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R E S E A R C H A R T I C L E

Pharmacological Evaluation of *Pavonia Odorata Willd* for Analgesic, Anti-Inflammatory and Anti-Ulcer Activity

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A B S T R A C T

The plant *Pavonia odorata willd* (*Malvaceae*) contains many active ingredients like ageratochromene, palmitic acid, hexahydrofarnesyl acetone, beta-eudesmol and beta-caryophyllene oxide as the major constituents. It is reported to have Analgesic Activity, Antibacterial Activity, Antifungal Activity, Antimicrobial, Antioxidant, Antiulcer Activity, Anti-inflammatory Activities and Reduction in Blood Pressure. It is been widely used in traditional system of medicine in India. Objective: The present study was aimed at evaluating the metabolic extract of aerial parts of *Pavonia Odorata Willd* at doses of 100 and 200 mg/kg body weight for analgesic, anti- inflammatory and antiulcer activities. Methods: The Analgesic activity was evaluated by hot Plate model. Anti-inflammatory activity (sub acute) of *Pavonia odorata willd* methanolic extract was evaluated by carrageenan induced hind paw edema. Aspirin induced ulcer model were employed for evaluating antiulcer activity for methanolic extracts of *Pavonia odorata willd*. Result: Methanolic extracts of *Pavonia odorata willd* was evaluated for Analgesic activity by hot Plate model. Methanolic extracts of *Pavonia odorata willd* produced anti-inflammatory activity at the various time intervals (1, 2, 3, 4, 5 and 24h) when it was evaluated for by carrageenan induced rat paw edema model. POM at both the doses exhibited good anti ulcer activity in aspirin induced ulcers model.

Keywords: *Pavonia odorata willd* –Analgesic, Anti-inflammatory; Antiulcer

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1. Introduction

Botanical name : *Pavonia odorata willd*

Vernacular Names

English: Fragrant swamp mallow, fragrant pavonia
Hindi: Bala, Sugandha-Bala, Sugandhabala
Kannada: Bala Raakshasi, Bala Rakkasi, Bala-Rakkasi-Gida, Balaraakshi Gida, Balarakkasi Malayalam: Iruveli, Kuruntotti
Marathi: Kaalaavaala, Kala-Vala, Kalavala, Randodaki, Sugandhabala, Sughandabala
Sanskrit: Ambu, Ambunamaka, Bala, Balaka, Barhishtha, Harivera, Hribera, Hrivela
Tamil: Anantai, Anantavariti, Anantavariti, Anantavariticceti, Antai, Antaiyitan, Arttavacceti
Telugu: Chirubenda, Chitlebunda, Chitti Benda, Chittibenda, Cittibenda, Erra-Kuti, Errakooti
Tibetan: Ba-La-Ka

TAXONOMY

Kingdom:	Plantae
Order:	Malvales
Family:	Malvaceae
Sub family:	Malvoideae
Tribe :	Hibisceae
Genus:	Pavonia
Species :	Pavonia odorata

Figure No. 7. Leaves of Pavonia odorata willd

Figure No. 8. Flower of *Pavonia odorata willd*

Therapeutic uses:

The roots of P. odorata are used for the preparation of perfumery like Hina. Moreover, the roots also have medicinal properties against intestinal haemorrhage, inflammation and stomachache. A white and soft fiber can be found in this species that is of good quality and finer texture(Randive and Hatekar, 2010).The wild P. odorata produces musk like aromatic odor from the roots. In Ayurveda the therapeutic application of its roots and aerial parts are mentioned in form cooling, demulcent, carminative, diaphoretic and fever along with its action against internal organ hemorrhage and inflammation (Selvan et al., 2007).Young shoots and leaves have been used as an emollient (Nadkarni, 1982; Chopra, 1994).The plant was reported to contain sesquiterpene alcohol known as pavonenol (C15H24O) (The wealth of India, 1992). The aromatic roots contain refrigerant, antipyretic, stomachic and astringent properties, and also plays role in controlling diabetes, tumor and blood pressure

Phytochemistry:

The volatile oil obtained from P. odorata has been assessed for its chemical properties employing Gas Chromatography-Mass Spectrometry (GC-MS) and its aroma active compounds were identified using Gas Chromatography-Olfactometry (GC-O) and Aroma Extraction Dilution Analysis (AEDA). Amongst the 85 compounds detected by GC-MS; the major constituents reported were a-eudesmol (4.53%), b-caryophyllene oxide (3.08%), ageratochromene (11.95%), hexahydrofarnesyl acetone (5.96%), and palmitic acid (9.95%) (Kashima et al., 2014). Using GC-MS, GC-O and AEDA techniques the most characteristic aroma compounds screened were 3-butylpyridine, 2-nonanone, a-caryophyllene oxide and (E)-pinocarveol. It was found that sweet and spicy odor that comes from its aerial parts is produced by these characteristic aromatic compounds. Earlier many other compounds were also identified in the volatile oil extracted from roots such as a-pinene, a-terpinene, aromadendrene, azulene, caproic acid, isovaleric acid, isovaleraldehyde, methyl heptenone, pavonene, pavoneol and palmitic acid (Baslas, 1959; Kumar et al., 1965).The chemical structures of typical constituents extracted from P. odorata.

Pharmacology:

The discussed traditional implications of P. odorata have been confirmed by the recent pharmacological studies. The traditional uses of this species revealed to possess a broad spectrum of medicinal properties. For example, it has been used to treat tumor, inflammation, microbial infection, diabetes, fever, skin disease, athletes' foot disease, dysentery, gonorrhea, intestinal haemorrhage, ulcers and bleeding disorders. But, based on the literature review, thorough pharmacological evaluations have been not carried out yet. Only a few biological activities have been examined from this species involving antioxidant, antitumor, anti-inflammatory, antimicrobial, antidiabetic, anthelmintic, mosquitocidal and reduction in blood pressure. Antioxidant Activity The antioxidant activity of the P. odorata volatile oil was examined by Kashima et al. (2014) through Oxygen Radical Absorbance Capacity (ORAC) assay employing fluorescein as the fluorescent probe.

The ORAC value of the oil was found to be 594.2±25.9 mM TE/g. The results signified that the volatile oil extracted from aerial parts of P. odorata could be considered as a natural antioxidant agent. Antitumour Activity Methanol extract of P. odorata, hydroalcoholic, and ethyl acetate fractions were evaluated for their

cytotoxic effects (Selvan et al., 2007). The result yields the fact that methanol extract, its hydroalcoholic, and ethyl acetate fractions indeed contain cytotoxic and anticancer property. Using acute toxicity study, it has been found out that methanol extract is non-poisonous and safe to the mark of 2000 mg/kg. The effectiveness of methanol extract with respect to clonogenic inhibition on human breast cancer (MDMB-231), lung cancer (Calu-6) and Prostate cancer (PC-3) was examined by Girish et al. (2016). It was seen that in the dose dependent manner, methanol extract could quite induce cytotoxic effect upon MD-MB-231, Calu-6 and PC-3 cell lines when subjected to different concentrations (0-500 µg/ml). Upon comparison, considerable cytotoxicity

2. Materials and methods

Materials

Plants:

The fresh aerial parts of *Pavonia odorata willd* was procured and authenticated by Dr.Madhava Chetty, Department of botany, Sri Venkateswara University, Tirupathi, A.P., India.

Drugs:

Table 1

S. No	Drug Name	Source
1	Asprin (Ecosprin)	(From USV)
2	Ranitdine (Rantac)	From J.B. Chemicals Pharmaceutical Ltd
3.	Indomethacin (Microid)	From Micro Labs
4	Tramadol (Tramazac)	From Cadila

Animals:

Healthy Albino Wistar rats of female and of approximately same age (12 to13 weeks), weighing between 150-200 g. The animals were acclimatized by keeping them in animal house facility of KGR institute of technology and management for a week. They were housed in polypropylene (32x24x16cm) cages containing bedding material as husk and maintained under controlled conditions of temperature (23±2^{0}C), humidity (55±5%) and 12h light and 12h dark cycles. They were fed with commercial pelleted rat chow (M/S Gold Mohur foods and feds, Mumbai.) with water *ad. Libitum.* The norms for Good Laboratory Practice (GLP) were followed for care of laboratory animals. The animals were maintained in accordance with the CPCSEA guide lines. The studies (Anlagestic, Antiulcer and Anti-inflammatory activities) were conducted after obtaining the approval from Institutional Animal Ethical Committee (IAEC) of KGR institute of technology and management.

