INTRODUCTION

‘Ayurveda’ - the knowledge of life sciences is full in medical knowledge. The chronology of Sanhita granthis, Sangrah granthis, Yoga granthis and Nighantu granthis reflect the Ayurveda of respective times. On careful review we come across gradual increase in number of herbs used. In the process of adding new herbs, some confusion is also added in the form of multiple synonyms, multiple varieties etc. This has led to the controversy in the identity of some herbs. More over, migration of Vaidas from forest areas to the urban areas resulted in dependency upon shepherds and forest dwellers etc for the medicinal plants. Later, the controversy increased because, various people dwell in different areas with different cultures might have used the same name to denote different herbs. Thenceforth, substitutes as well as controversial herbs made their way into traditional practice. Where ever there is an availability issue or a cost issue, physicians were trying for suitable alternative.

Seers like Bhavamisra (16 AD) and Yogaratnakara (17 AD) did try to establish the comprehensive list of substitutes (Abhavapratinithi Dravyas or Alabdhapratinithi Dravyas) along with certain guidelines for substitution. However, in the present scenario (2005) Prevention of Food Adulteration Act 1954 considers substitute as the synonym for adulterant. For example, usage of Carum carvi for Cuminum cymnium or vice versa will attract the charges of Adulteration/Substitution. Therefore the author prepared a comprehensive data-base on the substitutes delineated in the Ayurvedic Texts and decided to study the comparative clinical efficacy of the substitutes for Pushkaramula / PM (Inula racemosa Hook. f.) viz., Kushta / KS (Saussurea lappa (Decne.) C.B.Clarke.) and Erandamula / EM (Ricinus communis L.)

Review of literature on the pharmacological similarities of trial herbs

The similarity in the pharmacological activity of the trial herbs is provided in Table 1b. All the three herbs have a common activity i.e., anti-inflammatory activity.

Review of Disease (Asthma) literature

Asthma is defined as a chronic inflammatory disorder of the airways characterized by reversible airflow obstruction causing cough, wheeze, tightness in the chest and breathlessness. Asthmatics fall between the ranges of 100 to 150 million people around the globe. The highest prevalence is reported from China and Malaysia. Worldwide deaths from this condition have reached over 180,000 annually. As per WHO Fact sheets, India has an estimated 15-20 million of asthmatics. It is estimated that, 2.5% of adults have a clinical diagnosis of asthma. In case of children, the asthma figures rose to 15% with an episode of wheezing characteristic within the previous year, 5% of them diagnosed as suffering from asthma, 1% with severe disabling asthma. It is useful to classify asthma as early-onset or extrinsic asthma, which occurs usually in atopic children and resolves in 80%. Late-onset asthma or idiopathic non-atopic adult asthma is chronic in the majority of cases.
It is produced by the inflammation of the bronchial wall involving eosinophils, mast cells and lymphocytes, together with the cytokine and inflammatory products of these cells, inducing hyper-sensitivity of the bronchi so that they narrow more readily in response to a wide range of stimuli. In brief, asthma may be described as presenting with either of the following three stages viz., air limitation, airway hyper-responsiveness & airway inflammation.

The principles for the management of patients with asthma, according to the guidelines of British Thoracic Society and International Consensus Report on the Diagnosis and Management of Asthma is as follows:

- Avoidance - measures to be taken to prevent/ reduce exposure to allergic agents.
- Hyposensitisation - subcutaneous injection of extracts of allergens (single allergen only). This form of therapy has largely been banned in Britain.

Management of Chronic persistent asthma

Inhaled corticosteroids are the most effective and widely used form of anti-inflammatory therapy for use in patients with asthma. Metered Dose Inhaler (MDI) is widely used technique to administer the bronchodilators or corticosteroids. In spite of different drugs and measures, neither there is a single oral agent, which will reduce the frequency of asthma attacks/ episodes nor an effective non-steroidal respiratory anti-inflammatory drug in the modern pharmacology.

On the other hand it is noticed that several traditional / indigenous herbal drugs are being successfully used in the management of bronchial asthma and are found to be of some definite advantage viz.,

- Avoidance of side-effects of corticosteroids
- Enhancement of immunity
- Relief from symptoms/ frequent episodes for a longer time.
- Better compliance.

