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ORIGINAL RESEARCH ARTICLE

Antihypertensive and Antioxidant Potential of Borneol-A Natural Terpene in L-NAME – Induced Hypertensive Rats

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ABSTRACT

The present study was aimed to investigate the antihypertensive and antioxidant potential of borneol - a natural terpene, against N^{ω}-Nitro-L-arginine methyl ester hydrochloride (L-NAME) induced hypertension in rats. Hypertension was induced in adult male albino rats of the Wistar strain, weighing 180-220 g, by oral administration of the L-NAME (40 mg/kg bw/day) in drinking water for 4 weeks. Rats were treated with borneol (50 mg/kg bw/day) for 4 weeks. Systolic and diastolic blood pressure was measured every week and the toxic effect of L-NAME was determined using lipid peroxidative markers (thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxides (LOOH). We assessed the activity of enzymatic antioxidants (superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and measured the levels of non-enzymatic antioxidants (vitamin C, vitamin E and reduced glutathione (GSH)) levels in erythrocytes, plasma and tissues. Our results showed that oral administration of borneol (50 mg/kg bw/day) significantly attenuated systolic and diastolic blood pressure. In addition, borneol significantly reduced lipid peroxidation and increased the activities and level of enzymatic and non-enzymatic antioxidants. These results were supported by histopathalogical studies. The effect of borneol was comparable with nifedipine. These findings suggest that borneol affords a significant antihypertensive and antioxidant effect against L-NAME induced hypertensive rats.

Keywords: Hypertension, Borneol, Lipid peroxidation, Antioxidants, L-NAME.

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide, accounting for an estimated 14 million deaths in 1990 and projected to cause 25 million deaths in 2020[1]. Hypertension is considered to be a major risk factor in the development of CVD[2]. Therefore, it has been received increasing attention by researchers. Currently available antihypertensive drugs play an important role in the treatment of hypertension. However, commonly used antihypertensive drugs are expensive with many adverse effects. Therefore there is a need for population-based, cost-effective, adverse-effect free hypertension control strategies to be developed [3].

The development of a safe and effective way to manage hypertension has challenged medical researchers for centuries. In recent times, focus on plant research has increased all over the world and a large body of evidence was collected to show immense potential of medicinal plants used in various traditional systems. A wide variety of the traditional herbal remedies are used by hypertensive patients, especially in the third world countries and may therefore represent new avenues in the search for alternative antihypertensive drugs [4].

Monoterpenes are primary compounds of plant essential oils and the effects of many medicinal herbs have been attributed to them.Borneol, a bicyclic monoterpene, present in the essential oils of numerous medicinal plants is often used in traditional Chinese medicine and is a very important ingredient in many Japanese incense formulas with uplifting effects on the mind[5] and on the neurotransmitter GABA[6]. In folk remedies, borneol is used for the treatment of abdominal pain, particularly stomachache [7]. Borneol is used more frequently for topical applications such as to injuries, burns, rheumatic

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pains, hemorrhoids, skin diseases and ulcerations of the mouth, ear, eye, and nose. Moreover, it stimulates digestive system by increasing production of gastric juices; tones the heart and improves circulation; treats bronchitis, coughs and colds; reduces swelling; relieves stress; and can be used as a tonic to promote relaxation and reduce exhaustion[8]. It shows inhibitory effects on several Gram (-) and Gram (+) pathogenic microorganisms, exhibits a marked antifungal activity[9] and radical scavenging properties[10]. Immunomodulatory effects of borneol were studied by Juha's[11] showed that borneol was able to significantly suppress the pro-inflammatory cytokine mRNA expression in colonic inflammation in mice. In addition, borneol was reported to act as bioactive material in the cellular signal transduction system[12]. Recently borneol has been demonstrated to show antithrombotic and antiplatlet activity[13]. Our aim, therefore, was to examine whether administration of borneol could have positive effects on blood pressure and oxidative status in L-NAME induced hypertensive rats.

