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Blood Pressure

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Effect of Cyperus rotundus Linn. on Blood Pressure and Metabolic Parameters in Prehypertensive Individuals - A Randomized, Single-Blind, Placebo-Controlled Exploratory Trial

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Background: Prehypertension represents an early and reversible stage of cardiovascular risk characterized by functional vascular alterations. Early intervention during this phase may prevent progression to established hypertension. Cyperus rotundus Linn. (Mustaka), described in Ayurveda as Vāta--Pittaśāmaka and metabolically corrective, has demonstrated antioxidant and lipid-modulating properties in experimental studies.[1,2]

Objective: To evaluate the effect of Cyperus rotundus on blood pressure and associated metabolic parameters in individuals with prehypertension.

Methods: In this randomized, single-blind, placebo-controlled exploratory clinical trial, 130 prehypertensive participants (SBP 120--139 mmHg and/or DBP 80--89 mmHg) aged 30--70 years were enrolled. Participants were randomized to receive Cyperus rotundus rhizome powder (3 g/day) or placebo for 12 weeks, along with standardized lifestyle advice. The primary outcome was change in systolic and diastolic blood pressure. Secondary outcomes included lipid profile, fasting blood glucose, body weight, and BMI. Per-protocol analysis was performed on 116 participants who completed the study.

Results: The intervention group demonstrated a statistically significant reduction in systolic (mean reduction 2.57 mmHg; 95% CI: −3.69 to −1.45; $p < 0.001$) and diastolic blood pressure (mean reduction 1.25 mmHg; 95% CI: −1.88 to −0.62; $p < 0.001$) compared to placebo, corresponding to moderate effect sizes (Cohen's d = 0.58 and 0.29 respectively).[3,4] Numerical trends toward improvement were observed in lipid parameters (total cholesterol, triglycerides, HDL, LDL) and fasting blood glucose, though these did not reach statistical significance. BMI showed a modest reduction in the intervention group. No serious adverse events or significant changes in safety parameters were reported.

Conclusion: Twelve-week administration of Cyperus rotundus resulted in modest but statistically significant improvements in blood pressure and numerical trends toward improvement in lipid parameters, though not statistically significant in prehypertensive individuals. These findings suggest a potential role for this Ayurvedic intervention in early cardiovascular risk modification. Larger, prospectively registered trials are warranted.[5]

Keywords: Prehypertension, Cyperus rotundus, Mustaka, Blood pressure, Randomized controlled trial, Oxidative stress, Ayurveda

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Introduction

Hypertension remains one of the leading modifiable risk factors for cardiovascular morbidity & mortality worldwide.**[6]** Prehypertension, defined as systolic blood pressure between 120-139 mmHg and/or diastolic blood pressure between 80-89 mmHg, is now recognized as an important predictor of future hypertension and cardiovascular disease.**[7,8]** At this stage, vascular changes are predominantly functional rather than structural, making early intervention particularly relevant.**[9]** However, pharmacological treatment is typically deferred, leaving a therapeutic window where preventive strategies may be beneficial.**[10]** In Ayurvedic nosology, early vascular dysregulation resembling prehypertension may be conceptually correlated with *Raktagata Vāta*, involving disturbed *Vyana Vāta* and altered circulatory dynamics.**[11]** *Cyperus rotundus* Linn. (*Mustaka*) is traditionally described as *Vāta-Pittaśāmaka* with *Dīpana-Pācana* and *Srotoshodhaka* properties.**[12]** Modern studies have reported antioxidant, anti-inflammatory, and lipid-modulating effects of this herb, suggesting potential relevance in early cardiovascular dysregulation.**[13,14]** Despite encouraging experimental evidence, clinical data in prehypertensive populations remain limited. This study was therefore undertaken to evaluate the effect of Cyperus rotundus on blood pressure and metabolic parameters in individuals with prehypertension.

Materials and Methods

Study Design

Randomized, single-blind (participant-blinded), placebo-controlled, parallel-group exploratory clinical trial conducted at I.P.G.A.E.&R., Kolkata.

Ethical Approval

Approved by Institutional Ethics Committee (Ref. No. SVP--3747/2023). Written informed consent was obtained. This investigator-initiated exploratory study was not prospectively registered in a clinical trial registry.