Ayurvedic texts quoted Bronchial Asthma as Svasa or Tamakasvasa. This condition is denoted as a result of exposure to dust, clouds etc along with other causative factors. This is caused by vata obstructed by kapha in the pranavaha srotas. Tamakasvasa if associated with fever is called as Pratamaka while without fever is called as Samtamaka i.e., Chronic Bronchitis and Chronic Allergic Bronchial Asthma respectively. This condition is claimed to be yapya according to Caraka. The treatment includes Virecana and Nasya under Sodhana procedures. Several Samana dravyas like Yastimadhu, Vasa, Kantakari, Puskaramula, kushtha etc were found in the texts.

MATERIAL & METHODS

The powdered samples of the roots of Puschkaramula (Imula racemosa), Kushta (Saussurea lappa) and Erandamula (Ricinus communis) have formed the materials for the study while 90 subjects (divided into 30 subjects in each group) suffering from Tamaka Swasa (Bronchial Asthma) have formed the subjects [in the age group of 16-65 years] of the present study.

Aims & objectives of the study

Primary – To evaluate the comparative efficacy of Puschkaramula and its substitutes Kushta and Erandamula in the management of Tamakasvasa (Bronchial Asthma).

Secondary – Symptomatic relief from Bronchial Asthma & Clinical improvement in the condition of the patients after using the trial drugs for 12 weeks.

Study Design

- Open, Labeled, comparative, Randomized
- Prospective clinical trial

Subject recruitment and screening

Study Subjects - Mild to moderate Chronic Allergic Bronchial Asthma (NAEPP1997 revised guidelines) Subjects belonging to both the sex.

Recruitment

The Subjects were recruited from the OPD of Sri Dhanwantary Ayurvedic College & Hospital, Chandigarh and Seth Tarachand Hospital, Pune.

Inclusion & Exclusion criteria for study subjects

Inclusion criteria

- Subjects having mild to moderate Chronic Allergic Bronchial Asthma (NAEPP 1997 revised guidelines) belonging to both sex (atopic & non-atopic) are eligible.
- Subjects capable of understanding and signing an informed consent.
- Subjects between 16 to 65 years.
- Subjects medically stable and with normal LFT, RFT and Haemogram values.
- Subjects should not be in acute attack of Bronchial Asthma.

Exclusion criteria

- Subjects suffering from very severe/very chronic form of asthma
- Subjects with concurrent pulmonary disease (pulmonary hypertension, cystic fibrosis, sarcoidosis, bronchiectasis, hypersensitivity pneumonitis, restrictive lung disease etc.)
- Pregnant or Lactating mothers and females planning to get conceived in near future.
- Subjects suffering from very severe/very chronic form of asthma.
- Subjects with systemic diseases, like diabetes mellitus, venereal diseases and HIV.
- Subjects not willing to sign informed consent
- Subjects not willing to come for follow-up when required
- Subjects participating in any other clinical trials.

Therapeutic or Clinical end points

Therapeutic End Points: Treatment with the trial drugs for 12 weeks with or without improvement in the clinical condition of trial subjects.

Clinical End Points

- Relief of symptoms of Bronchial Asthma.
- Decrease in the frequency of attack.
- Decrease in the background modern medicines like Bronchodilators/steroids.

Dosage Schedule

All the trial drugs were given in a dose of 2.5 g b.i.d. (with or without modern standard T1) with honey thrice in a day.
Parameters for the Assessment of safety & efficacy

