

# Clinical Trial on The treatment of Chronic Obstructive Lung Disease Through the Oral Administration of *Siddha* Herbal Formulation *Swasakasathirku churnam*

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## ABSTRACT

Background: In *Siddha* medical texts, respiratory diseases are explained in the name of *Swasa noikal*. Objectives: In respiratory disease has been described to have symptoms close to chronic obstructive pulmonary disease (COPD), which is called as *swasa kasam* in *Tamil*. In this case study, we have recorded the effect of herbal medicine *Swasakasathirku churnam* (SKC) on the COPD patients. This case study was carried out in Post-Graduate Department of Pothumaruthuvam, Government Siddha Medical College, Palayamkottai, Tamilnadu, India. Material and Methods: Twenty patients were admitted as in-patients (12 male and 8 female, age group 21-60 years old) based on the severity of COPD and 20 out patients (12 male and 8 female, age group 12-60 years old) are treated with SKC. Patients of COPD selected on the basis of fixed inclusion and exclusion criteria. The trial patients were given SKC (dose of 1 g with honey) twice a day after meals for 40 days. Improvement of patients health was evaluated by pulmonary function test using Spirometry and blood chemistry parameters. Results: Treatment with SKC administration was found to be effective among COPD patients by regulating their respiratory rate to normal level. Further, analysis of blood profile before and after treatment with SKC indicated the safety of the herbal drug SKC. Moreover, studies on mechanism of action revealed that the *Siddha* formulation SKC might exhibits therapeutic effect through their anti-inflammatory, anti-spasmodic, anti-histamine and anti-microbial properties. Conclusions: Hence, *Siddha* formulation SKC could be explored as an effective herbal drug for COPD without any side effects.

**Keywords:** COPD, *swasa kasam*, *swasakasathirku churnam*, clinical trial, pulmonary function test.

## INTRODUCTION

Growing population, urbanisation, industrialization, deforestation and increasing number of vehicles results in air pollution, which leads to respiratory diseases<sup>1</sup>. In the past 2-3 decades, respiratory diseases are increased remarkably due to severe environmental pollution<sup>2</sup>. In India, a large number of people are affected by respiratory illness, especially with chronic obstructive type of airway disorder<sup>3</sup>.

Chronic obstructive lung disease (COPD, Tamil: *Swasakasam*) is a respiratory disease characterized by cough with expectoration, breath sound like hissing of snake, throat irritation, indigestion, flatulence, redness of the nose, low pitched voice and excessive salivation<sup>4</sup>. Major symptoms are cough, sputum production and exertional dyspnea frequently of long duration. It is a disease state characterized by air flow limitation that is not fully reversible. Different conditions of COPD are emphysema (characterized by destruction and enlargement of the lung alveoli), chronic bronchitis (chronic cough and phlegm) and small airway disease (small bronchioles are narrowed)<sup>5</sup>. Global initiative for chronic lung disease estimates that COPD will be increased from the sixth most

common cause of death worldwide by 2020<sup>6</sup>. According to American Centre for Disease control and Prevention (2014), more than 70% of COPD related healthcare expenditure goes to medication and in the US about \$10 billion is being spent annually for hospital care of COPD<sup>7</sup>. Smoking, respiratory infections, occupational exposure to pollutants and genetic factors are the major risk factors of COPD<sup>8</sup>.

Medicines currently available for COPD include anti-inflammatory therapies, bronchodilators and inhaled corticosteroids. But these therapies have been considered effective to reduce the disease symptoms and exacerbations. Excessive use of some therapies can induce side effects in some patients such as increased risk of initiating pneumonia and cardiac co-morbidities. So, an alternative treatment is very much essential for the COPD patients due to inefficiency of the modern medicines. One such alternative or add-on therapy is phytomedicine<sup>9</sup>. In this same problem peoples were selected alternatives medicines<sup>10</sup>. *Swasakasathirku churnam* (SKC) is a plant based traditional *Siddha* formulation used to treat respiratory diseases according to the *Siddha* medical text *Agathiyar Vaakiam 50*<sup>11</sup>. Herbal ingredients such as

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*Alangium ecapetalum*, *Zingiber officinale*, *Piper nigrum*, *Piper longum* and *Celastrus paniculatus* are used to prepare SKC<sup>12</sup>.