Methodology

Extraction:

The fresh aerial parts (leaves, flowers, stem, bark and fruits) of *Pavonia odorata willd* were procured and authenticated by Dr.Madhava Chetty, Department of botany, Sri Venkateswara University, Tirupathi, A.P., IndiaThe authenticated aerial parts were dried in shaded and make in to a uniform powder uhnsing a blender and stored in containers with cork. The aerial parts of Pavonia Odorata were thoroughly cleaned with water and dried in the shade at room temperature and made into a uniform coarse powder and stored in a closed vessel. The dired powder Pavonia Odorata aerial parts (1Kg) was extracted with 90% of Methanol in soxhlet apparatus for 5 cycles. The extract was then dried and stored in containers. THe extract obtained were concentrated under reduced pressure to yield methanolic extacts (18.70 %).

Acute toxicitystudies:

Acute oral toxicity study of methanolic extracts of *Pavonia odorata willd* was carried out according to OECD guidelines 423, (adopted December 17, 2001) for limit test.

Principle:

It is the principle of the test that is based on a stepwise procedure with the use of a minimum number of animals per step; sufficient information is obtained on the acute toxicity of the test substance to enable its classification. The substance is administered orally to a group of experimental animals at one of the defined doses. The substance is tested using a stepwise procedure, each step using three animals of a single sex (normally females). Absence or presence of compound-related mortality of the animals dosed at one step will determine the next step, i.e;

- No further testing isneeded,
- Dosing of three additional animals, with the samedose
- Dosing of three additional animals at the next higher or the next lower dose level.

Method:

- Nulliparous, non-pregnant, 8 – 12 weeks old female rats and its weight should fall in an interval within ± 20% of the mean weight of any previously dosed animals wereused.
- Methanolic solution of methanolic extract (2000 mg/kg b.w.) was administered to one animal each included in thestudy.
- Based on where animal survived or died, suitable tests were performed. (If died, main test was performed and if survived, same test was continued with remaining animals.)
- If three animals died, the limit test was terminated and main test wasperformed.
- The animals were observed continuously for first 2h under followingprofile.
- Behavioral profile: Spontaneous, restlessness, irritability andfearfulness.
- Neurological profile: Spontaneous activities, reactivity, touch response, pain response andgait.
- Autonomic profile: defecation and urination.

After a period of 24 and 72 h, they were observed for any lethality or death. If toxic signs or lethality is not observed, then 1/5th, 1/10th and 1/20th part of the limit test dose were considered as test doses for the present investigation.

Grouping of Animals:

Analgesic Activity: Alboino mice weighing 18-25 grams were grouped into four groups of six animals for hot plate Method and Group1 served as control. The II, III are

received POM (Pavonia Odorata Willd) at 100 and 200 mg/Kg b.w. and group IV received the standard drug tramadol 5 mg/kg body weight by i.p. route in case of hot plate test.

Anti-inflammatory activity: Albino Wistar rats weighing between 150-200 g were randomly divided into 4 groups of 6 animals each. Group I served as control, Group II to Group III were received *Pavonia odorata willd* methanolic extracts (100mg/kg and 200mg/kg b.w.) and Group IV indomethacin 10mg/kg b.w.respectively.

Antiulcer activity:

Albino Wistar rats weighing 200–250g were randomly divided into four groups of six animals in each group for aspirin induced ulcer model. Group I served as control. Group II served as standard. Group III to IV animals received POM 100 and 200 mg/kg body weight and ranitidine 20 mg/kg, p.o.respectively.

Experimental schedule:

Analgesic Activity:

The Emthanalic extractsof Pavonia Odorata willd wereevaluated for analgesic activity by hot plate method the result obtained as follows.