MATERIALS AND METHODS

Animals

Male albino Wistar rats, 7-8 weeks old (weighing 180–220 g) were procured from the Central Animal House, Department of Experimental Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University and maintained in an air-conditioned room (25 ± 1ºC) with a 12 h light/12 h dark cycle. Feed and water were provided *ad libitum*. All the experimental studies were conducted in the Department of Biochemistry, Faculty of Science, Annamalai University, in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (NIH 1985); the experimental study was approved by the Ethical Committee of Rajah Muthiah Medical College and Hospital (Reg No.160/1999/CPCSEA, Pro. No.597), Annamalainagar, Tamil Nadu.

A pilot study was conducted with three different doses of borneol (25, 50 and 100 mg/kg) to determine the dose dependent effect of borneol in L-NAME induced hypertensive rats. It was observed that after 14 days of experiment, borneol treatment at the doses of 25, 50 and 100 mg/kg significantly ($p< 0.05$) lowered the elevated blood pressure in L-NAME hypertensive rats. 50 mg/kg of borneol showed higher significant effect than lower dose 25 mg/kg and the higher dose 100. Hence, we have chosen the dose (50 mg/kg) for our study.

Chemicals

Borneol and N^{ω}-Nitro-L-arginine methyl ester hydrochloride (L-NAME) were purchased from Sigma-Aldrich Company (St. Louis, Missouri, USA). All other chemicals used were of analytical grade obtained from E. Merck, Mumbai and HIMEDIA, Mumbai, India.

Experimental design

The rats were randomly divided into five groups of six animals each as given below. The first group (n=6) served as a control and received tap water only. In the second group (n=6) served as a drug (borneol) control group received borneol at a dose of 50 mg/kg /day. The third group, L-NAME group (n=6), L-NAME was added to drinking water at a concentration of 0.4 mg/ml to account for a daily intake of 40 mg/kg[14].The fourth group (borneol group, n=6) received simultaneously L-NAME (40mg/kg/day) and borneol at 50 mg/kg/day and the last group (nifidipine group, n=6) received simultaneously L-NAME (40 mg/kg/day) and nifedipine (20 mg/kg/day). The borneol was suspended in 0.5% Dimethyl sulphaoxide (DMSO) vehicle solution and fed by intubation. Before initiating experimental protocols, measurements of baseline systolic (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MABP) and heart rate (HR) by non-invasive tail-cuff plethysmography (IITC, model 31, Woodland Hills, CA, USA) and initial body weight have been performed.

The experimental duration was 30 days. On 31st day the rats were sacrificed by cervical dislocation. Blood was collected in a dry test tube and allowed to coagulate at ambient temperature for 40 min. Serum was separated by centrifugation at 2000 rpm for 10 min. The blood, collected in a heparinised centrifuge tube was centrifuged at 2000 rpm for 10 min and the plasma was separated by aspiration. After the separation of plasma, the buffy coat, enriched in white cells, was removed and the remaining erythrocytes were washed three times with physiological saline. A known volume of erythrocyte was lysed with hypotonic phosphate buffer at pH 7.4. The hemolysate was separated by centrifugation at 2500 rpm for 10 min and the supernatant was used for the estimation of enzymic antioxidants. Heart,

liver and kidney tissues (250 mg) were sliced into pieces and homogenised in appropriate buffer in cold condition (pH 7.0) to give 20% homogenate (w/v). The homogenate was centrifuged at 1000 rpm for 10 min at 0 °C in refrigerated centrifuge. The supernatant was separated and used for various biochemical estimations.

Biochemical estimations

Lipid peroxidation was assessed by measuring the levels of thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxides in the plasma following the procedures of Niehaus and Samuelson[15] and Jiang[16], respectively. The activities of erythrocyte SOD, CAT and GPx were assayed by the method of Kakkar[17], Sinha[18]] and Rotruck[19].The levels of non-enzymatic antioxidants such as ascorbic acid, α-tocopherol and reduced glutathione were measured by Roe and Kuether[20], Baker[21] and Ellman[22], respectively.

Histological examination of cardiac tissues

Excised heart sample were cleared of blood and immediately fixed in a neutral buffered solution of 10% formalin for 24 h. 5µm-thick tissues section from heart of each animal were prepared from processed paraffin-embedded samples. Section were stained with Hematoxylin and Eosin (H&E) for light microscopic examination for evidence of hypertensive tissues changes. The cross-sectional area (CSA) of heart was evaluated from photographs of whole tissue sections taken at 40X magnification and scanned, digitized and analyzed by computer, using the Adobe Photoshop Imaging program (Adobe System Incorporation).

