha strotas*<sup>(9)</sup>. *Pippali* acts as *vrishya*, *rasayani*, *rechani* and alleviator of *kapha* and *vayu*. It is mentioned in the treatment of *shwas*, *kasa*, *udar*, *jwar*, *kushta*, *prameh*, *pleeha*, *arsha*, *shool* and *amavata*. Pharmacological outlinedisplays that it acts as an anti-tubercular, antimicrobial, hepatoprotective, respiratory, neuroprotective, anti-diabetic and an aphrodisiac along with bioavailability enhancer.<sup>(10)</sup>

Comment [IKK4]: Incomplete sentence

### Methodology

Type of trial - Double arm randomized placebo controlled single blind clinical trial Allocation ratio – Total 60 patients will be selected for the study which will be randomly divided into two groups. Both groups will continue their modern medicinal treatment suggested by pulmonologist. With this, group A (experimental group) will be given *pippalirasayan* and group B will be given placebo.

**Drug collection / authentication-** The raw material will be procured from *reliable* source and will be authenticated from Department of Dravayguna of Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H) ,Wardha.

Comment [IKK5]: Reliable source????

### Formulations:

**Table 1: PippaliRasayana**<sup>(11)</sup>

Sr.No.	Ingredient	Botanical Name	Part Used	Quantity
1.	<i>Pippali</i>	Pipperlougum	Fruit	1 Part
2.	<i>Palash</i>	ButiaMonosprema	Panchang	Ksharodak of panchangksharwill be used for trituration

### Study setting:

Patients will be selected from OPD and IPD of Kayachikitsaas well as specialized peripheral camps.

**Registration number** – The trial is registered under CTRI with trial number - REF/2020/11/029366.

**Inclusion criteria –**

- Age group of 40-70 years of both gender and irrespective of the *SharirikPrakruti*
- Patients having cardinal features of Chronic Obstructive Pulmonary Disease (COPD) i.e. Dyspnea, Chronic cough, Excessive production of Sputum.
- Patients of mild and moderate Chronic Obstructive Pulmonary Disease (COPD) on Spirometric criteria (given by GOLD 2006) . Mild  $FEV_1/FVC < 0.70$  ,  $FEV_1 = > 80\%$  predicted & Moderate  $FEV_1/FVC < 0.70$ ,  $FEV_1 = 50\% - 79\%$  predicted.

**Exclusion criteria-**

- **Known** Cases of lung cancer, bronchiectasis, interstitial lung disease, CHD, DM, Pneumonia, lung fibrosis, Pneumothorax, and Tuberculosis.

**Comment [IKK6]:** How did you rule out these conditions???

**Interventions:**

**Group A** (Experimental)– Treatment of Modern medicine prescribed by Pulmonologist. + *Pippali Rasayana* + *Pippali Rasayana* 2.5gm twice a day with honey for 45 days.<sup>(12)</sup>

**Group B** ( Placebo Control ) – Treatment of Modern medicine prescribed by pulmonologist + Placebo 250 mg twice a day with water for 45 day's.

**Screening investigations (baseline):** Pulmonary Function Test (PFT)

**Investigation (endline):** Pulmonary Function Test (PFT)

**Criteria for discontinuing or modifying allocated interventions:** From the study if any untoward incidence, features of drug sensitivity or any other disease or problem arises, Subject will be withdrawn and free treatment will be offered to the subject till the difficulty subsides. We will measure quantity of *Churna* for the consumption of appropriate dose for assessment and to check drug adherence during treatment the subject will be followed up.

**Follow up:** Patients will be followed up on 15<sup>th</sup> day, 30<sup>th</sup> day and 45<sup>th</sup> day during the period of treatment.

**Primary Outcomes:** The primary outcome is to check the effect of interventional drug on Pulmonary function test (PFT).

**Secondary Outcomes:** The secondary outcome is to compare its effect on frequency of attacks of Cough and Dyspnea.

**Statistical analysis: Statistical analysis:** Wilcoxon test. Paired as well as Unpaired t test will be used to analyse the data having objective criteria. The McNamara's test will be used to analyse the data with subjective criteria.

**Total follow up :** Patient will be followed up thrice during the trial. First on 15<sup>th</sup> day after initiating the treatment and then on 30<sup>th</sup> day and on 45<sup>th</sup> day.

**Patient recruitment:** By computerized random chart sampling method 60 patient will be recruited (30 in each group).

**Implementation:** Principle investigator will enrol and allocate the patient.

**Data collection method :**

**Subjective-** Dyspnea, Chronic cough, Excessive sputum production will be assessed by gradation of symptoms.

**Gradation with validation:** Symptoms will be seen before, during and after treatment using gradation of symptoms for clinical research methodology.

Table 2: Duration of attack

Grade	Duration of attack:
0	No episode of attack.
1	Attack lasting for duration of ½-1 hour.
2	Attack lasting for duration of 1-6 hours.