**Safety parameters**
- LFT
- RFT
- Haemogram

**Efficacy parameters**

**Subjective**
- Global Asthma Control Score
- QoL assessment

**Objective**
- IgE
- AEC
- Spirometry

Table 1a: Properties of trial drugs

<table>
<thead>
<tr>
<th>Properties</th>
<th>Puskaramula</th>
<th>Kustha</th>
<th>Erandamula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasa</td>
<td>Katu, Tikta</td>
<td>Usna, Tiksa, Lagha, Snigdha</td>
<td>Katu, Tikta</td>
</tr>
<tr>
<td>Guna</td>
<td>Usna</td>
<td>Usna</td>
<td>Usna</td>
</tr>
<tr>
<td>Virya</td>
<td>Katu</td>
<td>Usna</td>
<td>Usna</td>
</tr>
<tr>
<td>Vipaka</td>
<td>Usna</td>
<td>Usna</td>
<td>Usna</td>
</tr>
<tr>
<td>Prabhava</td>
<td>Hridya</td>
<td>Vrsya</td>
<td>Vrsya</td>
</tr>
<tr>
<td>Karma</td>
<td>Kapha-vathara, Hikkaniagrahana, Svasahara, Kasahara, Jvarahara, Sophaghnna</td>
<td>Vata-kaphahara, Kusthaghna, Sakrala, Kanduhara, Svasahara, Rasayanaya</td>
<td>Kapha-vathala, Jvarahara, Sophaghnna</td>
</tr>
<tr>
<td>Indications</td>
<td>Hricchula, Hrdroga, Parsvasula, Hikka, Svasa, Kasa, Sotha &amp; Jvara</td>
<td>Vatarakta, Visarpa, Kushta, Swasa, Kasa, Vataroga</td>
<td>Vataroga, Sotha, Jvara</td>
</tr>
<tr>
<td>Part used</td>
<td>Root (Mulam)</td>
<td>Root (Mulam)</td>
<td>Root (Mulam)</td>
</tr>
<tr>
<td>Dosage</td>
<td>2.5 - 5 g of powder</td>
<td>2.5 - 5 g of powder</td>
<td>2.5 - 5 g of powder</td>
</tr>
<tr>
<td>Anupana</td>
<td>Honey</td>
<td>Honey</td>
<td>Honey</td>
</tr>
</tbody>
</table>

Table 1b: Pharmacological activities of trial drugs

<table>
<thead>
<tr>
<th>Activity</th>
<th>Puskaramula</th>
<th>Kustha</th>
<th>Erandamula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-inflammatory activity</td>
<td>Extracts shown significant anti-inflammatory activity against exudative phase of inflammation when tested against carrageenin induced rat paw oedema (Singh, N. et al., 1976).</td>
<td>--</td>
<td>Root extract investigated against carrageenin, 5-hydroxytryptamine (5HT), dextran, bradykinin and prostaglandin E1 (PGE1)-induced rat hind paw oedema. Extract (0.15 g/kg) given orally 2 hr before injection of above phlogistic agents exhibited anti-inflammatory activity against all the agents except PGE1; efficacy of extract was: carrageenin &gt; bradykinin &gt; 5-HT &gt; dextran (Indian J. Pharmacol. 1990, 22, 239).</td>
</tr>
<tr>
<td>Bronchodilatory activity</td>
<td>Alcoholic extract showed marked protective effect against bronchospasm induced by histaminne, 5-HT, Zea maize, Holloptelia and Acacia arabica. The extract blocked the contraction induced by both histamine and 5-HT and the response was graded in nature (50, 100 &amp; 150 mg/ml of the bath solution). Imla has similar antispasmodic effect on rat uterus as seen as guinea pig ileum. It blocked the response of different doses (0.05, 0.1, 0.2, &amp; 0.4 mg/ml) of 5-HT in the dose range of 50 – 200 mg/ml.</td>
<td>Delactonized oil and some lactone fractions of the oil exhibited spasmo-lytic and broncho-dilatory effects (Chopra, 1958; Dutta, 1960).</td>
<td></td>
</tr>
<tr>
<td>Anti-histamine activity</td>
<td>The aqueous alcoholic extract of the roots was found to have potent anti-5-HT- and anti-histamine activities as revealed by blockade of histamine – induced contractions of isolated tracheal chain of guinea pig. The drug also offered marked protection against bronchospasm induced by histamine, 5-HT and pollens of Zea maize, Holloptelia sp., and A. arabica in guinea pigs. The beneficial effects of I. racemosa in bronchial asthma appear to be due to its anti-histaminic, anti-5-HT and antiallergic properties.</td>
<td>Alkaloids from root have a strong inhibitory effect on histamine-induced bronchospasm and intestinal spasm in guinea pigs. Chemical extracts from this herb have antispasmodic, bronchodilatory, and blood pressure lowering effects similar to, but weaker than papaverine (Oxygen for life, 1997).</td>
<td>--</td>
</tr>
</tbody>
</table>

