Natural Product Sciences
14(2) : 122-126 (2008)

Toxicity Studies on *Peristrophe paniculata* (Forssk) Brummitt – an Ayurveda Drug.

R.V. Pradeep Chandran[1]*, A. Saraswathy[2], B. Murali Manohar[3], and S. Vairamuthu[3]

[1]*K L R. Pharmacy College, Paloncha – 507 115, A.P. India*
[2]*Captain Srinivasa Murti Drug Research Institute for Ayurveda (CCRAS) Arumbakkam, Chennai – 600 106, India*
[3]*Department of Pathology, Madras Veterinary College, Vepery, Chennai – 600 007.*

Abstract – Chronic oral toxicity studies (90 days) on aqueous and methanol extracts of the whole plant of *Peristrophe paniculata* (Forssk) Brummitt were carried out in Wistar rats. The dosage was 200 mg/kg/day, p.o. for both the extracts. All external morphological and biochemical changes, in addition to body weight and vital organ weights were recorded. During this investigation, no significant mortality was observed. The results showed that both the extracts were devoid of any toxicity at the dose level studied as compared to the control group.
Keywords – *Peristrophe paniculata*; Acanthaceae; Chronic toxicity

Introduction

Peristrophe paniculata (Forssk) Brummitt. (Fam: Acanthaceae) (Syn: *Peristrophe bicalyculata* (Retz) Nees., *Dianthera paniculata* Forssk. and *Dianthera bicalyculata* Retz.). The plant is distributed through out India, Burma, tropical Africa and Afghanistan. The whole plant is used to alleviate consumption. The root is bitter, astringent, cooling and is useful in intermittent fever, intrinsic haemorrhage, ulcer, wounds, skin diseases, pruritus, worms, dental caries, leucorrhoea and insomnia (Anonymous, 1966; Anonymous, 2002; Billore *et al*., 2004). Indian tribes have been using the plant in the treatment of liver disorders, rheumatism, gout, antidote for snakebite, antinematode and pesticide (Chopra *et al*., 1956; Bapalala, 1999; Jain, 1991; Kirtikar and Basu, 1975). It is also useful in psychosomatic disorders and possesses anti-venom activity (Anonymous, 2002). The 50% hydro ethanolic extract of the plant showed good anti-inflammatory and analgesic activity (Rathi *et al*., 2003). The aqueous extract of the plant also showed anti-inflammatory, analgesic and wound healing activity (Hoda *et al*., 2000) and antimicrobial activity has also been reported (Qureshi *et al* 1977; Chopra and Chopra, 1959). The Ayurvedic preparation, Aragvadhadi kwatha churna contains this drug as one of the ingredients (Anonymous, 1978). Phytochemical studies previously reported the isolation and identification of petunidin-3-rhamnoglucoside (Rastogi, 1993), 14-methyltritriacont-14-en-15-ol and 35-hydroxynonatriacontanal (Singh *et al*., 2000).

In the present communication we report the results of acute and chronic toxicity studies on the aqueous and methanol extracts of the whole plant in rats.

Experimental

Plant material – The plant was collected from Chennai, Tamil Nadu, India during the month of November 2004. A voucher specimen (No. 53) was deposited in the herbarium of this institute and was authenticated by Dr. P. Brindha, Department of Botany, Captain Srinivasa Murti Drug Research Institute for Ayurveda, Chennai.

Extraction – Shade dried and coarsely powdered whole plant (2.5 kg) was extracted with methanol in the cold (48 h). The extract was distilled in rotary evaporator and concentrated to syrup mass (PPM, 3.60%). The same quantity of the plant material was extracted separately with water to get a dark brown solid (PPA, 3.64%).

Animals – Adult, healthy Swiss albino mice (18 - 20 g) and Wistar albino rats of either sex, (150 - 200 g) were used. The animals were housed under standard laboratory conditions of 12 h light/dark cycle, 25 ± 2 °C with free access to standard food and water *ad libitum*. The study was approved by the Institutional Animal Ethical

*Author for correspondence
Fax: +91-08744-258245; E-mail: chandbalki@yahoo.com

Committee of CSMDRIA, Chennai, India (IAEC/CSMDRIA/03/2005).