Hot Plate Method:

Albino mice were randomly grouped into six groups of six animals each. Group I served as control. POM and POA 100 and 200 mg/kg b.w., p.o., and the standard tramadol at 5 mg/kg b.w. i.p., was administered to the animals of group II to group VI respectively. The delay in response time (Jumping and hind paw licking response) of animals when placed on the hot plate which was maintained at 55 ± 1ºC was recorded at 0,30,45,60, 90,120 and 180 min. the percentage increase in reaction time was calculated. Percentage protection against thermal pain was calculated by applying the formula:

% protection against thermal pain = $(Ta - T_b) \times 100 / T_b$

Where, Ta – Mean reaction time of test and Tb – Mean reaction time of control.

Anti-inflammatory activity:

Carrageenan induced inflammation: Albino Wistar rats fasted for 12 h were randomly divided into 4-groups of 6 animals each. Group I served as control, Group II served as standard, III to IV received methanolic extracts (100mg/kg and 200mg/kg b.w.) of *Pavonia odorata willd* and indomethacin at the dose of 10mg/kg b.w. respectively through oral route. After 1h of drug administration 0.1ml of 1% suspension of carrageenan was injected into the sub-plantar region of the right hind paw of each rat. The paw volumes were measured using a plethysmograph immediately after injection and every 1 hour upto 6 h and at 24h. The percentage inhibition in paw volume was determined using the formula: (Control reading -Test reading)/Control Reading×100.

Antiulcer activity:

Aspirin induced ulcers in rats: Albino wistar rats were randomly divided into four groups of six animals each. Group I served as control. Group II served as standard. Animals of group III to IV animals received POM 100 and 200 mg/kg b.w. and ranitidine 20 mg/kg b.w. p.o. respectively for five days. On the day five, one hour after administration of extract/ standard, aspirin 200 mg/kgb.w. was administered to all the animals. After four hours, animals were sacrificed; stomach was removed and opened along the greater curvature. The intensity of gastric lesions was assessed and ulcer index was calculated.

3. Results and discussion

Acute toxicity study:

Acute toxicity studies for methanolic extracts of *Pavonia odorata willdLeguminaceae* was conducted as per OECD guidelines 423 using albino wistar rats. Each animal was administered methanolic solution of methanolic extracts by oral route. There was no change in normal behavioral pattern of animals and no sign and symptoms of toxicity were observed during the observations which was done continuously for the first two hours and then observed up to twenty four hours for mortality. The extracts were safe up to a maximum dose of 2000 mg/ kg b.w. The biological evaluation was carried out at doses of 100 and 200 mg/kgb.w

Analgesic activity (Hot plate method):

The methanolic extracts of *Pavonia odorata willd* were evaluated for analgesic activity by hot plate method, the result obtained are as follows: The methanolic extract significantly and dose dependently protected the mice against thermally induced pain stimulus. Methanolic extracts at both the doses produced increase in reaction time at the various time intervals at which they were tested. The comparison of analgesic activity with the standard drug Tramadol at various time intervals is as follows. At 30 min, POM 200 produced analgesic activity comparable to that of standard, as evident by the percentage increase in reaction time which was 47.42±30.9 respectively. The analgesic activity continued even at 45 min. At 60 min POM 100 and POM 200 produced significant *(P<0.05)* analgesic activity which was near to that of tramadol values, the percentage protection was 71±11.48 and 75.85±21.77, respectively. At 90 min, both the dose of methanolic extracts were equal result than that of tramadol, the percentage protection was 68.99±24.7 and 71.93±50.77 respectively. At 120 and 180 min. reaction time decreased when compared with standard.

Anti-inflammatory activity:

Carrageenan induced paw edema:

Pavonia odorata willd was evaluated for anti-inflammatory activity using carrageenan induced rat paw edema model. The paw volume was measured using plethysmograph. Carrageenan induced edema, was evident by increase in paw volume in the control animals at all the time intervals (1, 2, 3, 4, 5, 6 and 24 h) it was testedfor. The methanolic extracts of *Pavonia odorata willd* were found to reduce the edema produced by Carrageenan. The percentage reduction in paw volume was calculated. The percentage inhibition of edema of various doses (100 and 200 mg/kg) methanolic extracts of *Pavonia odorata willd* were compared with standard drug Indomethacin the following results were obtained,

1sthour:

It was found that POM 200, produced significantanti-inflammatory activity that was better than that of standard indomethacin.