SKC contain five herbal drugs and its main ingredient is bark of *Alangium ecapetalum*. In Siddha system it used as a alterative, anthelmintic, diuretic, emetic, febrifuge and laxative<sup>13</sup>. The same therapeutic uses was mentioned in the journal of Babeet Singh Tanwer and Rekha Vijayvergia, 2014<sup>14</sup>. Also its dry poeder was used for controll respiratory problems. Previously one review papper of Panara et.al, 2016 has explained that it has major phytochemicals of alangine, ankorine, tubulosine, alangicine, salsolin etc<sup>15</sup>.

Another ingredient of *Zingiber officinale* is therapeutically used to control the diseases of Wheezing, cough, pneumonia and indigestion<sup>13</sup>. Formerly it uses was mentioned in a article Rajalakshmi et.al, 2017 gastrointestinal tract such as indigestion, gastric reflexion, gastric ulcer, flatulence, diarrhea, vomiting and respiratory problems such as cough, cold, wheezing, head ache, head heaviness tonsillitis and sinusitis. It acts as a stomachic, carminative and stimulant and also used for ear pain, rectal problems, abdominal tuberculosis, anemia, body pain, viral fever, and tooth pain. External application of its paste for joint swelling, head ache and throat pain<sup>16</sup>.

Next one drug is *Piper nigrum* dyr fruit. It is act as an antitode for all toxins of food and insects. It controll lungs diseases, Dermal problems and gastra intestinal tract disorders. It is traditionally used for curing different aliments like cough, fever, swelling, joint pain and sinusitis<sup>13</sup>. Formerly Sruthi et al., 2013 has explained in their research article it has the phytochemicals of Piperidine, Piperine, pinene, sabinene, limonene, caryophyllene, and linalool<sup>17</sup>.

*Piper longum* has stimulant and carminative activity. It is used for controilling the respiratory problems and ulcer, anaemia, giddiness, tastelessness, flatulence, head ache, sinusitis, throat pain and diseases of ear, nose, eye. Gives streanth to seminal fluid and body<sup>13</sup>.

SKC contain the above explained drugs and it is prescribed with a dose of 1 g with honey twice a day after meals for 40 days. Even though, ancient *Tamil Siddha* literatures indicate the use of COPD, there is no experimental / clinical evidence for its effectiveness. Hence, for the first time we are recording the clinical case study for the treatment of COPD with SKC.

## MATERIALS AND METHODS:

### *Study subjects*

The clinical study was undertaken in Post-Graduate Department of *Pothumaruthuvam*, Government Siddha Medical College, Palayamkottai, Tamilnadu, India. To carry out this study patients identified with COPD satisfying the inclusion criteria were registered from OPD and IPD. Twenty patients were admitted as in-patients (12 male and 8 female, age group 21-60 years old) based on the severity of COPD and 20 out patients (12 male and 8 female, age group 12-60 years old).

### *Inclusion criteria*

Patients were selected based on the clinical symptoms of cough with expectoration, dyspnoea, tightness of chest, wheezing and hardly expectoration of scanty mucoid sputum with different duration of illness (6 months to 30 years). Among the patients, 15 were having smoking habit, 12 were occupationally exposed to dust and 13 were exposed to severe air pollution. Habits of smoking (15 patients), tobacco chewing (6 patients), betel nut chewing (2 patients) and alcoholic consumption (13 patients) were noted. Nineteen patients were clinically manifested with running nose, 14 with sneezing, 40 with difficulty in breathing, 10 with tightness of chest and 1 with sweating. These criteria were followed as given by GOLD Executive Summary, 2013<sup>18</sup>.

### *Exclusion criteria*

The major exclusion criteria were the presence of other complications of congestive heart failure, pneumonia, tuberculosis and bronchiectasis. Any of the following is regarded as a criterion for exclusion from the study. Some patients not fulfilling the inclusion criteria, not willing for trial and presented with complications were excluded from the study.

### *Treatment with SKC*

Herbal ingredients such as *Alangium ecapetalum*, *Zingiber officinale*, *Piper nigrum*, *Piper longum* and *Celastrus paniculatus* were purchased from local market, Palayamkottai and shade dried, powdered and mixed in equal portion to prepare SKC according to the book *Agathiar Vakkiam 50*<sup>11</sup>. Patients were administered with 1 g of SKC twice a day with honey for 40 days and patients are advised to undergo haematology (Nucleophils, Lymphocytes, Eosinophils and ESR) and biochemical profile of blood (Sugar, Urea, Haemoglobin and Cholesterol) and pulmonary function test using (PFT).

