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Evaluation of Analgesic, Anti-inflammatory and Antipyretic Potential of *Parkinsonia aculeata* Linn. Leaves

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ABSTRACT

The present study was aimed at evaluation of the analgesic, anti-inflammatory and antipyretic activity of total alcoholic and aqueous extract of leaves of *Parkinsonia aculeata* Linn in mice and rats. The alcoholic extract of *P. aculeata Linn.* leaves *at* a dose of 200 mg/kg body weight has shown significant analgesic, antipyretic and anti-inflammatory activity as compared to aqueous extract. The result of hot plate indicated that the total alcoholic extract shows a significant increase ($P<0.01$) in reaction time at a 3, 4and 6 hours comparable to the reference drug Pentazocin but lesser ($P<0.05$) at 2 hr. The tail immersion and hot plate test reveal that this plant has high analgesic activity. This is because some form of error may be introduced with the animal handing while the test is being elicited. Both test show highest degree of analgesia in alcoholic extract compared to aqueous extract. The total alcoholic extract of P. aculeata L leaves at the a dose of 200 mg/kg body weight has shown significant ($p<0.01$) antipyretic activity as compared to aqueous extract, it has shown significant fall in body temperature up to 4h following its admistraction. The antipyretic activity stared as early as 1h and the effect was maintain for 4h.The response was comparable to that antipyretic activity of paracetamol a standard antipyretic drug. Total alcoholic extract significantly inhibited Carrageenin-induced paw oedemas compared; it may be due to possible inhibition of lipooxygenase pathway.

KEYWORDS: *Parkinsonia aculeata,* Analgesic, Anti-inflammatory, Antipyretic, Tail immersion method, Eddy's Hot plate method. Paw edema method, Yeast induced pyrexia method.

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INTRODUCTION

The problem of uncontrolled pain led early human to seek remedies from any materials that they could lay their hand on. In resent times, focus on plant research has increase and non-steroidal anti-inflammatory drugs constitute one of the most widely used classes of drugs. Herbal drugs are being proved as effective as synthetic drugs with lesser side effects. Herbal medicines are in line with nature, with less hazardous reaction[1].

Parkinsonia (Leguminosae) is a small genus containing three species which are common in tropical America and have been recently naturalized in hotter regions, e.g. Egypt and India[2]. *Parkinsonia aculeata* is a tree from the family Fabaceae; common names include Mexican Palo Verde, Parkinsonia, Jerusalem thorn, or Jellybean tree[3]. Previous investigations showed that the leaves from the plant contains orientin, iso-orientin, vitexin, isovitexin, lucenin-II, vicenin-II, diosmetin 6-C-Bglucoside, apigenin, luteolin, kaempferol, chrysoeriol, epiorientin, parkinsonin-A, parkinsonin-B, and parkintin[2,4-6]. All the parts of the plant are known as antipyretic, diaphoretic, and abortifacient[7-8], reported to possess antimicrobial activity[9]. The alcoholic extract of the aerial part possess CNS depressant activity[3]. However, there is no report of the presence of analgesic, antipyretic and anti-inflammatory activity from ***P. aculeata*** L. leaves.

MATERIALS AND METHODS

PLANT MATERIALS

Leaves of ***Parkinsonia aculeata*** *Linn.* was collected from local areas of Ajmer road, Jaipur, Rajasthan. The taxonomical identification of the plant was done by Dr. Gajendra Pal Singh, Department of Botany, University of Rajasthan, Jaipur, and voucher specimens were deposited at the herbarium, Department of Botany, University of Rajasthan, Jaipur (Specimen No. RUBL20684). Bark was dried under shade, coarsely powdered and stored in airtight container for further use.

PREPARATION OF EXTRACT

The powdered leaves was Soxhlet-extracted with total alcoholic. The extract, on removal of solvent in vacuum, gave dark green semisolid residue (yield: 9.8% w/w). The leaves of *P. aculeata* was shade dried at room temperature, pulverized, and 100g of coarse powder was macerate exhaustively with water then being kept for 5 days in tightly sealed vessels at room temperature, protected from sunlight and shaken several times daily and add preservative(2% chloroform). Concentrate extract by distilling

off the solvent and then evaporating to dryness on water –bath, gave yellowish brown semisolid residue (yield: 11.8% w/w)[10-11].

PHYTOCHEMICAL SCREENING

Preliminary Phytochemical investigation was carried out for extracts. Presence of alkaloids was determined by Mayer's, Dragendorf's, Wagner and Hager's test, Flavonoids by Shinoda, Ferric chloride and lead acetate tests, Saponins by Foam and haemolysis test and sterols by Salkowaski and Libermann and Burchards tests[12].