Acute toxicity studies – Acute toxicity study of the aqueous and methanol extracts was carried out in Swiss albino mice of either sex (Ecobichon, 1997). The animals were made to fast for 4 h, but allowed free access to water throughout. The fasted mice were divided into seven groups of six animals each. Both aqueous and methanol extracts of *P. paniculata* were dissolved in distilled water and administered orally in varying doses 50, 100, 500, 1000, 1500 and 2000 mg/kg respectively. Negative control received a similar volume of water. They were continuously observed for 2 h to detect changes in the behavioral, neurological and autonomic responses, viz. awareness, irritability, spontaneous activity, convulsions, righting reflex, corneal reflex, urination, salivation, piloerection (Turner, 1965). The experimental animals were observed for further 7 days for any toxic symptoms and mortality. On the basis of the above study the dose level of 200 mg/kg of both the extracts was chosen for further experiments.

Chronic toxicity study – Albino rats of either sex were randomly divided into three groups of six animals each. They were treated orally as follows for a period of 90 days (WHO, 2000). Group I received normal diet and served as control. Group II received 200 mg/kg/day PPA. Group III received 200 mg/kg/day PPM.

The animals were observed for general behavioral changes through the period, the average pre- and post-treatment body weights, food-intake and vital organ weights. Twenty-four hours after the last administration (91st day of the experiment), the animals were sacrificed and blood samples were collected from each rat into non-heparinized tubes and were allowed to coagulate. Serum samples were analyzed for alkaline phosphatase (ALP), acid phosphatase (ACP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein, albumin, globulin, glucose, blood urea nitrogen (BUN), creatinine, bilirubin and uric acid using a 200 Semi autoanalyser (E-Merck). Sodium, potassium and calcium in serum were also measured using Digital Flame Photometer TDF-35 model.

The shape, size, color of internal organs viz. brain, liver, lung, heart, kidneys, spleen, adrenal glands, stomach, testis in male rats or ovary and uterus in female rats were observed for any signs of morbid changes. They were weighed immediately to determine the relative organ weights. Primary organs viz. liver, kidneys, spleen and stomach were washed, preserved in 10% formalin and stained with hematoxylin and eosin and examined for any pathological changes.

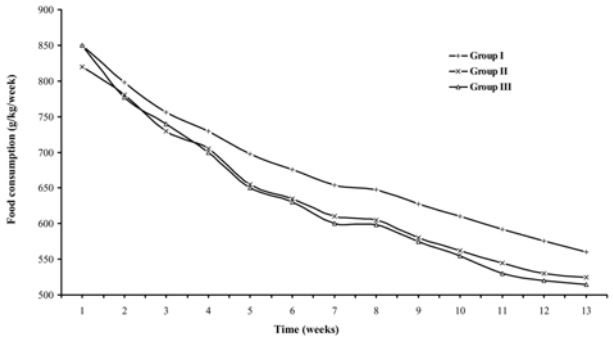

Fig. 1. Relative food consumption of rats receiving *Peristrophe paniculata* for 90 days.

Statistical analysis – Data were statistically evaluated using ANOVA, expressed as mean ± S.E.M followed by Post Hoc Dunnett T3 multiple comparisons test using the 10 version of SPSS computer software. Data were considered significant at $P < 0.05$.

Results and Discussion

The aqueous and methanol extracts of *P. paniculata*, PPA and PPM respectively, when administered in the dose range of 50 - 2000 mg/kg b.wt (p.o) to mice, did not produce any significant changes in the behavioral or autonomic responses during the experimental period which indicated that the extracts were non-toxic upto a dose of 2 g/kg b.wt.

In chronic toxicity studies at the dose of 200 mg/kg/day no significant alteration in behavioral, neurological and autonomic responses were seen, when compared to control group. The effect on average body weights at the dose of 200 mg/kg/day is shown in Table 1. It can be observed that both the extracts caused a significant increase in average body weight when compared to the control group. Relative food intake calculated on weekly basis of both control and treated animals did not show any appreciable change (Fig. 1). Rats treated with the extracts showed no change in relative organ weight viz. liver, lung, heart, spleen, adrenal glands, stomach and ovary. Male rats treated with the extracts had a slight lowering of the testis weight, female rats showed a slight increased in the uterus weight. However the changes were not significant in both cases (Table 1).

No significant difference in serum levels of ALP, AST, total protein, albumin, globulin, creatinine, sodium, potassium and calcium was found between extract-treated groups and the control group. Only a slightly significant increase in ACP, bilirubin and BUN levels was observed.