2nd hour:

POM 200 produced significantanti-inflammatory activity than the standard indomethacin (56.25±12.5 and 52.5±21 respectively).

3rd hour:

POM 200 produced anti-inflammatory activity which was comparable to that of standard (74.92±19.8Band 73±9.18respectively).

4th our:

POM 200 produced anti-inflammatory activity which was comparable to that of standard indomethacin (76.81±14.8 and 75.72±10 respectively).

5th hour:

All the extracts POM 100 and POM 200 produced good anti- inflammatory activity.

6th hour:

Anti-inflammatory activity of methanolic extract continued even at 6th hour. Higher dose of methanolic extracts produce better percentage inhibition of edema then lower dose.

24th hour:

All the extracts POM 100 and 200, produce similar anti-inflammatory activity than that of standard indomethacin. The percentage decrease in edema of POM 100 & 200, and indomethacin are 21.31±9.72, 28.93±8.28, and 31.47±17.33respectively. The various extracts were found to produce significant anti-inflammatory activity at all the time intervals it was tested for.

Antiulcer activity

At the end of the study, the stomach were isolated and washed with saline. The stomach was observed for ulceration and ulcers were scored, Ulcer index and percentage protection against ulcers was calculated. The recorded parameters were compared by statistical analysis with control and also with standard.

Aspirin induced ulcers in rats:

Significant decrease in ulcer score was produced by ranitidine, POM at both 100 and 200 mg/kg b.w. when compared to control. Higher dose of POM and produced maximum decrease in ulcer score, which was better than the lower dose of POM extracts. Percentage protection against ulcers by POM 200 was comparable to that of standard drug ranitidine. The percentage protection against ulcer by ranitidine, POM 100 and 200 mg/kg b.w. were found to be 96.58, 87.42 and 95.70, respectively.

Discussion

Analgesic activity:

Antinoiceptive or analgestic acitivty of Pavonia Odorata willd was evaluated by using thermal model of nociception in mice. The methanolic dose of PO dependently increased the reaction time at the various time intervals at which they were tested. At higher the reaction time at the various time intervals at which they were tested. At high doses the extracts showed activity which was comparable to that of tramadol (45 min) and was better than tramadol at 60 and 90 min. This indicates that the extracts exhibit analgesic effect.

Anti-inflammatory activity:

In the present study of carrageenan induced paw edema, the anti-inflammatory activity of *Pavonia odorata willd* methanolic extracts at the dose of 100 and 200 mg/kg b.w. took place at1, 2, 3, 4, 5, 6 and 24h after carrageenan injection suggesting that its mechanism of action may involve inhibition of prostaglandins. POM 200 showed better result in first two hours after carrageenan injection as compared to that of standard drug indomethacin. At 3, 4 and 5h POM 100, 200 showed the anti-inflammatory activity comparable to that of indomethacin. At 6 h all the extracts show the relatively same activity but at 24h POM 200 showed better activity which are comparable to that of standard drug. It is evident from the study that methanolic extracts of *Pavonia odorata willd* possess anti-inflammatory.

Antiulcer activity:

Methanolic extracts at both the doses, reduced ulcers significantly when compared to the control as evident by decrease in ulcer score. The results suggest possible involvement of prostaglandin and /mucus in antiulcer effect of extracts and may also be due to anti oxidant activity of theextracts. Methanolic extracts of *Pavonia odorata willd* at both the doses produced significant decrease in gastric volume, total and free acidity indicating its anti secretory activity when compare to that control group. The methanolic extracts at both the doses also produced decrease in the ulcer incidence as evident by decrease in ulcer score and provided protection againstulcers

