

EFFECT OF A NOVEL GRAPE SEED EXTRACT ON BLOOD PRESSURE IN SUBJECTS WITH PREHYPERTENSION

Bob Lu, BA, Melissa Robinson, MD, C. Tissa Kappagoda, MBBS, PhD
 Division of Cardiovascular Medicine, University of California, Davis School of Medicine



BACKGROUND

Hypertension has long been recognized as a significant risk factor for cardiovascular, cerebrovascular and renal disease. The most recent Joint National Committee guidelines for hypertension (JNC 7) reclassified this disease and added the new category of prehypertension (Table 1). Patients with pre-hypertension are at increased risk of cardiovascular events as well as progression to frank hypertension. Current treatment guidelines recommend lifestyle changes without pharmaceutical intervention. Meganatural BP® (Polyphenolics, Inc., Madera, CA) is a novel grape seed extract (GSE) which is manufactured through a patented extraction process (Figure 1). It has an average degree of polymerization of 2.6 and a total phenolic content of ~94% and is unique in lacking terminal gallate residues usually found in GSEs. This GSE has previously been shown to cause endothelium-dependent relaxation in rabbit aorta (Figure 2) resulting from activation of eNOS. We have also shown this to be mediated through the activation of the AKT/IP3 pathway (ref). In a previous trial of patients with metabolic syndrome, GSE was found to lower blood pressure significantly. We hypothesized that this novel grape seed extract would also lower blood pressure in subjects with prehypertension.