Table 1. Body weight (g) and relative organ weight (g/kg) of rats receiving *Peristrophe paniculata* for 90 days

Organs	Dose of *Peristrophe paniculata* (mg/kg/ day, p.o.)			*F*-ratio	d.f.
	Group I 10 ml/kg	Group II 200	Group III 200		
Initial body weight	182.83 ± 7.46	177.83 ± 9.36^{ab}	181.67 ± 7.26^{a}	0.11	2, 15
Final body weight	303.33 ± 4.41	340.33 ± 8.33^{a**b}	334.17 ± 7.12^{a**}	8.45	2, 15
Brain	1.06 ± 0.03	1.06 ± 0.04^{ab}	1.05 ± 0.03^{a}	0.03	2, 15
Heart	0.31 ± 0.02	0.28 ± 0.04^{a*b}	0.29 ± 0.01^{a**}	10.06	2, 15
Lungs	0.65 ± 0.03	0.69 ± 0.04^{ab}	0.70 ± 0.03^{a}	0.69	2, 15
Liver	5.76 ± 0.07	5.78 ± 0.07^{ab}	5.69 ± 0.03^{a}	1.08	2, 15
Stomach	0.45 ± 0.06	0.45 ± 0.03^{ab}	0.45 ± 0.05^{a}	0.13	2, 15
Spleen	0.24 ± 0.01	0.24 ± 0.02^{ab}	0.26 ± 0.02^{a}	0.53	2, 15
Kidneys	0.74 ± 0.03	0.77 ± 0.02^{ab}	0.76 ± 0.02^{a}	0.32	2, 15
Testis	1.25 ± 0.03	1.04 ± 0.04^{a*b}	1.04 ± 0.04^{a*}	13.67	2, 15
Adrenals	0.02 ± 0.02	0.02 ± 0.02^{ab**}	0.02 ± 0.01^{a}	3.12	2, 15
Uterus	0.18 ± 0.01	0.22 ± 0.01^{ab}	0.22 ± 0.02^{a}	2.67	2, 15
Ovaries	0.03 ± 0.03	0.02 ± 0.01^{ab}	0.03 ± 0.03^{a}	2.34	2, 15

Comparisions were made between a - Group I and II, III
b - Group II and III
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Table 2. Serum biochemical values of rats receiving *Peristrophe paniculata* for 90 days

Parameters	Dose of *Peristrophe paniculata* (mg/kg/ day, p.o.)			*F*-ratio	d.f.
	Group I 10 ml/kg	Group II 200	Group III 200		
ALP (U/L)	40.53 ± 6.30	42.82 ± 6.64^{ab}	42.61 ± 6.49^{a}	0.38	2, 15
ACP (U/L)	24.09 ± 0.13	25.18 ± 0.14^{a*b}	24.92 ± 0.18^{a**}	14.68	2, 15
ALT (U/L)	36.50 ± 4.56	29.96 ± 0.93^{ab}	29.54 ± 0.86^{a}	2.04	2, 15
AST 9U/L)	90.10 ± 2.82	90.41 ± 1.53^{ab}	92.86 ± 1.53^{a}	0.54	2, 15
Total protein (g/dL)	6.98 ± 0.03	7.12 ± 0.02^{a**b}	7.07 ± 0.02^{a}	7.18	2, 15
Albumin (g/dL)	4.95 ± 0.02	4.96 ± 0.03^{ab}	5.01 ± 0.05^{a}	1.10	2, 15
Globulin (g/dL)	2.82 ± 0.11	3.08 ± 0.03^{ab**}	3.19 ± 0.02^{a**}	7.94	2, 15
A/G	1.76 ± 0.07	1.61 ± 0.01^{ab}	1.57 ± 0.02^{a**}	6.00	2, 15
Bilirubin (mg/dL)	0.62 ± 0.02	0.68 ± 0.02^{a**b}	0.71 ± 0.02^{a***}	9.54	2, 15
BUN (mg/dL)	21.64 ± 0.22	20.49 ± 0.04^{a**b***}	22.63 ± 0.04^{a**}	66.66	2, 15
Creatinine (mg/dL)	0.76 ± 0.03	0.75 ± 0.02^{ab}	0.77 ± 0.03^{a}	0.18	2, 15
Glucose (mg/dL)	146.89 ± 2.40	158.78 ± 2.90^{a**b}	156.00 ± 1.95^{a**}	6.45	2, 15
Uric acid (mg/dL)	2.12 ± 2.07	2.13 ± 0.01^{ab}	2.14 ± 0.02^{a}	0.73	2, 15
Sodium (mmol/L)	141.29 ± 1.52	143.50 ± 0.99^{ab}	143.43 ± 0.88^{a}	1.16	2, 15
Potassium (mmol/L)	4.84 ± 0.20	4.91 ± 0.25^{ab}	5.00 ± 0.16^{a}	0.16	2, 15
Calcium (mmol/L)	2.13 ± 0.02	2.14 ± 0.02^{ab}	2.18 ± 0.02^{a}	2.09	2, 15

Comparisons were made between a - Group I and II, III
b - Group II and III
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Similarly a slight significant increase was observed in serum glucose level for the PPA treated group (Table 2). The results also showed that the level of ALT in both the extracts-treated groups was lower than that of control group, however the values were still within the normal range (CPCSEA, 2003; Gad, 1992).

