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Antihypertensive effect of methanolic extract of *Passiflora nepalensis*

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Abstract: The present study was designed to investigate the antihypertensive effect of methanolic extract of the whole plant of *Passiflora nepalensis* Walp., Passifloraceae, (MPN) in renal hypertensive and normotensive rats. The blood pressure, pulse pressure, and heart rate fell dose-dependently in renal hypertensive and normotensive rats after intravenous administration of 75, 150, and 225 mg/kg MPN, suggesting that MPN possesses antihypertensive, hypotensive and negative chronotropic effects. The effect at doses of 150 and 225 mg/kg of MPN were more pronounced than that of 75 mg/kg body weight. Thus, the present study reveals that MPN exerts antihypertensive effect against renal hypertension.

Short communication

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Introduction

High blood pressure is a prevalent risk factor for cardiovascular disease, affecting more than 72 million peoples in the United State and more than one billion people worldwide. In the United States, based on results of the National Health and Nutrition Examination Survey, 28.7% (age-adjusted prevalence) of U.S. adults or ~58.4 million individuals have hypertension. Hypertension prevalence is 33.5% in non-Hispanic blacks, 28.9% in non-Hispanic whites, and 20.7% in Mexican Americans. The prevalence of hypertension and stroke mortality rates is higher in the South-eastern United States than in other regions (Kotchen, 2008). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) recommends a blood pressure treatment goal of 140/90 mmHg for most patients and 130/80 mmHg for patients with diabetes mellitus or kidney disease (Cheng, 2008). When determined by these criteria, hypertension affects 20% to 30% of the adult population in most developed countries, and its prevalence appears to increase with the age of the patient (Brown et al., 2000; Pardell et al., 2000; Schoen, 2004).

The genus *Passiflora* consists of 500 species which are mostly found in warm and tropical regions. *Passiflora* comes from Latin word "Passio" that was first time discovered by Spanish discoverers in 1529 and was described as a symbol for "Passion of Christ" (Kinghorn, 2001; Dhawan et al., 2004). *Passiflora* is used widely in traditional medicine in West India, Mexico, Netherland, South America, Italia, and Argentina. One of species of this genus named as *Passiflora nepalensis* (Passifloraceae) is more popular than its other species in Eastern India. P. nepalensis is used in folklore medicine for treatment of hypertension and inflammation (Patel, 2009; Patel et al., 2009a). *Passiflora* contains several compounds including alkaloids, phenols, glycosyl flavonoids and cyanogenic compounds (Dhawan et al., 2004; Patel, 2009; Patel et al., 2009a). One of the most important glycosyl flavonoid vitexin has been isolated recently from the methanolic extract of *Passiflora nepalensis* Walp. and it showed antioxidant effect (Patel et al., 2009b; Kim et al., 2005). Hence the present study was designed to investigate the antihypertensive effect of methanolic extract of the whole plant of *P. nepalensis* in renal hypertensive and normotensive rats.

Materials and methods

Plant material

The whole plant of *Passiflora nepalensis* Walp., Passifloraceae, was collected in the month of October from the Eastern part of India (Sikkim Himalayas) and identified by Dr. K. Gauthaman of Pharmacognosy Department, Himalayan Pharmacy Institute, Sikkim, India. A voucher specimen number HPI 168 was deposited in the departmental herbarium.

Extraction

The whole parts were dried in shade and powdered (no. 60 mesh) and 100 g of the dried powder

was soxhlet extracted successively with petroleum ether, chloroform, and methanol. The weight of methanolic extract after drying was calculated as 11.8787 g.

Animals

Male Sprague-Dawley rats weighing 300-350 g were used. They were housed in standard environmental conditions and fed with rodent diet and water *ad libitum*. All animal experiments were carried out in accordance with the guidelines of Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA). The institute animal ethical committee has given approval for conducting animal experiments (HPI/08/60/IAEC/0060).

Acute toxicity study

The acute toxicity study of MPN was performed (Turner, 1965; Veerappan et al., 2007). The dead animals obtained from primary screening studies, LD50 value determination experiments, & the acute studies were subjected to post mortem studies. The external appearance of the dead animals, the appearance of the viscera, heart, lungs, and stomach, intestine, liver, kidney, spleen, & brain were carefully noted & any apparent & significant features or differences from the normal were recorded.

Effect on blood pressure

Male Sprague-Dawley rats weighing 300-350 g were used. The animals were anesthetized by intraperitoneal injection of 100 mg/kg hexobarbital sodium. PVC-coated Dieffenbach clip was placed onto the left hilum of the kidney. The renal artery was occluded (ischemia) for 3.5-4 h following the surgery; the animals were then anesthetized by intraperitoneal injection of 30-40 mg/kg pentobarbital sodium. To measure hemodynamic parameters, the cannula in the carotid artery was connected to Powerlab data acquisition system (8/30 and Lab Chart, ADInstrument, Australia). For administration of the test compound, a jugular vein was cannulated. After 3.5-4 h the renal arterial clip was removed called reperfusion. This led to a rise in blood pressure as a consequence of elevated plasma renin level. Within 15 min a stable hypertension was achieved due to renal ischemia and reperfusion (IR) (Vogel et al., 2002). The test substance was then administered by intravenous injection at doses of 75, 150, and 225 mg/kg to renal hypertensive and normotensive rats. Hemodynamic parameters were monitored continuously.