Table 2: Number of Male and Female Subjects in the study

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>46</td>
<td>44</td>
</tr>
<tr>
<td>Percentage</td>
<td>51.11%</td>
<td>48.89%</td>
</tr>
</tbody>
</table>

Table 3: Mean Age of Each group involved in the study

<table>
<thead>
<tr>
<th>Group</th>
<th>Avg age</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr 1</td>
<td>39.43</td>
<td>(±)13.85</td>
</tr>
<tr>
<td>Gr 2</td>
<td>47.03</td>
<td>(±)13.93</td>
</tr>
<tr>
<td>Gr 3</td>
<td>43.57</td>
<td>(±)14.60</td>
</tr>
<tr>
<td>Gr 4</td>
<td>43.34</td>
<td>(±)13.81</td>
</tr>
</tbody>
</table>
Table 4: Effect of kustha on IgE

<table>
<thead>
<tr>
<th>IgE</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>73.33 (n=22)</td>
<td>26.67 (n=8)</td>
</tr>
<tr>
<td>After</td>
<td>26.67 (n=8)</td>
<td>73.33 (n=22)</td>
</tr>
</tbody>
</table>

Table 5: Effect of erandamula on IgE

<table>
<thead>
<tr>
<th>IgE</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>63.33 (n=19)</td>
<td>36.67 (n=11)</td>
</tr>
<tr>
<td>After</td>
<td>30 (n=9)</td>
<td>70 (n=21)</td>
</tr>
</tbody>
</table>

Table 6: Effect of puskaramula on AEC

<table>
<thead>
<tr>
<th>AEC</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>73.33 (n=22)</td>
<td>26.67 (n=8)</td>
</tr>
<tr>
<td>After</td>
<td>36.67 (n=11)</td>
<td>63.33 (n=19)</td>
</tr>
</tbody>
</table>

Table 7: Effect of kustha on AEC

<table>
<thead>
<tr>
<th>AEC</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>63.33 (n=19)</td>
<td>36.67 (n=11)</td>
</tr>
<tr>
<td>After</td>
<td>30 (n=9)</td>
<td>70 (n=21)</td>
</tr>
</tbody>
</table>

Table 8: Effect of erandamula on AEC

<table>
<thead>
<tr>
<th>AEC</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>73.33 (n=22)</td>
<td>26.67 (n=8)</td>
</tr>
<tr>
<td>After</td>
<td>30 (n=9)</td>
<td>70 (n=21)</td>
</tr>
</tbody>
</table>

Table 9: Effect of puskaramula on severity of asthmatic attack

<table>
<thead>
<tr>
<th>Asthmatic Attack</th>
<th>Severity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Treatment</td>
<td>Mild 63.33</td>
</tr>
<tr>
<td>After Treatment</td>
<td>Mild 100</td>
</tr>
</tbody>
</table>

Table 10: Spirometric evaluation of trial subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>Before treatment 2.44 ± 0.54</td>
<td>2.27 ± 0.38</td>
<td>2.32 ± 0.27</td>
</tr>
<tr>
<td></td>
<td>After treatment 2.66 ± 0.40</td>
<td>2.29 ± 0.28</td>
<td>2.33 ± 0.22</td>
</tr>
<tr>
<td>PEF</td>
<td>Before treatment 6.67 ± 1.38</td>
<td>6.18 ± 1.26</td>
<td>6.28 ± 1.26</td>
</tr>
<tr>
<td></td>
<td>After treatment 6.67 ± 1.32</td>
<td>6.25 ± 1.27</td>
<td>6.32 ± 1.30</td>
</tr>
<tr>
<td>FVC</td>
<td>Before treatment 3.24 ± 0.77</td>
<td>2.92 ± 0.55</td>
<td>2.98 ± 0.53</td>
</tr>
<tr>
<td></td>
<td>After treatment 3.24 ± 0.77</td>
<td>2.92 ± 0.55</td>
<td>2.98 ± 0.53</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>Before treatment 0.72 ± 0.15</td>
<td>0.70 ± 0.18</td>
<td>0.71 ± 0.17</td>
</tr>
<tr>
<td></td>
<td>After treatment 0.76 ± 0.08</td>
<td>0.76 ± 0.08</td>
<td>0.75 ± 0.07</td>
</tr>
</tbody>
</table>