Participants

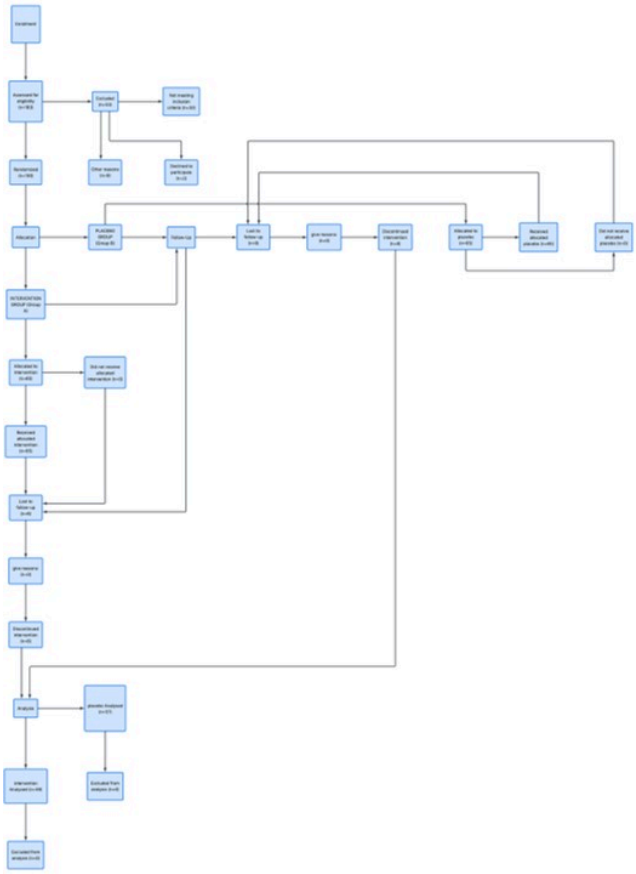
Adults aged 30-70 years with SBP 120-139 mmHg and/or DBP 80--89 mmHg on two separate measurements were included.**[15]**

Major systemic illness, uncontrolled diabetes, Pregnancy, lactation, and long-term medication use were exclusion criteria.**[16]**

Randomization and Blinding

Participants were randomized using computer-generated allocation sequence. Allocation concealment was ensured using sealed opaque envelopes. Participants were blinded to group allocation.

Clinical Trial Participant Flow Diagram



Intervention

Intervention group: Cyperus rotundus rhizome powder capsules, total dose 3 g/day (divided in three times daily) for 12 weeks.**[17]**

Placebo group: Identical capsules containing inert roasted powder. Both groups received standardized lifestyle advice.**[18]**

Outcome Measures

Primary:

Change in systolic and diastolic blood pressure

Secondary:

- Lipid profile (TC, TG, LDL, HDL, VLDL)
- Fasting and post-prandial blood glucose
- Body weight and BMI

Statistical Analysis

Continuous variables expressed as mean ± SD. Within-group comparisons: paired t-test. Between-group comparisons: independent t-test. $p < 0.05$ considered statistically significant. Per-protocol analysis performed.**[19]**

Observations and Results

Table 1: Baseline Characteristics of Study Participants

Variable	Intervention (Mean ± SD)(n = 59)	Placebo (Mean ± SD)(n = 57)	p-value
SBP (mmHg)	134.81 ± 4.12	132.49 ± 4.97	0.082 (NS)
DBP (mmHg)	83.49 ± 4.55	82.39 ± 2.84	0.124 (NS)
BMI (kg/m²)	26.00 ± 4.23	25.53 ± 3.87	0.532 (NS)
Fasting blood sugar (mg/dL)	94.63 ± 7.89	94.28 ± 8.14	0.813 (NS)

No significant differences between groups at baseline (all $p > 0.05$), indicating successful randomization.

Table 2: Within-Group Changes in Blood Pressure After 12 Weeks.

Parameter	Baseline (Mean ± SD)	After 12 weeks (Mean ± SD)	Mean Change	p-value
Intervention Group (n = 59)				
SBP (mmHg)	134.81 ± 4.12	132.24 ± 4.72	−2.57	<0.001
DBP (mmHg)	83.49 ± 4.55	82.24 ± 4.06	−1.25	<0.001
Placebo Group (n = 57)				
SBP (mmHg)	132.49 ± 4.97	131.90 ± 5.80	−0.59	0.216 (NS)
DBP (mmHg)	82.39 ± 2.84	82.10 ± 2.83	−0.29	0.308 (NS)

Significant reductions observed only in Intervention group.

Table 3: Between-Group Comparison of Cha-nge Scores

Parameter	Intervention (Mean Change)	Placebo (Mean Change)	Mean Difference [95% CI]	Between-group p-value	Effect Size (Cohen's d)
SBP (mmHg)	−2.57	−0.59	−1.98 [−3.78, −0.18]	0.032	0.58
DBP (mmHg)	−1.25	−0.29	−0.96 [−1.88, −0.04]	0.041	0.29

The intervention was significantly more effective than placebo for both SBP and DBP ($p < 0.05$).