There are a variety of pulmonary tests to perform in an effort to better define the type of lung disease and to the treatment. PFT test is done by the affected person by taking in a deep breath and then, as fast as he can, blow out all of the air. The patient will be blowing into a tube connected to a machine (spirometer). To get the best test result, the test is repeated three times. The patient will be given a rest between tests. The test is often repeated after giving breathing medicine (bronchodilator) to find out how much better he might breathe with this type of medicine<sup>19</sup>.

### *Mechanism of action*

In order to prove the mechanism of action, the anti-inflammatory activity of SKC was studied in rat model. Fifteen healthy albino rats weighing 100-150 g were divided into three groups each consisting of 5 rats. All the animals were given free access to food and water and acclimatized for one week. Cotton pellet weighing 10 mg was sterilized in autoclave and implanted in rats subcutaneously in the lower abdomen after making suitable incision and sutured carefully under anaesthesia. Group I is disease control and given distilled water, Group II is administered with standard drug Ibuprofen (20 mg/100 g BW) and Group III is given with SKC (200 mg/100 g BW) for one week. On the 8<sup>th</sup> day, all the rats were sacrificed and the cotton pellets surrounded by granulation tissue were removed and dried in the hot air

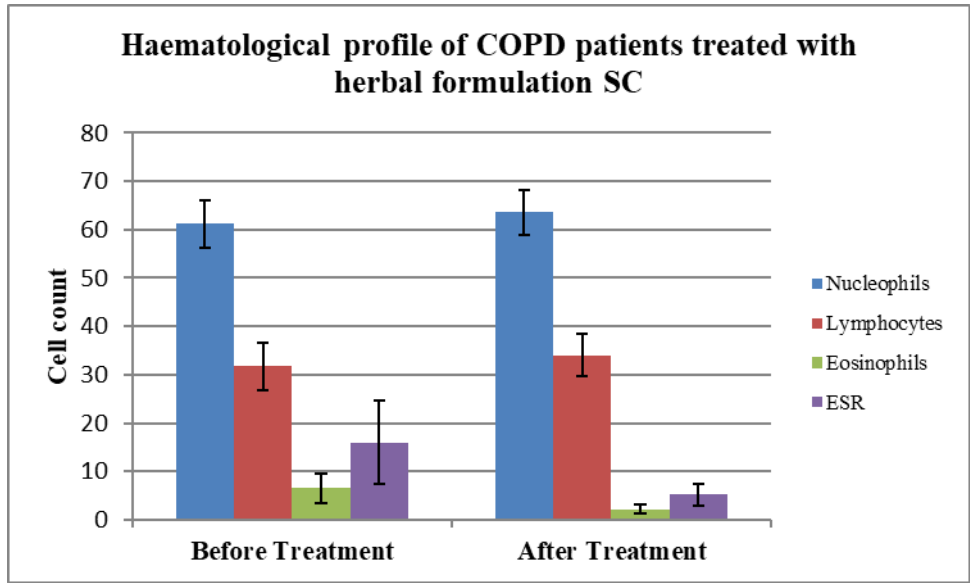


Figure 1: Haematology profile.