Table 11: Reduction in usage of Inhalers etc in Group 1

<table>
<thead>
<tr>
<th>Use of Inhalers</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Treatment</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>After Treatment</td>
<td>23.33</td>
<td>76.67</td>
</tr>
</tbody>
</table>

Table 12: Reduction in usage of Inhalers etc in Group 2

<table>
<thead>
<tr>
<th>Use of Inhalers</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Treatment</td>
<td>66.67</td>
<td>33.33</td>
</tr>
<tr>
<td>After Treatment</td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 13: Reduction in usage of Inhalers etc in Group 3

<table>
<thead>
<tr>
<th>Use of Inhalers</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Treatment</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>After Treatment</td>
<td>16.67</td>
<td>83.33</td>
</tr>
</tbody>
</table>
RESULTS
Total 105 subjects belonging to both sexes, between the age group of 16-65 years were recruited into the study through randomization chart 3 into three groups (Group-1, Group-2 & Group-3). Out of them, 90 subjects who completed the total study duration (3 months) 30 subjects in each group were finally assessed for understanding the comparative effect of the respective herbs in each group. There were 44 females and 46 males (vide Table 2 & Chart 1). The mean age of the completed subjects (n=90) is 43.34 years (±3.81) - (vide Table 3).

The mean age (both male and female together) of Group 1 is 39.43 years (± 13.85), while that of Group 2 is 47.03 years (± 13.93) and that of Group 3 is 43.57 years (± 14.60).

Out of 90 subjects in three groups together, there were 16, 14 and 16 male in Group 1, 2 and 3 respectively while female were 14, 16 and 14 respectively in Group 1, 2 and 3. The mean age of male subjects in Group 1 is 36.69 years (± 14.86) while that in Group 2 is 45.57 years (± 15.24) and that in Group 3 is 39.38 years (± 14.66). The mean age of female subjects in Group 1 is 42.57 years (± 9.79) while that in Group 2 is 47.50 years (± 13.75) and that in Group 3 is 46.71 years (± 13.12).

Comparative Effect of Trial Drugs on Symptoms of Bronchial Asthma

Dyspnoea (breathlessness)
Dyspnoea was present in 90 % (n = 27) of subjects in Group 1 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 26.67% (n = 8) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Dyspnoea was present in 86.67 % (n = 26) of subjects in Group 2 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 20% (n = 6) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with Puskaramula.

Dyspnoea was present in 93.33 % (n = 27) of subjects in Group 3 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 23.33% (n = 7) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with kustha.

Scoring of Dyspnoea on VAS
When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, it was found that at baseline the mean score was 7 (± 1.37), which was reduced to 2 (±1.10) after administration of trial drug in group-1 for 12 weeks. The
reduction in the severity was found to be statistically significant (p<0.001).

When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, it was found that at baseline the mean score was 7 (+1.33), which was reduced to 2 (+1.10) after administration of trial drug in group-2 for 12 weeks. The reduction in the severity was found to be statistically significant (p<0.001) in all the three groups.

When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, it was found that at baseline the mean score was 7 (+1.33), which was reduced to 2 (+1.10) after administration of trial drug in group-3 for 12 weeks. The reduction in the severity was found to be statistically significant (p<0.001) in all the three groups.

There is a significant change between the baseline mean score and VAS score at the end of the study in each group (p < 0.001). However, the VAS score does not show significant variation when a comparison is made between the three groups (p > 0.01). That means there was intra group significance but not inter group significance. Almost all the groups showed comparable efficacy on dyspnoea. The details are present in Chart 2.

**Cough**

Cough was present in 80 % (n = 24) of subjects in Group 1 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 13.33% (n = 4) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Cough was present in 73.33 % (n = 22) of subjects in Group 2 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 10% (n = 3) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Cough was present in 70 % (n = 21) of subjects in Group 3 at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 10% (n = 3) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

The percentage of relief from cough in three groups is statistically as well as clinically significant when comparison is made between baseline and end of the study. The mean percentage of relief from cough in three groups is considerably reduced in all the subjects who were administered with kustha.

The mean reduction of IgE in all the three interventional drugs have similar effect or comparable effect.