Statistical analysis

Data were analysed by one way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT) using a statistical software package (SPSS for Windows, V. 11.5, Chicago, USA). Results were presented as means ± S.D. *p*-values < 0.05 were considered as statistically significant.

RESULTS

Blood pressure measurements

As shown in fig. 1 and 2 administration of L-NAME in drinking water for 4 weeks significantly elevated SBP (182.3 ± 4.07 mm Hg), DBP (118.8 ± 1.69 mm Hg), as compared to that of control rats (SBP (112.3±2.74 mm Hg), DBP (72.2±2.41 mm Hg, $p< 0.05$). Treatments with borneol and nifedipine significantly attenuated development of high blood pressure (SBP (120.2±3.41mm Hg), DBP (74.65±1.69 mm Hg) and nifedipine (SBP (116.3±5.81 mm Hg), DBP (72.5±3.27 mm Hg $p< 0.05$).

Effect of borneol on body weight, tissue, water intake in normal, L-NAME induced hypertensive rats

Table 1 shows the body weight, tissue weights and water intake of all groups. The initial body weights (BW) were 181 ± 1.16, 183 ± 1.64, 185 ± 1.47, 184 ± 1.64,183 ± 2.42g (data not shown), and final bodyweights were 206 ± 1.75, 208 ± 1.47, 160 ± 3.61, 204 ± 1.94, 208 ± 3.25 for control, control + borneol, L-NAME (40mg/kg/day), L-NAME + borneol (50mg/kg/day), L-NAME + nifedipine (20 mg/kg/day) groups, respectively. L-NAME administered rats had significantly increased water intake, kidney and heart weight. Borneol and nifedipine significantly reduced the water intake, renal and heart weight in L-NAME rats. The BWs of rats in the five groups differ significantly at the beginning or at the end of study.

Table.1 Effect of borneol on body weight, relative tissue weights and water intake in control and L-NAME-induced hypertensive rats

		Relative organ weight g/100 g BW		Water intake (ml)
Groups	**BW (g)**	**Kidney**	**Heart**	
Control	206±1.75[a]	0.84±0.03[a]	0.80±0.07[a]	28.22±1.43[a]
Control+ borneol (50 mg/kg /day)	208 ±1.47[a]	0.83±0.03[a]	0.80±0.05[a]	27.45±0.98[a]
L-NAME (40mg/kg/day)	160±3.61[b]	1.93±0.06[b]	1.12±0.03[b]	39.38±1.65[b]
L-NAME + borneol (50 mg/kg/day)	204±1.94[a]	0.87±0.06a	0.85±0.04[a]	29.14±0.95[a]
L-NAME + nifedipine (20mg/kg/day)	208±3.25[a]	0.85±0.04[c]	0.83±0.05[c]	30.27±2.02[c]

Values are means ± SD for six rats
Values not sharing a common superscript differ significantly at p < 0.05 (DMRT)

Effect of borneol on lipid peroxidation

Table 2 shows the concentration of TBARS and lipid hydroperoxides (markers of lipid peroxidation) in the plasma and tissues (heart, liver and kidney) of control and L - NAME treated rats. The levels of TBARS and hydroperoxides were significantly increased in L-NAME rats. Oral administration of borneol and nifedipine significantly prevented the increase in lipid peroxidation marker level which was brought to near control.

Table 2. Effect of borneol on TBARS and lipid hydroperoxide in the plasma and tissues of normal and L-NAME induced hypertensive rats.

