Hypertension is the commonest cardiovascular disorder, posing a major public health challenge to population. The prevalence of hypertension among adults in developed countries is 25%. A similar prevalence has also been observed in developing countries ranging from 10 to 20%. It has been shown that there were 972 million people living with hypertension worldwide in the year 2000, and it is estimated that this number will escalate to more than 1.56 billion by the year 2025. Around two-thirds of those people with hypertension worldwide were living in developing countries (639 million) in 2000, and this number is projected to rise to three-quarters living in developing countries (1.15 billion) by 2025. Hypertension is an important independent predictor of cardiovascular disease (CVD), cerebrovascular accidents and death. The prevalence of hypertension has been increasing in India, both in rural and urban regions. The prevalence of prehypertension in India is also increasing. This implies accompanying raise in other CVD risk factors in the Indian population. In India, CVDs are estimated to be responsible for 1.5 million deaths annually. Indeed, it is estimated that by 2020, CVDs will be the largest cause of mortality and morbidity in India. Trials completed within the last five years clearly indicate that overall cardiovascular risk is reduced by blood pressure (BP) lowering to levels below 140/90 mmHg. Greater cardiovascular risk reduction is not seen, however, by driving BP to levels well below 130/80 mmHg. Greater cardiovascular risk reduction is not seen, however, by driving BP to levels well below 130/80 mmHg. This is true across the spectrum of cardio renal risk with few exceptions, stroke prevention possibly being one. Antihypertensive drugs work in different ways to lower BP. Some drugs lower BP by removing extra fluid and salt from the body (e.g. diuretics). Others lower BP by slowing down the heartbeat (e.g. β-blockers), or by relaxing, widening or preventing the narrowing of

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**ABSTRACT**

Aims and objectives: The primary objective of the study was to evaluate and document the evidence-based efficacy and safety of the study drug in lowering blood pressure (BP). The secondary objectives included efficacy of the study drug in improving symptoms, quality-of-life (QOL) and biochemical parameters including treadmill and Doppler echocardiography. Study design: Phase IV post-marketing/surveillance study. Material and methods: Thirty-five subjects with prehypertension and hypertension (Stage 1 and Stage 2), attending the OPDs and camps of Heart Care Foundation of India were enrolled for the nonplacebo-controlled prospective study. The subjects were given homeopathic combination BPA (study drug) in liquid dosage for 12 weeks. Baseline clinical and biochemical parameters, treadmill test and Doppler echocardiogram were compared with the same parameters at the end of 12 weeks. Sixteen subjects completed the study. Results: There was a mean fall in systolic BP (SBP) of 15.75 mmHg and mean fall in diastolic BP (DBP) of 10.31 mmHg without any side effects. This significant decline in BP was evident from 4th week onwards. There was an appreciable increase in the exercise tolerance as evident by the 8.6% increase in metabolic equivalents (METs) and 8.2% increase in exercise time. No significant changes were observed in systolic or diastolic function parameters on Doppler echocardiography at three months. There was decrease in blood sugar from 96.5 ± 13.938 at baseline to 92.56 ± 12.329 at 12 weeks (p = 0.046). Serum uric acid levels also decreased from 5.681 ± 0.8998 at baseline to 6.031 ± 0.8822 at 12 weeks (p = 0.053) suggesting a beneficial effect of the combination on insulin resistance (IR). There were positive changes in the QOL as assessed by SF36 Questionnaire. The average Rand score improved from 54.53 ± 21.9991 to 77.55 ± 10.493 at 12 weeks (p < 0.001). All data are presented as mean ± standard deviation (SD). Conclusion: The results of the study showed that the study drug can be safely used as monotherapy in patients with prehypertension or hypertension with no complications.

Keywords: Homeopathic combination BPA, prehypertension, hypertension

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blood vessels (e.g., angiotensin-converting enzyme [ACE] inhibitors, calcium channel blockers [CCBs]).

A review has described the main homeopathic medicines whose center of action includes the heart, especially medicines commonly used in mother tincture form for hypertension.7 The study drug is a combination of seven drugs8-15 used for reducing high BP. They are well-known homeopathic medicines and help relieve associated symptoms of BP too. The drugs included are Rauwolfia serpentina 2X (5.00% v/v), Viscum album 3X (1.00% v/v), Crataegus oxyacantha 2X (1.00% v/v), Arnica montana 3X (0.25% v/v), Valeriana officinalis 3X (0.50% v/v), Melilotus alba 3X (0.25% v/v), Cactus grandiflorus 3X (0.25% v/v), Excipients q.s. and alcohol (7.00% v/v).