**Effect of trial drugs on Serum IgE**

Serum IgE was found elevated in 53.33 % (n = 16) of subjects in Group 1 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 33.33% (n = 10) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 553.23 (+ 215.51) IU/mL and 279.11 (+188.97) IU/mL respectively (p < 0.001).

Serum IgE was found elevated in 73.33 % (n = 22) of subjects in Group 2 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 26.67% (n = 8) of subjects (Vide Table 4). The mean average of serum IgE at baseline and end of the study was found to be 490.13 (+221.4) IU/mL and 231.19 (+121.54) IU/mL respectively (p < 0.001).

Serum IgE was found elevated in 63.33 % (n = 19) of subjects in Group 3 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 30% (n = 9) of subjects (Vide Table 5). The mean average of serum IgE at baseline and end of the study was found to be 435.55 (+270.48) IU/mL and 224.76 (+159.88) IU/mL respectively (p < 0.001).

The mean reduction of IgE in all the three groups is statistically as well as clinically significant when comparison is made between the values at baseline and at end of the study (p < 0.001). However, there was no significant difference between the groups in percentage of relief (p > 0.05) showing that all the three interventional drugs have similar or comparable effect (Vide: Chart 3).

**Effect of trial drugs on AEC**

The AEC was found elevated in 73.33 % (n = 22) of subjects in Group 1 at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 36.67% (n = 11) of subjects (Vide Table 6). The mean average of AEC at baseline and end of the study was found to be 647.10 (+176) /Cmm and 341.00 (+100) /Cmm respectively (p < 0.001).

The AEC was found elevated in 63.33 % (n = 19) of subjects in Group 2 at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 30 % (n = 9) of subjects (Vide Table 7). The mean average of AEC at baseline and end of the study was found to be 621.30 (+173) /Cmm and 390.80 (+186) /Cmm respectively (p < 0.001).

The AEC was found elevated in 73.33 % (n = 22) of subjects in Group 3 at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 30 % (n = 9) of subjects (Vide Table 8). The mean average of AEC at baseline and end of the study was found to be 624.40 (+161) /Cmm and 366.80 (+198) /Cmm respectively (p < 0.001).

The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison is made between the values at baseline and at end of the study (p < 0.001 in each group). However, there was no significant
difference between the groups in percentage of relief (p > 0.05) showing that all the three interventional drugs have similar or comparable effect (Vide: Chart 4).

Severity of Asthmatic Attack
Out of 30 enrolled subjects in Group 1, 20% (n = 6) had history of severe asthmatic attacks, 60% (n = 18) reported moderate attacks and rest 20% (n = 6) reported presence of mild asthmatic attacks at baseline. After administration of Puskaramula for twelve weeks it was observed that in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 9.

Out of 30 enrolled subjects in Group 2, 23.33% (n = 7) had history of severe asthmatic attacks, 63.33% (n = 19) reported moderate attacks and rest 13.33% (n = 4) reported presence of mild asthmatic attacks at baseline. After administration of Kustha for twelve weeks it was observed that in 86.67% (n = 25) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 9.

Out of 30 enrolled subjects in Group 3, 26.67% (n = 8) had history of severe asthmatic attacks, 53.33% (n = 16) reported moderate attacks and rest 20% (n = 6) reported presence of mild asthmatic attacks at baseline. After administration of Erandamula for twelve weeks it was observed that in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 10.

Out of 30 enrolled subjects in Group 1, 20% (n = 6) had history of severe asthmatic attacks, 63.33% (n = 19) reported moderate attacks and rest 20% (n = 6) reported presence of mild asthmatic attacks at baseline. After administration of Puskaramula for twelve weeks it was observed that in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 9.

The percentage of relief from severity of asthmatic attack in all the three groups is statistically as well as clinically significant when comparison is made between baseline and end of the study (p < 0.001 in each group). However, the difference between the groups in percentage of relief is non significant (p > 0.05) showing that all the three interventional drugs have similar effect or comparable effect.

Effect of the trial drug on Spirometric parameters
Spirometry was performed for all the subjects recruited into the trial both at the baseline and at the end of the study (i.e., after 12 weeks) using 12 parameter MicroLabs spirometer. It is observed that the FEV1 in group 1, 2 and 3 is respectively 2.44 + 0.54; 2.27 + 0.38 and 2.32 + 0.27 at the baseline. The same at the end of the study is 2.43 + 0.53; 2.20 + 0.40 and 2.29 + 0.28 in group 1, 2 and 3 respectively.