Histopathological examination of primary organs showed normal architecture suggesting no detrimental

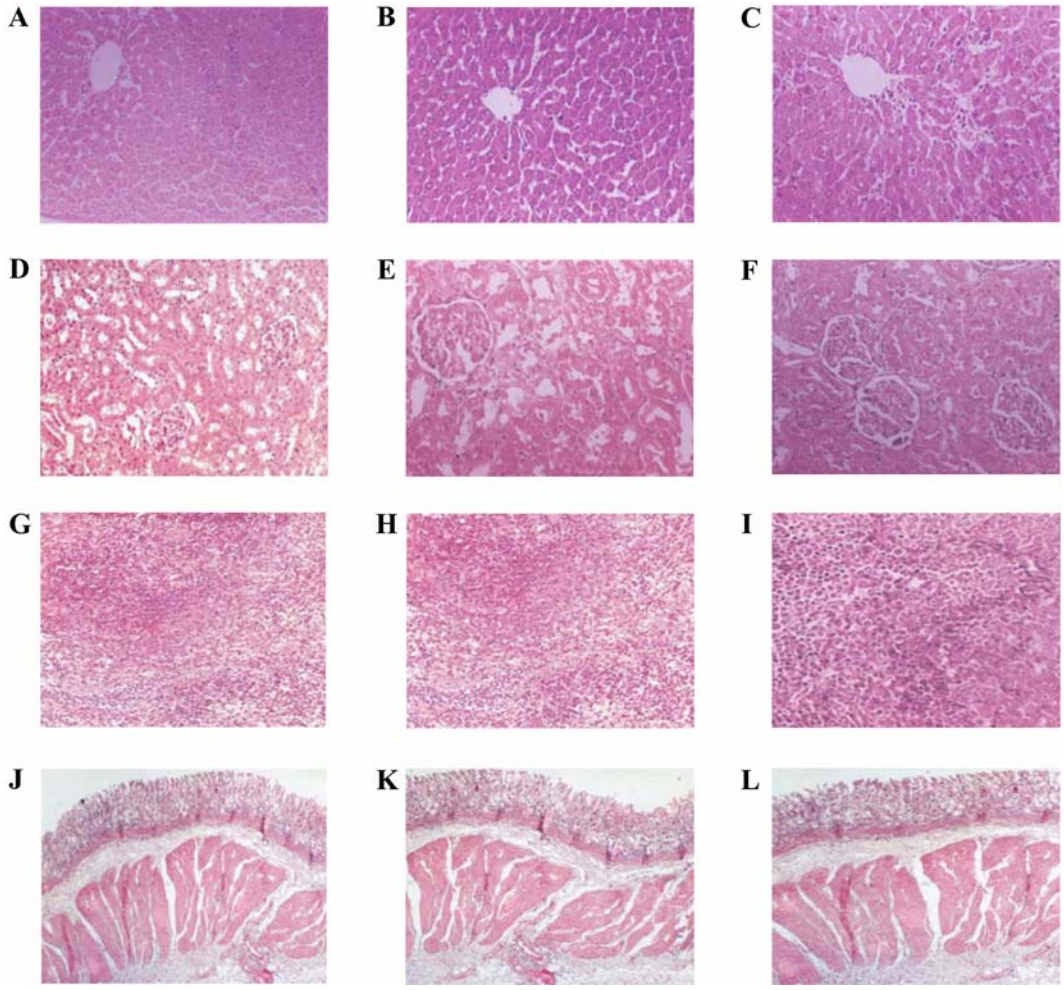

Fig. 2A-L. Histological examination of - (**A**) liver tissue from control rat showing normal architecture; (**B**) PPA treated rat showing slight fatty change; (**C**) PPM treated rat showing mild mononuclear cell infiltration and fatty change; (**D**) kidney tissue from control rat showing normal architecture; (**E**) PPA treated rat showing slight inclusions; (**F**) PPM treated rat showing slight inclusions; (**G**) spleen tissue from control rat showing normal architecture; (**H**) PPA treated rat showing apparently normal architecture with no pathologic changes; (**I**) PPM treated rat showing apparently normal architecture with no pathologic changes; (**J**) stomach tissue from control rat showing normal architecture; (**K**) PPA treated rat showing normal architecture with no pathologic changes; (**L**) PPM treated rat showing normal architecture with no pathologic changes (H & E × 100).

change and morphological disturbances were caused by the daily oral administration of PPA and PPM at the dose level of 200 mg/kg/day for 90 days. However, liver showed incidence of slight fatty changes in both the groups. Similarly, kidney showed slight inclusions (Fig. 2A-L).