Figure 1 GRAPE SEED EXTRACT

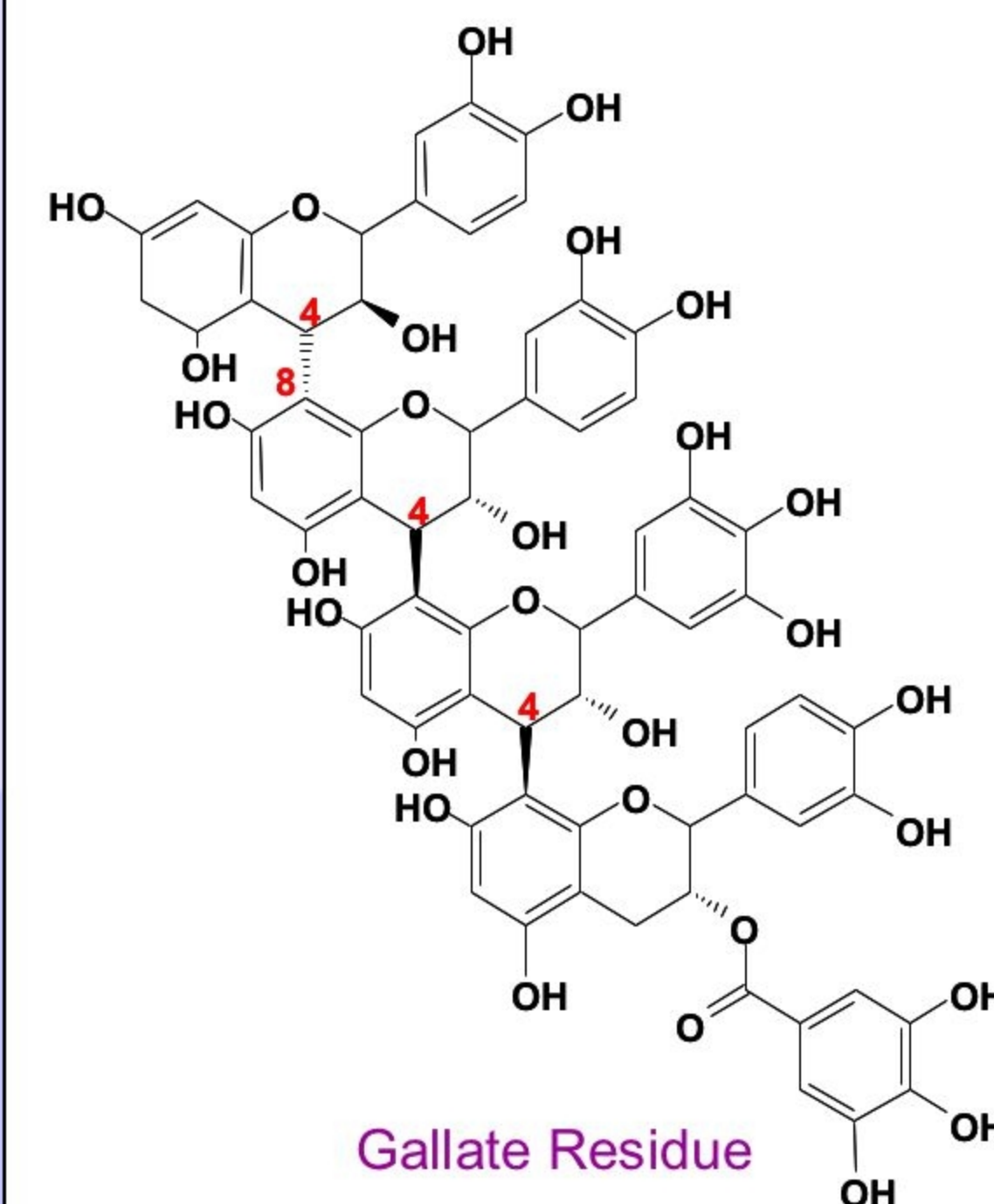
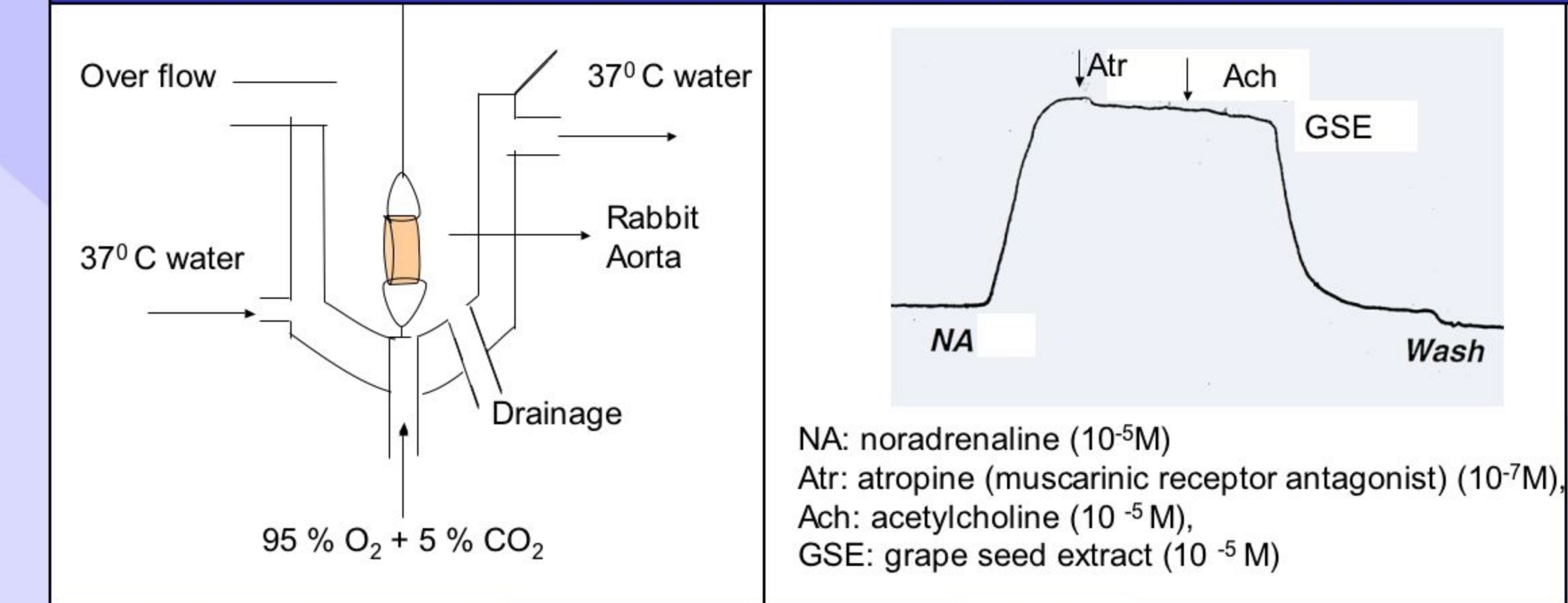