AIMS AND OBJECTIVES

Primary objective: To evaluate and document the evidence-based efficacy and safety of the study drug in lowering BP.

Secondary objectives:
- To assess the efficacy of the study drug in relieving symptoms associated with hypertension.
- To assess the efficacy of the study drug in improving quality-of-life (QOL) in hypertensive subjects.
- To assess the improvement or changes, if any, in necessary investigations performed at the beginning and end of study especially lipid profile, treadmill test and Doppler echocardiograms.

MATERIAL AND METHODS

Study Design

A phase IV post-marketing/surveillance study was done to delineate additional information on long-term benefits, optimal use and any side effects after approval of the study protocol from the Ethics Committee. The duration of the study was 15 months (October 2010 to December 2011). Subjects with prehypertension or hypertension without target organ damage attending the OPD and camps of Heart Care Foundation of India were included in the study. A total of 67 subjects were screened. There were 32 screen failures. A total of 35 subjects were enrolled, out of whom 16 subjects completed the study. There were 19 dropouts (lost to follow-up). Informed consent was obtained from each study subject. The study drug was dispensed in 30 ml bottle pack duly labeled as per the Drug Authority requirements. No placebo was used during the study. It was a nonrandomized nonblind open study.

Inclusion Criteria

- Adults of both sexes aged 25-75 years.
- Newly diagnosed or subjects with prehypertension (diastolic BP [DBP] 80-89 mmHg and systolic BP [SBP] 120-139 mmHg) of less than one year duration.
- Patients with stage 1 (SBP >140 and <160 and DBP >90 and <100 mmHg) and Stage 2 (SBP >160 and DBP >100 mmHg) hypertension. All subjects were subjected to a washout period of two weeks.
- Written informed consent for the use of the study drug as stand-alone treatment and necessary investigations.

Exclusion Criteria

- Known secondary hypertension
- Body mass index (BMI) >35 kg/m²
- Pregnant and lactating women
- Poorly-controlled hypertension and/or complications
- Target organ damage
- Diabetes
- Abnormal lab screening: Hemoglobin (Hb) <75% of lower limit, serum cholesterol >300 mg/dl
- Abnormal resting ECG
- Pre-existing chronic debilitating illness
- Subjects on hormonal contraceptives, steroids or nonsteroidal anti-inflammatory drugs (NSAIDs)

Investigations

Complete blood count (CBC), lipid profile, fasting blood sugar, serum creatinine, serum uric acid, serum glutamic pyruvic transaminase (SGPT), routine urinalysis, treadmill test and Doppler echocardiography were done at baseline and after 12 weeks of treatment.

Drug Dose Protocol

Each subject was given 20 drops of the study drug diluted with 30 ml water twice-daily. Patients who were intolerant to the study drug were instructed to start with 10 drops of the study drug diluted with 30 ml water twice-daily and increase the dose gradually to 15 and then 20 drops.

Follow-up

The subjects were clinically assessed every week and their BP readings were recorded. Investigations were done at baseline and after 12 weeks of treatment (completion of the study period).
**Statistical Methods**

Statistical analysis was done using the SPSS statistical package (version 17.0). Results are expressed as mean ± standard deviation (SD). Paired test was used to compare normally distributed continuous variables from pre- and post-intervention. BP values over time within the groups were analyzed using repeated measures analysis of variance (ANOVA) followed by Bonferroni’s post-hoc testing; p < 0.05 was considered statistically significant.

**RESULTS**

**Fall in Systolic BP**

Means of SBP starting from 0 week to the 12th week were analyzed. There was statistically significant (p < 0.001) mean fall in SBP of 15.75 mmHg at 12 weeks (95% confidence interval [CI] 9.25 to 22.25) (Table 1 and Fig. 1). Post-hoc tests using Bonferroni correction revealed that the reduction in SBP values was significant from 4th week onwards.