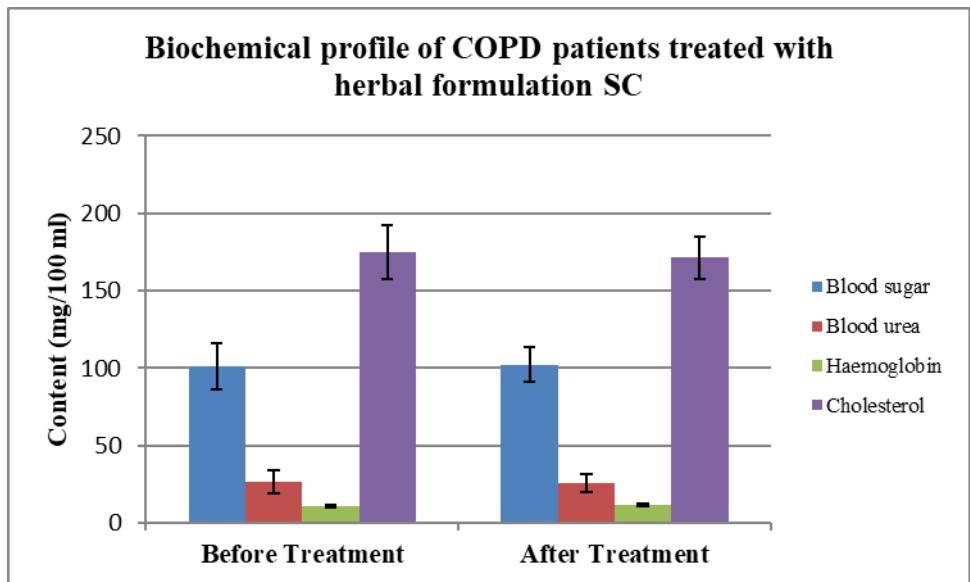


Figure 2: Biochemical profile.

Table 1: Pulmonary function test.

S.No.	Parameter	Level
1	Forced expiratory flow (FEF, %)	25-75
2	Peak expiratory flow rate (PEFR, %)	< 70
3	Forced expiratory volume (FEV) / Forced volume vital capacity (FVC, %)	91.28 ± 8.54
4	Forced volume vital capacity (FVC, %)	> 80
5	Respiratory rate before treatment (%)	23.30 ± 1.02
6	Respiratory rate after treatment (%)	19.93 ± 0.86

oven at 60°C and average weight of granuloma was calculated.

The anti-spasmodic effect of SKC was studied in rabbit model. A rabbit weighing 1.1 kg was selected and starved for 48 h, but allowed to drink water and sacrificed; abdomen was opened to expose the viscera. Then the ileum was dissected out and placed on a shallow glass dish containing warm aerated tyrode solution. Lumen of the ileum was gently rinsed by saline and in fully relaxed state, the ileum was cut into required segments of about 4 cm length. Sutures were made to tie either ends with the help of the needle in such a way that it was suspended in an inner tube of isolated organ bath maintained at 37°C. The tube is connected with a jar containing nutrient solution supplemented with atropine sulphate (0.25 mg/L). The inner tube thus obtained the nutrient solution was connected with the outlet tube as well as oxygen tube. The ileum segment got oxygen by the aeration and fresh

Table 2: Mechanism of action.

S. No.	Parameter	Disease control (Without treatment)	Treated with standard drug (Ibuprofen)	Treated with herbal drug (SC)
1	Dose (mg) / 100 g BW	--	20	2.0
2	Cotton pellet weight (mg)	10	10	10
3	Granuloma weight (mg)	250	55	120
4	Inflammation level (%)	100	22	48
5	Inhibition of inflammation (%)	0	78	52

solution was filled after every test preceded by the removal of old nutrient solution through the outlet tube. Acetylcholine stock solution (100 mg/mL) was prepared and different concentrations (0.2, 0.4, 0.6, 0.8 and 1.0 ml) for standardizing the optimum concentration required for contracting the tissue in 30 min incubation time. Then the trial medicine (SKC, 0.5 ml) was given to study the inhibitory effect of acetylcholine induced contractions and the tissue contraction was measured by Kymograph.

Anti-histamine activity of SKC was investigated in Guinea pig model. An over-night fasted Guinea pig weighing about 400 g was sacrificed and the abdomen was opened and the ileo-caecal junction was dissected. A small portion of ileum (3 cm) was cut and placed in a dish containing warm aerated tyrode solution and the contents of lumen of ileum was gently rinsed. Both the ends of ileum were tied without closing the lumen and mounted in an organ bath containing tyrode solution at 37°C and bubbled with oxygen. One millilitre of test drug was added after the addition of 0.2 ml of histamine and the drum was allowed to run for 30 sec to record the inhibitory action of the drug. Anti-microbial activity of SKC was tested against cultures of *Escherichia coli*, *Klebsiella sp.*, *Proteus sp.*, *Staphylococcus aureus*, *Streptococcus pneumonia*, *Pseudomonas aeruginosa* and *Candida albicans* which were inoculated on Muller-Hinton agar plates. Disc containing herbal drug extract (SKC) was placed over the inoculated plate and incubated for 24 h at 37°C and observed for zone of inhibition.