Parameter	Samples	Groups				
		Control	**Control + borneol (50 mg/kg BW.)**	**L-NAME (40mg/kg BW.)**	**L-NAME+ borneol (50mg/kg BW.)**	**L-NAME+ nifedepine (20mg/kg BW.)**
TBARS	Plasma (mmoles / dL)	9.10±0.43^{a}	8.86±0.61^{a}	21.78±1.46^{b}	10.83±0.66^{c}	12.50±0.95^{d}
	Liver(mmoles/100 g wet tissue)	77.97±6.93^{a}	76.19±5.83^{a}	108.92±8.06^{b}	86.30±4.74^{c}	91.07±2.98^{dc}
	Kidney(mmoles/100g wet tissue)	63.09±6.25^{a}	62.50.±8.67^{a}	158.92±7.40^{b}	75.00±8.45^{c}	79.76±9.22^{d}
	Heart(mmoles/100 g wet tissue)	65.47±8.65^{a}	64.76±3.24^{a}	136.90±7.02^{b}	79.76±9.22^{c}	87.50±8.06^{d}
LOOH	Plasma (mg/dL)	0.13±0.16^{a}	0.12±0.22^{a}	0.43±0.56^{b}	0.18±0.18^{c}	0.19±0.02^{d}
	Liver(mmoles/100 g wet tissue)	0.87±0.06^{a}	0.85±0.07^{a}	2.55±0.18^{b}	1.22±0.14^{c}	1.37±0.11^{d}
	Kidney(mmoles /100g wet tissue)	1.40±0.77^{a}	1.37 ±0.11^{a}	3.80±0.30^{b}	1.67±0.17^{c}	1.92±0.11^{d}
	Heart(mmoles/100 g wet tissue)	0.52±0.15^{a}	0.50±0.154^{a}	3.02±0.34^{b}	0.75±0.16^{c}	0.95±0.18d^{d}

Values are means ± SD for six rats
Values not sharing a common superscript differ significantly at p < 0.05 (DMRT)

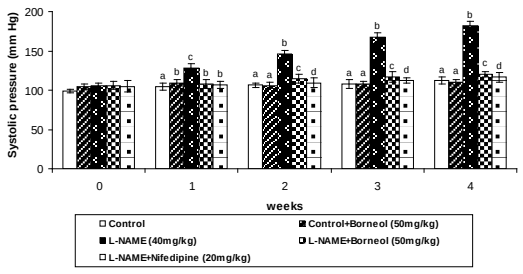
Enzymatic antioxidants

Tables 3 show the activities of SOD, CAT, and GPx in erythrocyte, liver, kidney and heart of control, L-NAME and borneol treated hypertensive rats, respectively. The activities of these enzymatic antioxidants were significantly restored in erythrocyte and tissues on treatment with borneol and nifedipine in L-NAME induced hypertensive rats.

Non-enzymatic antioxidants

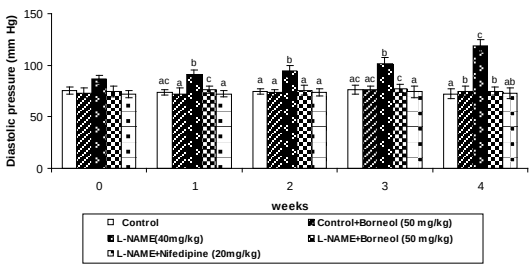
Tables 4 show the levels of non-enzymatic antioxidants (vitamin C, vitamin E and GSH) in the plasma and tissues (liver, kidney and heart) of control,L-NAME and borneol treated hypertensive rats. Our results show that the levels of non-enzymatic antioxidants were significantly decreased in L-NAME induced hypertensive rats. Oral administration of borneol and nifedipine brought back these parameters to near control.

Fig 1. Effect of borneol on the systolic blood pressure (SBP) in control and L-NAME - induced hypertensive rats.



Values are given as mean ± SD for six rats in each group. Values not sharing a common superscript differ significantly at p < 0.05 DMRT).

Fig 2. Effect of borneol on the diastolic blood pressure (DBP) in control and L-NAME - induced hypertensive rats.



Values are given as mean ± SD for six rats in each group. Values not sharing a common superscript differ significantly at p < 0.05 DMRT).