Statistical analysis

The results are expressed as mean±SEM, (n=6). Statistical significance was determined by ANOVA followed by Tukey tests.

Results and discussion

The dead animals obtained from the acute toxicity experiments were found with effects of respiratory arrest and convulsion. Apart from these characteristic observations, no other significant

Table 1. Effect of methanolic extract of the whole plant of *Passiflora nepalensis* Walp., Passifloraceae, on mean arterial pressure, pulse pressure, systolic BP, diastolic BP, and heart rate.

S. No.	Treatment	Mean Arterial Pressure (mm Hg)	Pulse Pressure (mm Hg)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart Rate (beats/ min)
1.	Normotensive rats	97.3±0.32	30.2±0.31	118.4±0.29	91.9±0.34	440.1±0.47
2.	Normotensive+ MPN 75 mg/kg	94.1±0.35‡	28.0±0.59†	99.5±0.51*	86.1±0.37*	437.5±0.67‡
3.	Normotensive+ MPN 150 mg/kg	58.2±0.52*	20.1±0.63*	79.4±0.69*	66.8±0.66*	431.1±0.30*
4.	Normotensive+ MPN 225 mg/kg	48.3±0.75*	15.6±0.29*	65.7±0.41*	55.6±0.85*	428.8±0.47*

*p<0.001 versus control; ‡p<0.01 versus control; †p<0.05 versus control.

Table 2. Effect of methanolic extract of the whole plant of *Passiflora nepalensis* Walp., Passifloraceae, on mean arterial pressure, pulse pressure, systolic BP, diastolic BP, and heart rate.

S. No.	Treatment	Mean Arterial Pressure (mm Hg)	Pulse Pressure (mm Hg)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart Rate (beats/ min)
1.	Normotensive rats	97.1±0.31	32.6±0.45	119.1±0.39	95.0±0.42	438.5±0.42
2.	Renal IR	159.5±0.68[a]	44.8±0.79[a]	142.3±0.34[a]	114.4±0.29[a]	448.0±0.3[3a]
3.	Renal IR + MPN 75 mg/kg	144.1±1.19*	42.0±0.25‡	137.0±0.49*	108.2±0.39*	445.6±0.33‡
4.	Renal IR + MPN 150 mg/kg	128.6±0.32*	35.4±0.52*	126.8±0.37*	99.3±0.43*	441.6±0.33*

[a]p<0.001 versus control; *p<0.001 versus Renal IR; ‡p<0.01 versus Renal IR; IR, ischemia and reperfusion.

observation deviants from the normal were seen in these dead animals. The LD50 value of MPN was calculated as 1566.82 mg/kg. The mean arterial pressure (MAP), pulse pressure, systolic and diastolic blood pressure, and heart rate obtained in normotensive rats before and after MPN treatment are reported in Table 1. Reduction in MAP, pulse and blood pressure in normotensive rats is a direct indication of hypotensive effect (Mojiminiyi et al., 2007). MAP, pulse and blood pressure, and heart rate raised significantly in renal hypertensive rats (p<0.001 versus control), whereas MAP, blood pressure, pulse pressure and heart rate fell dose-dependently in renal hypertensive rats after intravenous administration of 75, 150 and 225 mg/kg MPN, suggesting that MPN possesses antihypertensive and negative chronotropic effects (p<0.01 versus renal IR; p<0.001 versus renal IR group), reported in Table 2. In rats, renal hypertension is induced by clamping the left renal artery. After reopening of the vessel, accumulated renin is released into circulation. The protease renin catalyzes the first and rate-limiting step in the formation of angiotensin II leading to acute hypertension (Vogel et al., 2002). Blockade of renin angiotensin system is one of the important mechanisms for antihypertensive effect in this regards (Kotchen, 2008). These findings confirm the antihypertensive activity of MPN previously reported in literatures (Patel, 2009; Patel et al., 2009a). The MPN is having antioxidant effect on kidney (Patel et al., 2009b) thereby preventing oxidation of renal tubular cells during ischemia and reperfusion, resulting in the antihypertensive activity. The results of present study also showed that MPN dose dependently lowered heart rate in all groups. The fall in heart rate is also in agreement with the finding of Tiamjan (Tiamjan, 1999) and this suggests a negative chronotropic action.

In conclusion this study provides further experimental evidence that justifies the folkloric use of this plant in the treatment of hypertension.

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