Grade	Gradation of Dyspnea
0	Not trouble in breathing difficulty excluding during vigorous workout.
1	Worry by breathlessness when speeding or walking up a slight hills.
2	Gait is gentle than individual of the similar age due to rapid breathing or has to take rest for breathing while walking at personal place on a flat surface.
3	Breathing is stopped while breathing out after walking of out 100 meter on a flat surface.
4	breathlessness while leaving the house or feel breathless while dressing or undressing.
3	Attack lasting for duration of 6-12 hours.
4	Attack lasting for duration of 12 hours.
5	Attack lasting for duration of more then 12 hours.

Table 3: Gradation of Dyspnea

Table 4: Frequency of Sputum formation

Grade	Frequency of Sputum formation
0	Absent.
1	Only in the early morning.

2	2-3 times daily.
3	Continuously.

### Objectives - Pulmonary Function Test ( PFT ).

Mild FEV1 / FVC<0.70 ,FEV 1 =>80 % predicted.

Moderate FEV1 / FVC<0.70, FEV1 =50%–79% predicted.

In healthy person FEV1 / FVC 80% - 120% is obtained.<sup>(10)</sup>

If the value of pulmonary function test is lies in between the FEV1 / FVC is 80% - 120% or FEV1 / FVC will < 80%<sup>(10)</sup>then we concluded that *Pippalirasayana* is effective on patients of chronic obstructive pulmonary disease.

**Plan to promote participant’s retention and complete follow up-** We will stay in touch with the patient by taking contact number and timely advise them proper medication practices and follow up and the data regarding follow up will be stored in the documentation with valid reasons.

**Data management:** The data will be collected from patients by assessor by doing clinical assessment after taking written consent form from the patient. Data will be entered in master sheet and analysed by using appropriate statistical technique and data coding will be done by principal investigator.

### Ethics and dissemination :

**Research Ethics Approval :**Approval from research ethics committee has been taken. Ref. No. MGACHRC / IEC / July – 2020 / 59.

**Consent or assent :** The written consent will be taken before starting the study from the patient. During the study the confidentiality of each patient will be properly maintained.

**Dissemination policy :**The data will be disseminated by paper publication.

**Results:** We (~~We hypothesised~~) ~~are hypothesising~~ that in the group of *pippali rasayana* we may get improvement in pulmonary function test ( PFT ) than placebo group because '*Rasayana*' are rejuvenators possessing strong antioxidant activity and antagonistic actions on the oxidative stressors.<sup>(13)</sup>*Pippali* has a number of components, including volatile oil, alkaloids, isobutyl amides, ligansans ester. Piperine, which is a crucial component is having significant anti-inflammatory action. *Pippali* reduces inflammation of both acute and sub-acute phase <sup>(14)</sup>. *Pippali* has a property of antibacterial antifungal activity of various pathogenic bacteria and fungi respectively. Clinical studies have revealed that *pippali* is very effective in the treatment of bronchial asthma <sup>(15)</sup>.

### Discussion:

Study will observe that *Pippali Rasayana* along with treatment of Modern medicine will effectively reduce signs and symptoms of COPD. The *Pippali rasayana* is made up of *pippali churna* and *palashksharaudak*. *Pippali* possesses the qualities of *Katu Rasa*, *laghu*,

**Comment [IKK7]:** The result presentation is not formal, where are the comparison tables or figures, how did you arrive at these results??/? kindly format and improve

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**Comment [IKK8]:** The discussion also is grossly inadequate and did not bring adequate relevant information about your finding, reframe

*Tikshanguna*, *tikshnagunais* helpful in *bedha* of *kapha*, which is stuck to the *strotas* by *picchila* and *Sandra guna*. *Oncethedoshais* separated from *strotas*, *ushnavirya* of the drug causes *vilayana* of *kapha* and generates easy expectoration. *Kaphasthivana* causes *strotoshuddhi*, and hence, *vatasanga* and *vimarga-gamana* are corrected. That leads to *vyadhishm ana*<sup>(16)</sup>. *Palash* possesses the quality of *Katu Tikta Kashay rasa*, *Laghu Rukshaguna*, *Ushnavirya*, *Katuvipaka*. Various chemical constituent like flavonoid, alkaloids, butrin, palasonic acid, glycoside, galic acid etc. which are responsible for pharmacological activity like antioxidant, antibacterial, antifungal, anti-inflammatory, anticonvulsive, hepatoprotective, anti-fertility, wound healing etc<sup>(17)</sup>. Therefore, collectively this drug helps in *strotoshuddhi* and rejuvenate respiratory system which is the key factor in pathogenesis of COPD<sup>(18)</sup>. Related studies by Sourya et. al.<sup>(19)</sup> and Patil et. al.<sup>(20)</sup> were reviewed. Gupta et. al. reported critical appraisal of *pipasa* in chronic obstructive pulmonary disease<sup>(21)</sup>. Studies on COPD from India were reviewed<sup>(22-26)</sup>.

The study highlights the efficacy of " Ayurveda " which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

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