Evaluation of Bronchodilator Activity of Siddha Herbo Mineral Drug “Vasanthakusumakara Mathirai” by Exposing Guinea Pig in Histamine Aerosol

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Abstract
Asthma is an inflammatory disease of the small airways characterized by episodic, reversible bronchial obstruction, polyphonic wheeze, dyspnoea, and cough which may be relieved spontaneously or as a result of therapy. Asthma cannot be cured but it could be controlled. Combined medications possess both reliever and controller properties are very good for asthmatic treatment. Siddha herbo mineral preparations are bio-safe and have its own fast acting properties to control broncho constriction and relieves from asthmatic symptoms early. And they probably don’t cause any adverse drug reactions. Vasanthakusumakara Mathirai (VKM) was indicated for respiratory illness includes sneezing, fever and bronchial asthma. To evaluate the Siddha herbo mineral drug VKM by exposing guinea pig in histamine aerosol for bronchodilator activity. Four group each group contain six animal. All the doses were given orally once a day for 5 days. Prior to drug treatment each animal was placed in the histamine chamber and exposed to 0.2 % histamine aerosol. The pre convulsive time (PCT) was determined from the time of exposure to onset of convulsions. These animals were again subjected to histamine aerosol after 1hour of drug administration and PCT was determined, then results were tabulated. Hence the test drug has significant effect on bronchodilator and proves to be the best drug for treating asthma.

Keyword: Bronchodilator, Vasanthakusumakara Mathirai, Siddha, Pre-convulsion time.

Introduction
Asthma is one of the most important non communicable diseases in the world. It is a Greek word which means ‘breathless’ or ‘to breathe with open mouth’. Asthma is an inflammatory disease of the small airways characterized by episodic, reversible bronchial obstruction, polyphonic wheeze, dyspnoea, and cough which may be relieved spontaneously or as a result of therapy. These episodes are usually associated with widespread, but variable, air flow obstruction within the lung that is often reversible either spontaneously or with treatment. It can be triggered by various factors like allergens, drugs,
respiratory infection, dust, cold air, exercise, emotions, occupational stimuli, chemicals, histamine and also hereditary\(^{(5)}\). Asthma cannot be cured but it could be controlled\(^{(6)}\). Intensive research during the last several decades has highlighted the role of lymphocytes, immunoglobulin’s, mast cells, and various autacoids in the pathogenesis of allergic conditions \(^{(7,8)}\).

More than 235 million people are currently affected by asthma in various countries and 100 million will be affected by 2025\(^{(9)}\). To control asthma, there are two ways one is medication and another is to improve surrounding environmental hygiene. Proper management of asthma enables people to enjoy a good quality of life. Medication for asthmatic comes under two groups. They are reliever medications and controller medications. Reliever medications are usually bronchodilator that quickly relieves broncho spasm. Reliever group of medication includes \(\beta_{2}\)-agonist Bronchodilators, Anti cholinergic Bronchodilators and are majorly used for Bronchial asthma treatment. Controller group medications in bronchial asthma management act by providing anti inflammatory action to prevent or diminish the inflammatory process and it helps to control the immune reactions that cause asthma attacks. A controller medication helps to reduce the incidence of attacks and sometimes preventing them from occurrence. Mast cell stabilizers, Leukotrienes modifiers and corticosteroids come under this classification. In present days Mast cell stabilizers provide dry cough and throat irritation while Leukotrienes modifiers produce side effects like headache, nausea, stomach upset and diarrhoea\(^{(10)}\). Combined medications possess both reliever and controller properties are very good for asthmatic treatment. It contains both bronchodilator and mast cell stabilizing properties. Unfortunately this type of medication is very rare now. Assessing the current status of health care system, there has been an alarming increase in number of diseases or disorders caused by synthetic drugs promoting a switch over to traditional medical system\(^{(11)}\).

In Siddha system the symptoms of Bronchial asthma can be correlated with the symptoms of Swasa kasam as quoted by Yugi muni\(^{(12)}\). Siddha herbo mineral preparations are bio-safe and have its own fast acting properties to control broncho constriction and relieves from asthmatic symptoms early. And they probably don’t cause any adverse drug reactions. In classical Siddha literature (Siddha Vaithiya Thiratu\(^{(13)}\), Vasanthakusumakara Mathirai was indicated for respiratory illness includes sneezing, fever and bronchial asthma. Screening of potential functional group, particle size etc were already done to standardize this drug\(^{(14)}\). Thus the present study was focused to evaluate the bronchodilator of a herbo mineral drug on experimental animal models.

**Materials and Methods**

**Selection of drug**

The trial drug VKM will be prepared as per Siddha literature “Siddha Vaithiya Thiratu.”