Table 3.Effect of borneol on the activity of SOD, catalase and GPx in the erythrocyte and tissues of normal and L-NAME induced hypertensive rats

Parameter	Samples	Groups				
		Control	Control + borneol (50 mg/kg BW.)	L-NAME (40mg/kg BW.)	L-NAME+ borneol (50 mg/kg BW.)	L-NAME + nifedepine (20 mg/kg BW.)
SOD	Erythrocyte*/mg Hb)	6.88±0.92^{ad}	7.29±0.76^{b}	3.39±0.78^{c}	7.61±0.59^{d}	7.39±0.60^{e}
	Liver (U*/mg protein)	8.85±0.65^{a}	9.02±0.76^{a}	4.56±0.96^{b}	6.50±0.94^{c}	6.06±0.72^{cd}
	Kidney(U*/mg protein)	15.40±1.05^{a}	16.86±1.11^{a}	8.86±1.42^{b}	14.87±1.24^{c}	13.25±1.23^{d}
	Heart(U*/mg protein)	5.99±0.55^{a}	6.44±0.88^{a}	2.64±0.34^{b}	4.92±0.42^{c}	4.65±0.58^{d}
Catalase	Erythrocyte*/$^{mg}_{Hb}$)	172.62±4.01^{a}	174.55±3.8	99.97±7.81^{b}	160.75±6.56^{c}	155.0±9.11^{d}
	Liver(U*/mg protein)	73.12±6.70^{a}	74.13±7.03^{a}	45.25±5.06^{b}	67.65±7.74^{ca}	62.65±7.48^{d}
	Kidney(U*/mg protein)	36.52±3.13^{a}	37.14±4.03^{a}	16.90±2.80^{b}	28.04±2.54^{c}	25.01±1.96^{d}
	Heart (U*/mg protein)	50.96±8.36^{a}	50.99±6.27^{a}	27.99±9.23^{b}	44.01±6.67^{ca}	41.39±5.04^{cd}
GPx	Erythrocyte*/mg Hb)	14.31±0.47^{a}	13.28±0.78^{a}	5.98±0.26^{b}	13.34±0.48^{c}	13.09±0.22^{ac}
	Liver(U*/mg protein)	8.91±2.09^{a}	9.28±0.59^{a}	4.67±0.21^{b}	7.28±0.68^{c}	7.22±0.34^{d}
	Kidney(U*/mg protein)	8.66±0.48^{a}	8.93±0.87^{b}	4.36±0.68^{c}	7.48±0.49^{d}	6.44±0.24^{e}
	Heart (U*/mg protein)	8.41±0.88^{a}	8.87±0.99^{a}	3.58±0.65^{b}	8.05±0.29^{ca}	7.72±0.32^{d}

U = enzyme concentration required to inhibit the chromogen produced by 50% in one minute under standard condition. $U^{\#}$ = µmole of H_2O_2 consumed/minute. $U^{\$}$ = µg of GSH utilized/minute.Values are means ± SD for six rats. Values not sharing a common superscript differ significantly at p < 0.05 (DMRT)*

Table 4. Effect of borneol on Vitamin-C, Vitamin-E and GSH, in the plasma and tissues of normal and L-NAME induced hypertensive rats

Parameter	Samples	Groups				
		Control	Control + borneol (50 mg/kg BW.)	L-NAME (40mg/kg BW.)	L-NAME+ borneol (50 mg/kg BW.)	L-NAME+ nifedipine (20 mg/kg BW.)
Vitamin C	Plasma (mg/dL)	2.42±0.16^{a}	2.57±0.15^{b}	0.93±0.05^{c}	2.30±0.89^{a}	2.80±0.89^{d}
	Liver (µg/mg protein)	0.83±0.07^{a}	0.84±0.09^{a}	0.57±0.09^{b}	0.77±0.11^{ca}	0.74 ±0.05^{cda}
	Kidney (µg/mg protein)	0.84±0.08^{a}	0.86±0.10^{a}	0.37±0.07^{b}	0.66±0.07^{c}	0.62±0.10^{d}
	Heart (µg/mg protein)	0.52±0.07^{a}	0.54±0.08^{a}	0.29±0.05^{b}	0.48±0.04^{ca}	0.43±0.08^{cd}
Vitamin E	Plasma (mg/dL)	2.62±0.09^{a}	2.81±0.11^{b}	0.97±0.12^{c}	1.92±0.11^{d}	1.72±0.16^{c}
	Liver (mg/100 g wet tissue)	6.36±0.70^{ab}	6.79±0.47^{b}	3.77±0.33^{c}	5.84±0.31^{a}	4.93 ±0.48^{d}
	Kidney(mg/100gwet tissue)	4.66±0.30^{a}	4.74±0.63^{a}	1.86±0.47^{b}	3.30±0.27^{c}	2.74±0.41^{cd}
	Heart (mg/100 g wet tissue)	4.40±0.52^{a}	4.55±0.34^{a}	1.89±0.30^{b}	3.56±0.34^{ca}	3.18±0.65^{cd}
GSH	Plasma (mg/dL)	34.84±2.30^{a}	36.26±2.23^{a}	20.97±1.98^{b}	30.75±1.41^{c}	28.08±1.74^{c}
	Liver (mg/100 g wet tissue)	13.20±1.35^{a}	14.85±1.02^{b}	5.45±0.85^{c}	10.12±1.09^{d}	8.44 ±0.91^{e}
	Kidney(mg/100gwet tissue)	11.91±1.14^{a}	12.09±1.23^{a}	4.17±1.07^{b}	9.21±1.16^{c}	8.96±1.22^{c}