## RESULTS AND DISCUSSION

### Pulmonary Function Test

Lung disease is any disease or disorder where lung function is decreased. Pulmonary tests may consist of Pulmonary Function Testing, Bronchoscopy, Cardiopulmonary Exercise Testing, Home Oxygen Testing, Respiratory Management Training (Patient education on inhaler technique, incentive spirometry, peak flow monitoring, etc.), Pulmonary Rehabilitation, Smoking Cessation and Nicotine Addiction<sup>20</sup> (The Metro Health Foundation, Inc). This PFT breathing tests to find out how well the patients move air in and out of lungs and how well oxygen enters into the body.

Pulmonary function test showed obstructive lung disease among the investigated patients (Table 1). Forced expiratory flow among the investigated patients is ranged from 25 to 75% while the peak expiratory flow rate is below 70%. Below 80% of forced volume vital capacity was noticed among the patients, whereas the ratio of FEV / FVC was found to be 91.28%. Overall respiratory rate was decreased after treatment with herbal formulation

SKC (19.93%) when compared to initial pathological condition (23.30%). So, the herbal formulation SKC is effective in controlling the respiratory rate to the normal level among the presently investigated COPD patients. Previously a clinical trial was carried out to test the Ayurvedic medicine *Vasadi Syrup* and *Shwasaghna Dhuma* for COPD<sup>6</sup>.

### Haematology profile

Haematology profile of patients treated with the herbal drug SKC was shown in Figure 1. Haematology investigation showed total count of nucleophils (61.23) and lymphocytes (31.70) were slightly increased during treatment to 63.55 and 34.03, respectively. Eosinophil count was drastically reduced from 6.58 cells (before treatment) to 2.15 cells (after treatment). Erythrocyte sedimentation rate (ESR) was also found to be decreased from 15.98 to 5.20% after the treatment of COPD patients with herbal formulation SKC. The same blood parameter was noted in a Siddha clinical trial conducted by Merlin Kumari et al, 2014<sup>21</sup>.

### Biochemical profile

Biochemical investigation of blood was done during the admission and at the end of the treatment for every case and the results were given in the Figure 2. There was no significant change in the blood sugar (101.13 and 102.24 mg/100 ml), urea (26.61 and 25.66 mg/100 ml), cholesterol (174.92 and 171.27 mg/100 ml) and haemoglobin (10.95 and 11.59 mf/100 ml) levels of patients before and after treatment with herbal formulation SKC, respectively.

### Mechanism of action

Among the investigated mechanisms of action, the herbal formulation SKC was found to show effective anti-inflammatory activity. The granuloma weight as an inflammatory response to cotton pellet was measured in rat model and the results are shown in the Table 2. Granuloma weight in the disease control group was 250 mg, which was reduced to 55 mg in Ibuprofen treated animals and 120 mg in herbal drug treated animals. So, by considering the inflammation level in disease control animal 100%, the Ibuprofen and herbal drug treated animals were observed to exhibit inflammation level of 22 and 48%, respectively. Herbal drug SC was found to exhibit 52% of anti-inflammatory activity, which is comparable to that of standard drug Ibuprofen (78%). Mahalakshmi et al. 2015 explained the same study in siddha medicine *Elathi kuligai*<sup>22</sup>. Further, the anti-spasmodic and anti-histamine effects of the Siddha formulation SKC were experimentally observed in rabbit and Guinea pig models whereas the antimicrobial effect also recorded against the selected pathogens by Meena & Ramaswamy, 2015 in their research work<sup>23</sup>.

**CONCLUSION**

Even though COPD is a serious respiratory problem in many developing countries, the available treatment methods are neither not effective nor safe. Hence, while looking for alternative therapy for COPD, a Siddha formulation SKC received attention and in the present work the effect of SKC was proved in COPD patients. Patients administered with SKC twice a day with honey for 40 days resulted in improvement of respiratory rate to the normal level and hence it is effective to treat COPD. When analyzing the blood profile of patients before and after administration of SKC, there is no significant variation in the blood chemistry, which indicates the safety of the herbal formulation. Further, the mechanism of action of the currently studied Siddha drug SKC might be through their anti-inflammatory, anti-spasmodic, anti-histamine and anti-microbial properties. So, the herbal formulation SKC could be further explored as efficient, safe and cost-effective medicine with global acceptance to treat the world-wide problem of COPD. However, the botanical and chemicals must be fixed to maintain the use of authentic ingredients in the formulation of SKC to maintain their therapeutic efficacy in treatment.

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