Table 2 – BASELINE CHARACTERISTICS

	Placebo	GSE
Age (yr)	54 +/- 3	50 +/- 2.5
BMI	26.9 +/- 1	26.3 +/- 2
Male/Female	9/6	7/8
Systolic (mmHg)	135 +/- 2	133 +/- 2
Diastolic (mmHg)	79 +/- 2	79 +/- 2
Total Chol (mg/dL)	204 +/- 9	200 +/- 10
LDL (mg/dL)	134 +/- 9	128 +/- 9
HDL (mg/dL)	48 +/- 3	55 +/- 4
Glucose (mg/dL)	87 +/- 4	90 +/- 3

Figure 2 GSE Causes Endothelium Dependent Relaxation



METHODS

A convenience sample of 66 subjects with a resting systolic blood pressure (SBP) between 120 and 139 mm Hg and/or a diastolic blood pressure (DBP) between 80 and 89 mmHg were recruited. Subjects underwent 24 hour ambulatory blood pressure monitoring (Tiba Medical, Inc.). Patients were excluded if they had frank hypertension on baseline monitoring, were currently taking anti-hypertensive medication or nutritional supplements. Thirty subjects met criteria for entry (Table 2). There were no significant differences in any baseline characteristics. After a placebo run-in period of two weeks, patients were blindly randomized to either GSE 300mg orally daily or placebo (maltodextrin) for eight weeks. Labs and blood pressure monitoring was then repeated.

RESULTS

Results are presented in Table 3 and Figures 3. One patient in the placebo group developed frank hypertension requiring therapy. There was no significant changes in serum lipids, blood glucose, renal function or blood count.