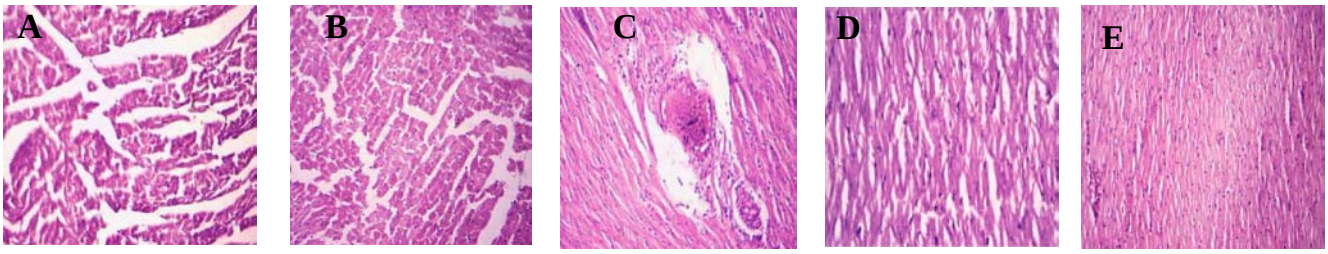
Heart (mg/100 g wet tissue)	8.37±0.58[a]	8.71±0.80[a]	3.34±0.77[b]	7.38±0.69[c]	6.97±0.63[cd]

Values are means ± SD for six rats. Values not sharing a common superscript differ significantly at p < 0.05 (DMRT)

HISTOPATHALOGICAL EXAMINATION

In control, heart tissue sample showed consistently normal histology **(Fig. 3**).Heart tissue samples were normal in control, control+borneol groups (**Fig.3A and B**).There were mild hypertensive arteriole changes in L-NAME group (**Fig.3C**). Such changes were notably borneol treated and nifedipine in L-NAME groups (**Fig.3D and E**).

Fig.3.Representative photomicrograph of histological changes in heart: (A) Control, myocardial fibres looked normal.(B) Control+borneol, similar to control group.(C) L-NAME, there was myocardial fibres destruction with mononuclear cell infiltration, thickened arteriole medial hypertrophy.(D) L-NAME + borneol, vascular changes were milder than L-NAME group mainly in the form of mild mononuclear inflammatory cells seen in interstitum.(H&E paraffin section,5 µm thick, 40x).



DISCUSSION

Nitric oxide (NO) synthesis and release by endothelial cells play an important vascular relaxation effect contributing to the modulation of vascular tone[23]. In addition, NO has been identified as important in other cellular events, such as vascular smooth muscle cell proliferation and neural transmission. Chronic inhibition of NO produces volume-dependent elevation of blood pressure and its physiological and pathological characteristics resemble essential hypertension. Besides, it is well established that acute inhibition of nitric oxide biosynthesis by in vivo administration of L-NAME, an L-arginine analogue, leads to arterial hypertension and renal vasoconstriction [24]. This effect is due to several factors like; inhibition of the NO production, increase in sympathetic tone, increase in the rennin-angiotensin system activity[25] and increase in the vascular resistance[26]. Also, the reactivity to vasoconstrictor agents is increased and the responsiveness to endothelial dependent vasodilators is reduced in this model of hypertension[27].Our results showed that oral administration of borneol significantly attenuated SBP and DBP in L-NAME rats.