In conclusion, the results indicate that the aqueous and methanol extracts of *P. paniculata* given orally at dose of 200 mg/kg/day for 90 days did not show any evidence of toxicity in rats as evidenced by biochemical and histopathological investigations.

Acknowledgement

The authors wish to thank The Director, Central Council for Research in Ayurveda & Siddha, New Delhi for financial support.

References

Anonymous., *The Ayurvedic Formulary of India*, Part - I (Ist edition), Ministry of Health and Family Planning, Government of India (eds.), New Delhi, 45 (1978).

Anonymous., *The Wealth of India*. Raw materials, Vol. VII, Publication and Information Directorate (C S I R), New Delhi, 313 (1966).

Anonymous., Wound healing and pain killer Chaksini, *Natural product radiance*, Vol. 1, National Institute of Science Communication (CSIR), New Delhi, 44 (2002).

Bapalala, G.V., *Nighantu Adarsh (Uttarardha)*. V-II, Chaukhamba Bharati Academy Publishers, 2nd edition, Varanasi, 225 (1999).

Billore, K.V., Yelne, M.B., Dennis, T.J., and Chaudhari, B.G., Kakajangha

(*Peristrophe paniculata*), *Data base on medicinal plants used in Ayurveda*. Vol. 6, CCRAS, Ministry of Health and Family welfare, Government of India (eds.), New Delhi, pp. 74-76 (2004).

Chopra, R.N., Nayar, S.L., and Chopra, I.C., *Glossary of Indian Medicinal Plants*. National Institute of Science Communication. 1st edition, New Delhi, 67 (1956).

Chopra, I.C. and Chopra, C.L., Antibacterial properties of *Peristrophe bicalyculata*. *Ind. J. Med. Res*., **47**, 161-163 (1959).

CPCSEA (Committee for the Purpose of Control and Supervision of Experimentation on Animals)., CPCSEA guidelines for laboratory animal facility. *Ind. J. Pharmacol.,* **35**, 257-274 (2003).

Ecobichon, DJ., The Basis of Toxicology Testing, New York: CRC Press, p. 43 (1997).

Gad, S.C., The rat: pathology, Gad, S.C. and Chengellis, C.P. (eds.), Marcel Dekker, New York, pp. 111-113 (1992).

Hoda, S., Afaq, S.H., and Tajuddin., Pharmacological studies of "*Chaksini*" *Peristrophe bicalyculata* Nees. for analgesic and anti-inflammatory effect on albino rats. *Hamdar Medicus,* **43,** 40-46 (2000).

Jain, S.K., *Dictionary of Indian folk medicine and Ethnobotany*. Deep Publication; 140 (1991).

Kirtikar, K.R. and Basu, B.D., *Indian medicinal plants*. Leader Press, Allahabad, 1910 (1975).

Qureshi, S., Rai, M.K., and Agrawal, S.C., Invitro evaluation of inhibitory nature of extracts of 18-plant species of Chhindwara against 3-keratinophilic fungi. *Hindustan Antibiot. Bull.* **39**, 56-60 (1977).

Rastogi Ram P. and Mehrotra B.N., Compendium of Indian medicinal plants. In: Rastogi Ram P, editor, vol. 2, New Delhi: Publication and Information Directorate, CDRI, 522 (1993).

Rathi, A., Rao Ch.V., Khatoon, S., and Mehrotra, S., Ethnopharmacological evaluation of *Peristrophe bicalyculata* Nees. for anti-inflammatory and analgesic activity. *Nat. Prod. Sci*. **9**, 195-199 (2003).

Singh, R.S., Pandey, R.P., Singh, B.K., and Singh. R.G., Aliphatics from *Peristrophe bicalyculata*. *Fitoterapia* **71**, 80-81 (2000).

Turner, RA., Screening Methods in Pharmacology, vol. I. New York: Academic Press; pp. 26-34 (1965).

WHO., General guidelines for methodologies on research and evaluation of traditional medicine, Geneva, WHO, 29 (2000).

(Accepted June 14, 2008)