Figure 3 CHANGE IN BLOOD PRESSURE

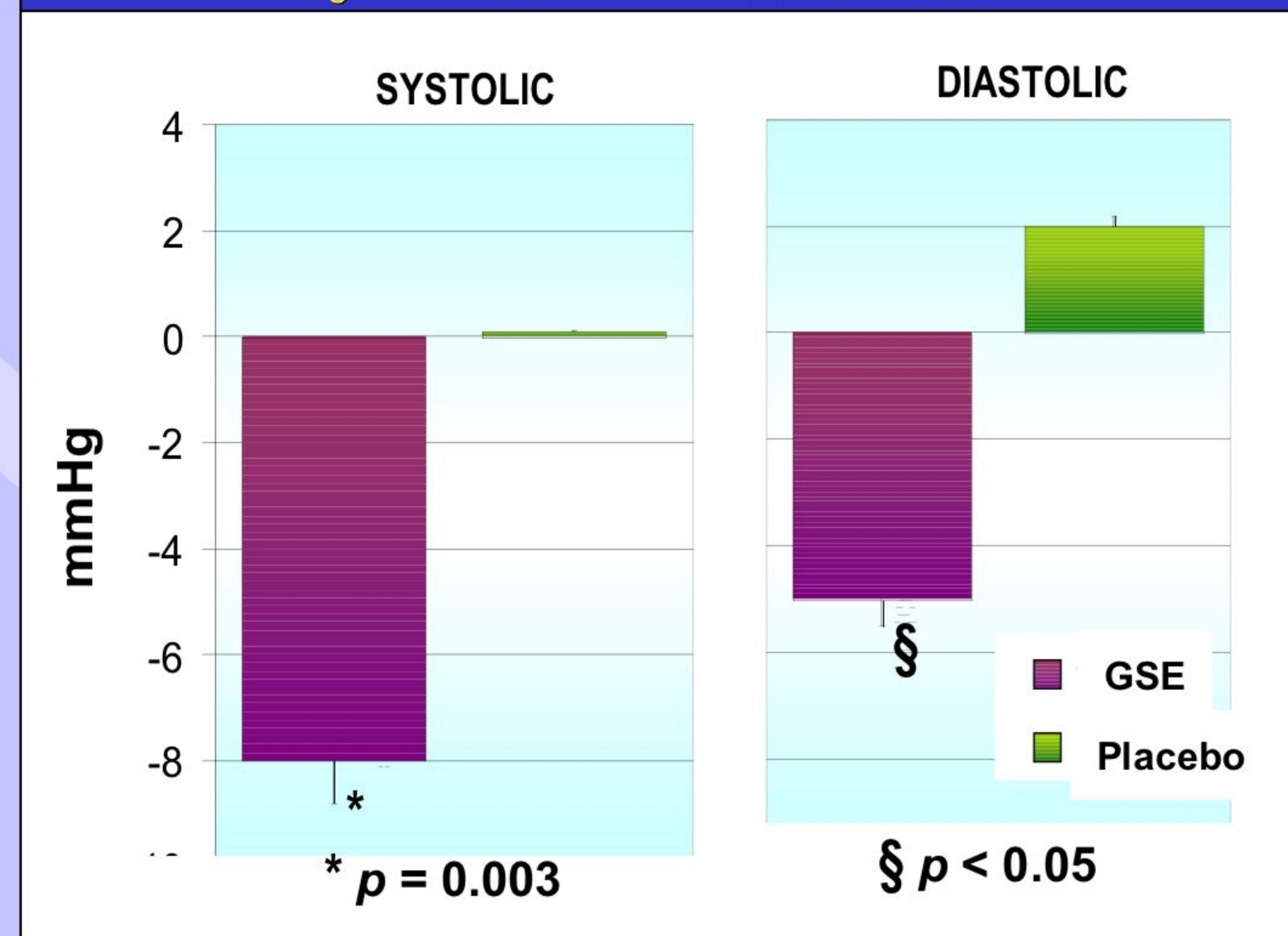


Table 3 - RESULTS

	GSE (n=15; mmHg)		Placebo (n=15; mmHg)	
	Systolic BP	Diastolic BP	Systolic BP	Diastolic BP
Baseline	134 ± 2	79 ± 2	133 ± 1.9	79 ± 2
Final	126 ± 2	74 ± 2	133 ± 2.3	81 ± 2
P	0.003	<0.05	NS	NS
Power (α=0.05)	0.86	0.50		

Table 1 JNC 7 CLASSIFICATION

Blood Pressure Classification	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	<120 and	<80
Prehypertension	120-139 or	80-89
Stage 1 hypertension	140-159 or	90-99
Stage 2 hypertension	≥ 160	≥ 100

DISCUSSION

Pre-hypertension affects 31% of the adult U.S. population between 30 - 65 years of age. Nine out of ten of these will develop overt hypertension by the age of 65. The current JNC 7 guidelines recommend these individuals should be managed with lifestyle changes including diet, exercise and weight management. The current dietary recommendations for healthy Americans include the consumption of up to five servings of fruits and vegetables daily. Such a diet would contain significant quantities of polyphenolic compounds which have vasodilatory properties. In fact, clinical trials have demonstrated a reduction in blood pressure with consumptions of such diets (ref). However, currently these dietary recommendations are generally not followed.

The present study has shown that this novel polyphenolic extract derived from grape seeds can in fact lower blood pressure even in patients without frank hypertension. In this and other small studies, there were no observed side effects or evidence of toxicity with the extract.

CONCLUSION

This study shows that this novel grape seed extract, Meganatural BP®, is an effective antihypertensive in patients with pre-hypertension and may prevent the development of frank hypertension. This represents a safe addition to current dietary and lifestyle recommendation. Further long-term studies are needed to evaluate the effect of this extract on clinical outcomes.

References

Edirisinghe, B. Lu, M. Nalbandyan and C. Kappagoda, (2007) Grape seed extract induced nitric oxide mediated endothelial-dependent relaxation through Akt/PI3 kinase pathway, 2007 Experimental Biology meeting abstracts [on CD-ROM], Abstract #A117.
 Wang Y, et al. The Prevalence of Prehypertension and Hypertension Among US Adults According to the New Joint National Committee Guidelines: New Challenges of the Old Problem. *Arch Intern Med.* 2004;164:2126-2134.

Disclosure

The study was funded by a grant from Polyphenolics, Inc. of Madera, California.