**Ingredients**

<table>
<thead>
<tr>
<th>Meanings</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lingam (Cinnabar)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Vengaram (Borax)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Lavangam (Syzygium aromaticum)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Thipilli (Piper longam)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Kostam (Costus speciosus)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Akirakaaram (Anacyclus pyrethrum)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Adhimathuram (Glycyrrhiza glabra)</td>
<td>¼ palam (8 g)</td>
</tr>
<tr>
<td>Korosanam (felbovinum purifactum)</td>
<td>1 varagan (4.2 g)</td>
</tr>
<tr>
<td>Kanguma poo (Crocus sativus)</td>
<td>1 varagan (4.2 g)</td>
</tr>
<tr>
<td>Pachaikarpoooram (Borneo camphor)</td>
<td>1 varagan (4.2 g)</td>
</tr>
<tr>
<td>Ginger juice</td>
<td>60 ml</td>
</tr>
<tr>
<td>Milk</td>
<td>60 ml</td>
</tr>
</tbody>
</table>

**Identification and Authentication**

All raw drugs were identified and authenticated by the botanist and experts from Gunapadam department (Pharmacology) at Government Siddha Medical College, Arumbakkam, Chennai. The specimen samples of the identified raw drugs were preserved in the laboratory of P.G Gunapadam for future references.

**Method of preparation**

All the ingredients were purified as above, the purified drugs are grounded separately, then mixed together and first the ginger juice was added; ground in stone mortar it for two days. The
final product was again grounded for another two days along with milk, then rolled it as tablet, dried in shadow.

Administration of the drug
Form of the medicine: pills
Route of administration: Enteral
Dose: green gram (65 mg), 1-2 pills
Time of administration: Twice a day
Adjuvant: Honey.
Indication: Kabakasam (Asthma), Thummal (Sneezing), Suram (Fever).

Ethical approval
The experimental protocol was approved by the Institutional Animal Ethical Committee (IAEC) under CPCSEA (approval no: IAEC/XLIV/22/CLBMCP/2014) by the institution C. L. Biad Metha college of pharmacy, Thuraipakkam, Chennai.

Experimental procedure of bronchodilator activity
Overnight fasted guinea pigs were divided into six groups each containing 6 animals.
- Group 1 was treated as control,
- Group 2 received standard drug Salbutamol (5 mg/kg).
- Group 3 VKM 200 mg/kg.
- Group 4 VKM 400mg/kg.
All the doses were given orally once a day for 5 days. Prior to drug treatment each animal was placed in the histamine chamber and exposed to 0.2 % histamine aerosol. The PCT was determined from the time of exposure to onset of convulsions. As soon as the PCT were noted, the animal were removed from the chamber and placed in fresh air.
Group 2 received Salbutamol. These animals were again subjected to histamine aerosol after 1 hour of drug administration and PCT was determined. The protection offered by treatment was calculated by using the formula (15).
Percentage Protection = (1 - T1/T2) X 100
Where,
T1 = the mean of PCT before administration of test drugs.
T2 = the mean of PCT after administration of test drugs.

Statistical analysis
All the results for this study were expressed as mean ± SEM of six animals in each group. Analysis of variation was performed by one way ANOVAs method followed by Dunnet’s multi comparision test using a computer software programme GRAPH PAD INSTAT-3 version.

Result and Discussion
Table: 1 Bronchodilator Activity of VKM

<table>
<thead>
<tr>
<th>S. No</th>
<th>Group</th>
<th>Onset of Convulsion (sec)</th>
<th>% protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>93.83±0.04</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>Standard (salbutamol 5mg)</td>
<td>992.4±0.46**</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>VKM (200mg/kg)</td>
<td>426.03±0.84</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>VKM (400mg/kg)</td>
<td>564.23±10.54*</td>
<td></td>
</tr>
</tbody>
</table>

*Values are expressed as mean ± SEM (Dunnet’s test) *p<0.05 – Significant, **p<0.01-Highly significant, ***p<0.001-Extremely significant n=6
Discussion
Here, the onset of convulsion to test drug group was significant when compare to standard and control. While increasing the dose the effect of the drug is increasing. By these we concluded the test drug VKM was best anti asthmatic drug.

Conclusion
In conclusion, the result of the test drug VKM has significant effect in bronchodilator activity. In experiment, the animals are subjected to histamine aerosol after 1 hour administration. The PCT was significant when compare to control and standard. Hence the VKM was scientifically evaluated and concluded that the test drug have new hope in the treatment of bronchial asthma which is cost effective also.

Reference
1. World health organisation, Asthma Fact Sheet (Updated 2013 Nov; Cited 2014 May 8) http://www.who.int/mediacentre/factsheets
6. World Health Organization fact sheet no.206
9. World Health Organisation, Asthma, 10 Facts on asthma. (Updated 2013 Nov; Cited 2014 May 8) http://www.who.int/features/factfiles/asthma