<table>
<thead>
<tr>
<th>Week</th>
<th>SBP Number of patients</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Change from Week 0 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16</td>
<td>146.25</td>
<td>9.83</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>135.75</td>
<td>9.74</td>
<td>–7.18%</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>138</td>
<td>14.17</td>
<td>–5.64%</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>134.06</td>
<td>12.89</td>
<td>–8.34%</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>131.75</td>
<td>9.03</td>
<td>–9.91%</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>133.69</td>
<td>13.46</td>
<td>–8.59%</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>132.63</td>
<td>12.92</td>
<td>–9.31%</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>131.88</td>
<td>11.01</td>
<td>–9.83%</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>131.81</td>
<td>10.37</td>
<td>–8.87%</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>134.75</td>
<td>11.13</td>
<td>–7.86%</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>131.44</td>
<td>10.84</td>
<td>–10.13%</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>133.88</td>
<td>13.65</td>
<td>–8.46%</td>
</tr>
<tr>
<td>12</td>
<td>16</td>
<td>130.5</td>
<td>11.97</td>
<td>–10.77%</td>
</tr>
</tbody>
</table>

**Fall in Diastolic BP**

There was statistically significant mean fall in DBP of 10.31 mmHg from 0 to 12 weeks (95% CI 5.57 to 15.05) (p < 0.001) (Table 2 and Fig. 2). Post-hoc tests using Bonferroni correction revealed that the reduction in DBP values was again significant from the 4th week onwards.

<table>
<thead>
<tr>
<th>Week</th>
<th>DBP Number of patients</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Change from Week 0 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16</td>
<td>95.44</td>
<td>7.92</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>86.69</td>
<td>7.49</td>
<td>–9.17%</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>85.69</td>
<td>10.21</td>
<td>–10.22%</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>86.69</td>
<td>7.49</td>
<td>–9.17%</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>85.06</td>
<td>7.64</td>
<td>–10.88%</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>87.06</td>
<td>7.84</td>
<td>–8.78%</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>84.63</td>
<td>10.58</td>
<td>–11.33%</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>86.38</td>
<td>7.94</td>
<td>–9.49%</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>85.38</td>
<td>10.06</td>
<td>–10.54%</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>89.06</td>
<td>9.70</td>
<td>–6.68%</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>85.25</td>
<td>6.06</td>
<td>–10.68%</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>86.94</td>
<td>8.43</td>
<td>–8.91%</td>
</tr>
<tr>
<td>12</td>
<td>16</td>
<td>85.13</td>
<td>8.76</td>
<td>–10.80%</td>
</tr>
</tbody>
</table>

Figure 1. Reduction in SBP.

Figure 2. Reduction in DBP.
There was no statistical significant change in Echo parameters after three months of treatment.

- No significant differences were observed in the means of E/A (ratio of mitral E-wave velocity to mitral A-wave velocity) at baseline (1.15 ± 0.32) and after three months (1.10 ± 0.34) (p = 0.535). The observed mean difference was 0.05 (95% CI –0.11 to 0.19).
- There were no significant differences in the means of E/E' ratio (ratio of early mitral inflow to early mitral annular velocity) at baseline (9.03 ± 1.97) and after three months (9.22 ± 2.5) (p = 0.788). The observed mean difference was 0.19 (95% CI –1.65 to 1.27).

No significant differences were observed in the means of left ventricular (LV) end-diastolic dimension at baseline (40 ± 4.81) and after three months (39.08 ± 4.43) (p = 0.156). The observed mean difference was 0.93 (95% CI –0.39 to 2.24).

No significant differences were observed in the means of aortic diameter (Ao) at baseline (29.86 ± 3.44) and after three months (29.54 ± 3.35) (p = 0.682). The observed mean difference was 0.32 (95% CI –1.31 to 1.95).

There was no significant difference in the means of left atrial (LA) diameter at baseline (28.75 ± 3.05) and after three months (28.49 ± 3.01) (p = 0.529). The observed mean difference was 0.26 (95% CI –0.98 to 1.28).

There was no significant difference in the means of LV septum at baseline (9.78 ± 1.29) and after three months (9.77 ± 1.17) (p = 0.969). The observed mean difference was 0.01 (95% CI –0.69 to 0.72).

There was no significant difference in the means of LV end-diastolic dimension at baseline (40 ± 4.81) and after three months (39.08 ± 4.43) (p = 0.156). The observed mean difference was 0.93 (95% CI –0.39 to 2.24).