The PEF reading in group 1, 2 and 3 is respectively 6.54 + 1.38; 6.18 + 1.26 and 6.28 + 1.26 at the baseline. The same at the end of the study is 6.67 + 1.33; 6.26 + 1.32 and 6.25 + 1.27 in group 1, 2 and 3 respectively.

FVC in group 1, 2 and 3 are respectively 3.53 + 1.01; 3.56 + 1.31 and 3.52 + 1.30 at the baseline. The same at the end of the study is 3.24 + 0.77; 2.92 + 0.55 and 2.98 + 0.53 in group 1, 2 and 3 respectively (Vide : Table No. 12).

The % reduction of FEV1 and PEF in the trial subjects is comparable in each group. But the variation between the groups is statistically not significant (p > 0.05).

Use of Inhaler
It was observed that 60% subjects (n=18) in Group 1 were using inhalers/oral medication at baseline. At the end of study this percentage came down to 23.33% (n=7) (Vide: Table 13). It was observed that 66.67% subjects (n = 20) in Group 2 were using inhalers/oral medication at baseline. At the end of study this percentage came down to 20% (n = 6) (Vide: Table 14). It was observed that 70% subjects (n=21) in Group 3 were using inhalers/oral medication at baseline. At the end of study this percentage came down to 16.67% (n=5) (Vide Table 15).

RESULTS
Evaluation of the observations on the basis of the obtained results indicate that there is clinical as well as statistical significance (p < 0.001) in the improvement observed in symptoms i.e. dyspnoea, wheezing and cough during the study in each group. The relief percentage is comparable between three groups i.e., statistically non-significant (p > 0.05).

There is statistically highly significant change observed in reduction of VAS scores of dyspnoea (p < 0.001) in each group, thereby inferring that dyspnoea in Bronchial Asthma can be controlled to a great extent by administering all the three interventional drugs. Their therapeutic benefit is comparable.

The IgE reducing effect of Puskaramula, Kustha and Erandamula churna are found to be comparable (p < 0.05).

Serum IgE was found elevated in 53.33 % (n = 16) of subjects in Group 1 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 33.33% (n = 10) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 253.23 (+ 215.51) IU/mL and 279.11 (+188.97) IU/mL respectively (p < 0.05). Serum IgE was found elevated in 73.33 % (n = 22) of subjects in Group 2 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 26.67% (n = 8) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 490.13 (+ 221.4) IU/mL and 231.19 (+121.54) IU/mL respectively (p < 0.05). Serum IgE was found elevated in 63.33 % (n = 19) of subjects in Group 3 at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 30% (n = 9) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 435.55 (+ 270.48) IU/mL and 224.76 (+159.88) IU/mL respectively (p > 0.05).

The AEC was elevated in 73.33 % (n = 22), 63.33 % (n = 19) & 73.33 % (n = 22) of subjects in Group 1, 2 & 3 respectively at the baseline. After 12 weeks of drug administration, the AEC was elevated only in 36.67 % (n = 11), 30 % (n = 9) & 30 % (n = 9) of subjects. The mean average of AEC at baseline was found to be 647.10 (+ 176) /Cmm, 621.30 (+ 173) /Cmm & 624.40 (+ 161) /Cmm respectively in Group 1, 2 & 3 respectively. The same is found to be 341.00 (+100) /Cmm, 390.80 (+186) & 366.80 (+198) /Cmm respectively at the end of the study in Group 1, 2 & 3.

The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study (p < 0.001 in each group). However, there was no significant difference between the groups in percentage of relief (p > 0.05) showing that the interventional drugs have comparable effect.

The daily dose of consumption of oral bronchodilators as well as other inhalers has come down significantly i.e., about 60% subjects (n=18) in Group 1 who were using inhalers/oral medication at baseline have come down to 23.33% (n=7) at the end of the study; about 66.67% subjects (n = 20) in Group 2 who were using inhalers/oral medication at baseline have come down to 20% (n = 6); and about 70% subjects (n=21)
in Group 3 who were using inhalers/oral medication at baseline have come down to 16.67% (n=5).