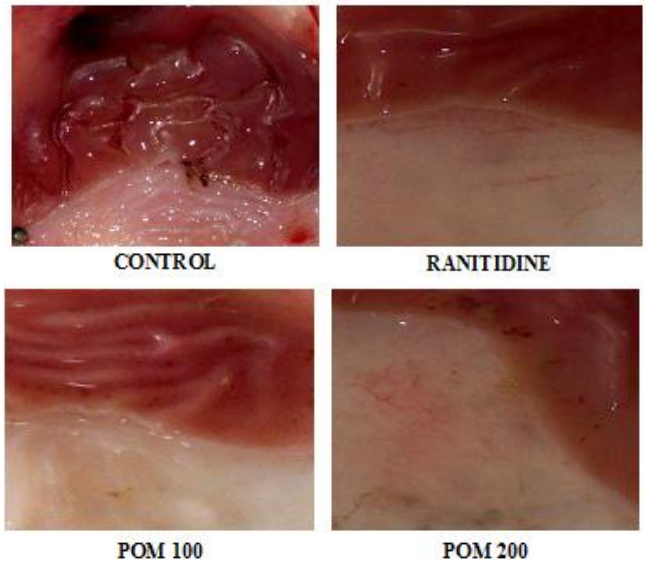

Figure No.1 Asprin induced ulcers.

4. Conclusion

The study was taken up to evaluate methanolic extracts of aerial parts of *Pavonia odorata willd* for analgesic, anti-inflammatory and antiulcer activities. The acute toxicity study conducted for methanolic and extract indicates that theya re sale upto to 2000 mg/kg b.w. Methanolic extract pf *Pavonia odorata willd* produced significant analgesic activity in hot plate in mice. This was evident by increase in reaction time of hot plate. Methanolic extracts of *Pavonia*

odorata willd produced anti-inflammatory activity at the various time intervals (1, 2, 3, 4, 5 and 24h) it was evaluated for, by carrageenan induced rat paw edema model. This indicates that the extracts of aerial parts of *Pavonia odorata willd* produce anti-inflammatory activity. Evaluation of anti ulcer activity was done by aspirin induced ulcer model in rats. Ulcers were scored; ulcer index and percentage protection against ulcers was calculated. It was evident from the results that *Pavonia odorata willd* extracts produced significant antiulcer activity. Results of the study suggest that it can be used in therapeutics for the treatment of analgesic, inflammation and ulcers. So it can be concluded that *Pavonia odorata willd* has the potential of being used as analgesic, anti-inflammatory and antiulcer agent.

Table 2: *Analgnesic effect of Pavonia Odorata willd aerial parts extracts and tramadol by hot plate method*

Groups	Dose (Mg/Kg)	Percentage increase in reaction time					
		30 Min	45 Min	60 Min	90 Min	120 Min	180 Min
Control	—	—	—	—	—	—	—
Standard (Tramadol)	5	49.06+32.88	77.98+47.95	80.68+34.21	74.67+41.15	63.55+36	44.97+33.94
POM	100	24.39+18.13	62.88+13.11	71+11.48*a	68.99+24.7*a	52.99+27.85	25.77+18.81
POM	200	47.42+30.9	66.47+23.34	75.85+21.77*a	71.96+50.77*a	37.55+16.38	24.87+18.47

n=6, vaules represent mean+ SD Where POM 100 and 200 indicates Pavonia Odorata WIlld doses 100 and 200 mg/kg body weight respectively.* Symbols represent statistical significance. **P < 0.01., *P < 0.05, 'a' as compared with standard tramadol.

Table 3: *Effects of methanolic extracts of aerial parts of Pavonia odorata willd on carrageenan induced paw edema in Albino wistar rats:*

Groups	**Dose (mg/kg)**	**Percentage inhibition of edema at various time intervals**						
		1h	**2h**	**3h**	**4h**	**5h**	**6h**	**24h**
Control	--	0.1ml	--	--	--	--	--	--
Indomethacin	10	25±28.8	52.5±21	73±9.18	75.72±10.4	72.22±11.11	78±16.6	31.47±17.33
POM	100	12.5±25	47.5±5	69.23±12.5	69±6.9	68.88±10.8	76.66±10	21.31±9.72
POM	200	37.5±25	56.25±12.5	74.92±19.8	76.81±14.8	78.88±20.32	82.10±20	28.93±8.28

n=6, values represent mean ±SD. Where, POM 100 and 200 indicates Pavonia odorata willd methanolic extracts at doses 100 and 200 mg/kg b.w. respectively compared with indomethacin.

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