Biochemistry

There was no significant difference in the means from baseline to the end of study for Hb (14.406 ± 1.3463 at baseline and 14.106 ± 1.3102 at 12 weeks [p = 0.193]); erythrocyte sedimentation rate (ESR) (15.69 ± 13.553 at baseline and 16.25 ± 8.497 at 12 weeks [p = 0.847]); serum creatinine (0.888 ± 0.1854 at baseline and 0.85 ± 0.1838 at 12 weeks [p = 0.315]); SGPT (51.38 ± 40.516 at baseline and 44.63 ± 19.677 at 12 weeks [p = 0.534]); total cholesterol (183.88 ± 39.16 at baseline and 194.25 ± 35.21 at 12 weeks [p = 0.191]); low-density lipoprotein (LDL) cholesterol (122.56 ± 36.30 at baseline and 127.20 ± 29.25 at 12 weeks [p = 0.476]); VLDL cholesterol (25.66 ± 8 at baseline and 28.48 ± 10.59 at 12 weeks [p = 0.209]); high-density lipoprotein (HDL) cholesterol (42.38 ± 9.14 at baseline and 41.38 ± 8 at 12 weeks [p = 0.315]); and triglycerides (128.31 ± 40.01 at baseline and 142.31 ± 53.15 at 12 weeks [p = 0.213]).

Blood sugar decreased at three months (96.5 ± 13.938 at baseline and 92.56 ± 12.329 at 12 weeks [p = 0.046]). A similar decrease was seen in the serum uric acid levels (5.681 ± 0.8998 at baseline and 6.031 ± 0.8822 at 12 weeks [p = 0.053]). Both these changes suggested a beneficial effect on the insulin resistance (IR). There was no change in BMI (28.62 ± 5.69 at baseline and 28.32 ± 5.83 at 12 weeks [p = 0.160]).
Changes in QOL
Change in QOL was assessed by SF36 Questionnaire and each subject was scored before and after completion of study. The average Rand score improved from 54.53 ± 21.9991 at baseline to 77.55 ± 10.493 at 12 weeks (p < 0.001).

Safety Evaluation
No serious adverse events were reported during the entire course of the study.

DISCUSSION
In a review of short-term studies on antihypertensives including CCBs, diuretics, ACE inhibitors, α-blockers, β-blockers, angiotensin II receptor blockers, the change in SBP and DBP was a negative value ranging from −2 to even −12 points, which is comparable to that observed in the current study with mean fall in SBP of 13.75 mmHg and mean fall in DBP of 10.31 mmHg without any side effects observed during the entire study duration. The change however was observed for over a period of 12 weeks with a statistically significant fall observed from 4th week onwards, so the study drug can be used safely used for prehypertension, Stage 1 hypertension and for Stage 2 excluding hypertensive emergencies and urgencies. There were appreciable increase in METs by 8.6% and exercise time by 8.2%, though no change was observed in echo parameters as duration of observation was just 12 weeks during which a change in echo is not expected as the trends go in other such studies.

CONCLUSION
The results of the study showed that the study drug can safely be used as monotherapy in patients with prehypertension or hypertension without complications. This is only a preliminary study and more data needs to be collected for further collaboration. A prolonged study for a period of at least six months to one year is needed for an in-depth analysis of the medicine.

Acknowledgment
The study product BPA (Bee Pee Aid) was supplied by Bakson Drugs and Pharmaceuticals Pvt. Ltd.

Disclaimer
It was an independent study and not influenced by any market forces.

REFERENCES
One trial examined the efficacy of pumpkin seed extract alone. In this placebo-controlled, year-long study, 476 patients were randomly assigned to receive placebo or 500 mg/day of seed extract. Although, there was an identical effect in both groups in $Q_{\text{max}}$, quality-of-life, and PVR at study end, the group that received phytotherapy showed a decrease in International Prostate Symptoms Score (IPSS) (6.7 points) over the placebo group (5.5 points). This 1.2 point is statistically significant.\(^9\)

**CONCLUSION**

Uncontrolled studies with low patient numbers and of short duration, not performed according to accepted standards and guidelines, are of questionable value. Meta-analysis are only acceptable if the quality of the studies included is assessed and shown to be appropriate. Due to the widely controversial and partly insufficient ‘hard’ data about the efficacy of phytotherapy for the treatment of LUTS due to BPH, the International Consultation on BPH were reluctant to recommend phytotherapy. However, a review of the role of phytotherapy in the management of LUTS due to BPH is needed.

**REFERENCES**