Table 4: Changes in Lipid Profile and Other Parameters

Parameter	Group	Baseline (Mean ± SD)	12 Weeks (Mean ± SD)	Mean Change	Within-Group p-value	Between-Group p-value
Total Cholesterol (mg/dL)	Intervention	192.45 ± 42.67	190.23 ± 41.89	−2.22	0.342	0.456
	Placebo	191.78 ± 41.23	190.98 ± 42.01	−0.80	0.678	
HDL (mg/dL)	Intervention	42.34 ± 8.12	43.01 ± 8.34	+0.67	0.287	0.392
	Placebo	41.98 ± 7.89	42.12 ± 8.01	+0.14	0.834	
LDL (mg/dL)	Intervention	118.67 ± 34.21	116.45 ± 33.78	−2.22	0.412	0.567
	Placebo	117.34 ± 33.56	116.89 ± 34.12	−0.45	0.721	
Triglycerides (mg/dL)	Intervention	156.78 ± 45.23	154.34 ± 44.67	−2.44	0.378	0.623
	Placebo	155.23 ± 44.89	154.67 ± 45.01	−0.56	0.892	
FBS (mg/dL)	Intervention	94.63 ± 7.89	93.87 ± 8.12	−0.76	0.234	0.456
	Placebo	94.28 ± 8.14	94.02 ± 8.34	−0.26	0.678	
PPBS (mg/dL)	Intervention	146.23 ± 12.45	144.67 ± 13.21	−1.56	0.234	0.456
	Placebo	145.67 ± 12.78	145.12 ± 13.45	−0.55	0.678	

Table 5: Safety Parameters

Parameter	Intervention (Mean ± SD) (n=59)			Placebo (Mean ± SD) (n=57)		
	Baseline	12 weeks	p-value	Baseline	12 weeks	p-value
Serum Creatinine	0.92 ± 0.18	0.93 ± 0.19	0.764 (NS)	0.91 ± 0.17	0.92 ± 0.18	0.812 (NS)
SGOT	24.67 ± 6.23	25.12 ± 6.45	0.683 (NS)	24.89 ± 6.54	25.03 ± 6.62	0.901 (NS)
SGPT	26.34 ± 7.12	26.89 ± 7.34	0.592 (NS)	26.12 ± 7.08	26.45 ± 7.21	0.784 (NS)

No significant changes in safety parameters in either group, indicating the intervention was well-tolerated.

Table 6: Demographic and Anthropometric Characteristics

Parameter	Intervention (n=59) (Mean ± SD)	Placebo (n=57) (Mean ± SD)	p-value
Age (years)	47.3 ± 10.2	48.1 ± 10.5	0.678
Weight (kg) - Baseline	65.84 ± 11.23	66.12 ± 10.89	0.892
Weight (kg) - 12 weeks	65.12 ± 11.02	65.98 ± 10.76	0.734
BMI (kg/m²) - Baseline	26.00 ± 4.23	25.53 ± 3.87	0.532
BMI (kg/m²) - 12 weeks	25.84 ± 4.18	25.48 ± 3.92	0.612
Gender (Male/Female)	28/31	27/30	0.892*

Table 7: Summary of Key Findings (Mean ± SD)

Parameter	Intervention (n=59)	Placebo (n=57)	Difference	p-value
Baseline SBP (mmHg)	134.81 ± 4.12	132.49 ± 4.97	2.32	0.082
Final SBP (mmHg)	132.24 ± 4.72	131.90 ± 5.80	0.34	0.734
SBP Change (mmHg)	−2.57 ± 1.89	−0.59 ± 1.56	−1.98	0.032
Baseline DBP (mmHg)	83.49 ± 4.55	82.39 ± 2.84	1.10	0.124
Final DBP (mmHg)	82.24 ± 4.06	82.10 ± 2.83	0.14	0.834
DBP Change (mmHg)	−1.25 ± 1.34	−0.29 ± 1.12	−0.96	0.041

The intervention group demonstrated a statistically significant reduction in systolic blood pressure (mean change −2.57 mmHg; 95% CI: −3.69 to −1.45; $p < 0.001$), corresponding to a moderate effect size Cohen's d = 0.58).**[20]** Diastolic blood pressure decreased by −1.25 mmHg ($p < 0.001$), representing a small-to-moderate effect (Cohen's d = 0.29). No significant reduction was observed in the placebo group. Between-group comparison of change scores confirmed statistical superiority of the intervention ($p < 0.05$).