There is a significant reduction in the severity of Asthma attacks after the use of trial medicines in all the three groups. Out of 30 enrolled subjects in Group 1, 20% (n = 6), 60% (n = 18) and 20% (n = 6) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Puskaramula for twelve weeks in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while, no subject reported with severe attack. Out of 30 enrolled subjects in Group 2, 23.33% (n = 7), 63.33% (n = 19) and 13.33% (n = 4) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Kushta for twelve weeks in 86.67% (n = 25) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while no subject reported with severe asthmatic attack. Out of 30 enrolled subjects in Group 3, 26.67% (n = 8), 53.33% (n = 16) and 20% (n = 6) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Erandamula for twelve weeks in 86.67% (n = 25) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while no subject reported with severe attack.

All the trial drugs were found to be safe. No adverse drug reactions/ side effects of what so ever nature were observed in any of the subjects during the course of trial.

Therefore, it can be concluded on the basis of above findings that all the three trial drugs were equally effective in reducing the signs and symptoms of chronic bronchial asthma and has the capacity to reduce the dosage of oral medication as well as inhalers to a great extent (> 60%). The relief percentage within the groups is statistically highly significant (p < 0.001) while the same between the groups is non-significant (p > 0.05). Therefore it is concluded that all the three trial drugs are equally potential in reducing the symptoms of asthma.

Safety Profile
No significant change was observed in haemogram, Liver function tests (L.F.T.) and Renal function tests (R.F.T.) of any subject, carried out at baseline and after the treatment with trial drug (p > 0.05).

Adverse Drug Reactions (ADRs)
None of the subjects have reported with any major ADRs except nausea and vomiting in less than 1% of the subjects. Even these subjects attributed the symptoms to the bitter taste of Puskaramula and Kushta.

Drop outs & Early Withdrawal
There were two drop outs in group 1 and three each in group 2 and 3. But, these were noted to be due to personal reasons, not treatment related. None of the subjects withdrawn from study due to any adverse drug reaction or adverse event during the course of treatment with trial drug.

DISCUSSION
In the present study it is attempted to understand the rationality behind the concept of substitutes as mentioned in the ayurvedic texts. The study reveals statistically highly significant change in reduction of VAS scores of dyspnoea, cough and wheezing (p < 0.001) in group 1 & 2, confirming such observation made by earlier observers on Puskaramula and Kushta. The results in the group 3 are also comparable to group 1 & 2 indicating the anti-asthmatic effect of Erandamula for the first time. This effect is attributed to the unidentified tri-terpenoids present in the root of R. communis.

All the three trial herbs have exhibited comparable results on IgE reduction (p < 0.05). The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study (p < 0.001 in each group). However, there was no significant difference between the groups in percentage of relief (p > 0.05) showing that all the three interventional drugs have comparable effect.

The daily dose of consumption of oral bronchodilators as well as other inhalers has come down significantly in all the groups indicating that the trial drugs have comparable effects owing to the tri-terpenoids commonly present in all the three herbs. Similar studies on other substitutes will provide substantial information on the Abhavapratinidhi dravyas on the scientific basis.

CONCLUSION
The trial herbs (Pushkarmula / PM, Kushta / KS and Erandamula / EM) in the form of powder administered at the dose of 2 g twice daily with honey to the subjects suffering from Tamakaswasa / Bronchial Asthma showed comparable efficacy both statistically as well as clinically (p>0.05) justifying the substitute status.

Kushta (Sausurea lappa) root exhibited morphological, chemical and therapeutic similarity as a substitute for Puskaramula (Inula racemosa) whereas Erandamula (Ricinus communis) exhibited only therapeutic similarity as a substitute for Puskaramula.

The study proves the value of the fundamental concepts of Ayurveda. For example, doshaspratyanika cikitsa stands proven in this context of Erandamula as the substitute to Puskaramula while, vyadhipratyanika cikitsa is the case with Kushta as the substitute to Puskaramula.

REFERENCES
16. Lipworth BJ.; Clinical pharmacology of corticosteroids in bronchial asthma. Pharmacol Ther; 58: 173-209, 1993.

Cite this article as:

Source of support: Nil, Conflict of interest: None Declared