Lipid peroxidation is reported to be a significant factor in pathologic conditions such as hypertension, diabetes mellitus and myocardial infarction [28]. An increased concentration of lipid peroxidation end products is noticed in hypertension. To evaluate the protective role of borneol against hypertension-associated oxidative stress, TBARS and hydroperoxide levels in plasma and tissues such as liver, kidney and heart were examined in all experimental rats. In the present study, both plasma and tissue levels of TBARS and hydroperoxides were enhanced in L-NAME administered rats as compared to normal control rats. L-NAME rats treated with borneol for 30 days significantly reduced both plasma and tissue lipid peroxidation levels.

The body has evolved a complex defense strategy to minimize the damaging effects of various oxidants. Central to this defense, are the antioxidant enzymes of the blood (SOD, CAT and GPx), which act in concert to protect the organism from oxidative damage. SOD scavenges the superoxide anion to form hydrogen peroxide, hence diminishing the toxic effect caused by this radical. The selenium-containing enzyme GPx detoxifies H_2O_2 by utilizing GSH and H_2O_2 as substrates to yield H_2O and oxidized glutathione[29]. Catalase removes H_2O_2 by breaking it down directly to O_2[30]. In the present study, our results showed that the activities of SOD, CAT and GPx were reduced in erythrocytes and tissues of L-NAME administered rats when compared to control rats. When borneol was administered, the reduction in antioxidant enzyme activities found in L - NAME rats was reversed to values closer to those found in untreated, control rats. The increased activities of SOD, CAT and GPx could be the result of decreased utilization

being that the lipid peroxidation was low in the borneol-treated group.

Several studies have suggested an inverse association between dietary intake and plasma concentration of antioxidants and vitamins and cardiovascular disease [31]. The decrease in the levels of β-carotene, ascorbic acid and α-tocopherol may be the result of their increased utilization to trap the ROS in L-NAME administered rats compared to the control rats. Our results showed that treatment with borneol increased the concentration of β-carotene, ascorbic acid and α-tocopherol in L-NAME administered rats. It has been reported that α-tocopherol treatment lowers blood pressure in rats[32]. Similarly, several cross-sectional studies revealed highly significant inverse relationships between blood pressure and ascorbic acid[33]. The conjugated system of beta-carotene reacts with peroxy radicals, thus breaking chain reaction of lipid peroxidation[34]. The tripeptide GSH is one of the most important endogenous antioxidants. It plays the role of a sulfhydryl group provider for direct scavenging reaction catalyzed by GPx and as a scavenger of vitamin C and vitamin E radicals. Treatment with borneol caused an increased generation of glutathione in the liver of rats[35]. By increasing the levels of glutathione and by decreasing lipid peroxidation, borneol may enhance resistance of cells membrane to free-radical–mediated injuries. Morphological studies of the heart showed that treatment with borneol minimized myocardial fibres destruction with mononuclear cell infiltration, arteriolar thickening, glomeruloscelrosis with marked arterial hypotrophy changes that were hypertension, increased activity of the renin-angiotension and sympathetic system and significant production of ROS and inflammatory mediators.

. A variety of terpenoids have been shown to be effective against coronary heart disease [36]. Recently, it has been reported that borneol has an antithrombotic and antiplatelet activity in rats [13].This may be one of the reason for reduction of blood pressure which is noticed in our study. Further, because of its strong antioxidants properties, borneol scavenging free radicals that enhancing levels of enzymic and non-enzymic antioxidant and exerts cardioprotective properties. Therefore, we suggest that daily consumption of borneol might be effective in lowering possible oxidative damage in hypertensive rats, indicating its therapeutic potential as an antihypertensive drug. In conclusion, NO a paracrine vasodilator has been implicated in regulating vascular tone and myocardial contractility and an inhibitor of platelet aggregation contributing be critically in the development of hypertension. In our present study suggests that borneol have antioxidant and antihypertensive potential effect in L-NAME induced hypertensive rats.

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