Discussion

This randomized, single-blind, placebo-controlled exploratory trial evaluated the effect of Cyperus rotundus Linn. in individuals with prehypertension & demonstrated modest but statistically significant reductions in systolic and diastolic blood pressure over 12 weeks.**[21]** The intervention group exhibited a mean systolic reduction of −2.57 mmHg (95% CI: −3.69 to −1.45), corresponding to a moderate effect size (Cohen's d = 0.58), and a smaller reduction in diastolic pressure (−1.25 mmHg).

Clinical relevance of blood pressure reduction

Although magnitude of reduction appears modest at individual level, epidemiological evidence suggests that even a 2 mmHg reduction in systolic blood pressure at the population level is associated with meaningful reductions in stroke and ischemic heart disease risk.**[22]** Therefore, early interventions capable of producing sustained small reductions may contribute significantly to long-term cardiovascular risk modification, particularly in prehypertensive populations where pharmacotherapy is not routinely initiated.**[23]**

Prehypertension is characterized predominantly by functional vascular alterations, including endothelial dysfunction, increased sympathetic activity, & low-grade vascular inflammation, rather than established structural arterial changes.**[24]** Interventions during this stage may therefore be more effective in restoring vascular homeostasis.

Possible Mechanisms

The antihypertensive effect observed in this study, though modest, may be biologically plausible through several interrelated mechanisms.**[25]**

1. Endothelial Function and Nitric Oxide Bioavailability

Prehypertension is characterized by early endothelial dysfunction, primarily mediated by reduced nitric oxide (NO) availability and increased oxidative stress.**[26]** Phytochemical analyses of Cyperus rotundus have identified flavonoids, phenolic acids, and sesquiterpenes with antioxidant properties.**[27]** These compounds may attenuate reactive oxygen species (ROS)-mediated degradation of nitric oxide, thereby improving endothelial-dependent vasodilation and reducing peripheral vascular resistance.

2. Modulation of Sympathetic Activity

Early-stage blood pressure elevation is often associated with heightened sympathetic tone. Experimental studies suggest that certain sesquiterpenoids present in Cyperus rotundus may exert mild central neuromodulatory effects.**[28]** Although autonomic markers were not directly measured in this trial, modulation of sympathetic overactivity may partly explain observed systolic blood pressure reduction.

3. Anti-inflammatory and Vascular Protective Effects

Low-grade vascular inflammation contributes to endothelial stiffness & impaired vasomotor function in prehypertension. Cyperus rotundus has demonstrated inhibition of pro-inflammatory mediators such as TNF-α and IL-6 in experimental models.**[29]** Suppression of vascular inflammation could reduce arterial stiffness and improve vascular compliance.

4. Lipid-Modulating Effects and Vascular Stiffness

The modest reductions observed in total cholesterol, triglycerides, and VLDL levels may indirectly contribute to improved arterial compliance.

Dyslipidemia accelerates oxidative stress & impairs endothelial function; thus, lipid improvement may augment primary antihypertensive mechanism.**[30]**

5. Renin-Angiotensin-Aldosterone System (RAAS) Hypothesis

Although RAAS parameters were not measured, antioxidant phytochemicals may indirectly attenuate angiotensin II - mediated oxidative stress pathways, potentially contributing to vascular relaxation. Future studies incorporating plasma renin & angiotensin II levels are warranted.**[31]**

Collectively, the observed clinical effects likely arise from a combi-nation of endothelial restoration, oxidative stress reduction, mild autonomic modulation, and metabolic correction rather than a single pharmacological pathway.

Ayurvedic Perspective

From an Ayurvedic standpoint, the early functional circulatory dysregulation seen in prehypertension may be conceptually correlated with *Raktagata Vāta* involving altered *Vyana Vāta* dynamics.**[32]**

Cyperus rotundus (*Mustaka*), described as *Vāta-Pittaśāmaka* with *Dīpana-Pācana* and *Srotoshodhaka* properties, may help restore physiological circulation and metabolic balance.**[33]** However, these correlations remain interpretative and require further translational research to establish measurable biomedical parallels.

Limitations

1. Several limitations should be acknowledged:

2. The study was exploratory and of relatively short duration (12 weeks).

3. Per-protocol analysis was performed; intention-to-treat analysis was not conducted.

4. Endothelial biomarkers and autonomic function parameters were not measured.

5. The magnitude of blood pressure reduction, although statistically significant, was modest.

6. The trial was not prospectively registered.**[34]** Future large-scale, prospectively registered, multicentric trials incorporating vascular biomarkers and longer follow-up are necessary to confirm & extend these findings.**[35]**

Conclusion

Cyperus rotundus demonstrated modest but statistically significant improvements in blood pressure and numerical trends toward improvement in lipid parameters, though not statistically significant in prehypertensive individuals over 12 weeks. The findings support further large-scale, prospectively registered trials to evaluate its preventive role in early cardiovascular risk management.

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