ANIMALS USED

Wister rats of either sex weighing 180-200g and Swiss mice weighing 18-28g were maintained under standard nutritional and environmental conditions throughout the experiment. The animals were of food for 24 h before experimentation but allowed access to tap water throughout. Animal were divided into five (n=6) for each experimental model, control, standard, two extract. The experimental protocol was approved by institutional ethical committee (IAEC) of Sri Balaji College Of Pharmacy, Benad road, Jaipur (Letter No. IAEC/SBCP/10-461/2010-11) with CPCSEA Registration no. 1212/AC/08/CPCSEA Dated O5.O6.2008.

TOXICITY STUDY[13]

P. aculeata was tested in single doses in each experimental model as per following the OECD guideline no. 420 fixed dose method procedure, the safest dose of total alcoholic extract and aqueous extract are 2000mg/kg body weight. The safe dose was found to be 2000mg/kg body weight; hence $1/10^{th}$ of the dose was taken as effective dose which was found to be 200mg/kg body weight. Pentazocine 5mg/kg was used as the standard analgesic in hot-plate and Acetyl salicylic acid 640mg/kg p.o in tail immersion in mice. Paracetamol was used as standard drug (positive control) in anti-pyretic models in the dose of 150 mg/kg and required quantity was dissolved in normal saline. In the anti-inflammatory model aspirin was used as the standard drug in a dose of 150 mg/kg.

ASSESSMENT OF ANALGESIC ACTIVITY[14-16]

Hot Plate Method

In the hot plate method albino mice (18-28) were divided into four groups each consisting of six animals. One group served as a control (received vehicle), second group served as a standard (received

Pentazocine 5mg/kg) while the third group received the alcoholic extract (As per b/w), and four group received the aqueous extract (As per b/w). The basal reaction time was noted before and 30, 60, 90 and 120 minutes after the administration of the drugs.

Tail Immersion Method

In the Tail immersion method albino rats (180-200g) were divided into four groups each consisting of six animals. One group served as a control (received vehicle), second group served as a standard (received Acetyl salicylic acid 640mg/kg p.o) while the third group received the alcoholic extract (As per b/w), and four group received the aqueous extract (As per b/w).The time in second to withdraw the tail clearly out the water was taken as the reaction time.

ASSESSMENT OF ANTI- PYRETIC ACTIVITY[16-17]

Induction of yeast-induced pyrexia

Rats were divided into four groups of six each for this experiment. The normal body temperature of each rat was measured rectally at predetermined intervals and recorded. The rats were trained to remain quiet in a restraint cage. A thermister probe was inserted 3-4 cm deep into the rectum and fastened to the tail by adhesive tape. The temperature was measured on a thermometer. After measuring the basal rectal temperature, animals were given a subcutaneous injection of 10 ml/kg body wt. of 15% w/v yeast suspended in 0.5% w/v methyl cellulose solution. Rats were then returned to their housing cages. After 19 h of yeast injection, the animals were again restrained in individual cages for another recording of their rectal temperature as described above.

Drug administration

After 19 h of yeast injection, the total alcoholic and aqueous extracts were administered orally at doses of 200 mg/kg body wt. to two groups of animals, respectively. A similar volume (5ml/kg body wt.) of normal saline solution was administered orally to the control group. The fourth group of animals received the standard drug paracetamol (150 mg/kg body wt.) orally. Rats were restrained for recording of their rectal temperature at the nineteenth hour, immediately before total alcoholic and aqueous extract, saline or paracetamol administration, and again at one-hour intervals up to the twenty-third hour after yeast injection.

ASSESSMENT OF ANTI- INFLAMMATORY ACTIVITY[16,18-19]

Carrageenin-induced rat paw oedema

The rats were divided into four groups, each groups consisting of six animals. Oedema was induced by sub plantar injection of 0.1 ml of 1% freshly prepared suspension of Carrageenin into the right hind paw of each rat. The paw volume was measured before (O h) and 1 h after the injection of Carrageenin using a Plethysmometer. The total alcoholic and aqueous extract bark in 2% Tween 80 solution (200 mg/kg) was administered orally to two groups of rats, 30 min before the injection of Carrageenin. The third and fourth group of rats received 2% aqueous Tween 80 solution 10 ml/kg orally (control) and Aspirin 150 mg/kg as a reference drug.

STATISTICAL ANALYSIS

Values are expressed as mean ± S.E.M Statistical significance was analyzed using one way ANOVA.

RESULTS AND DISCUSSION

The OECD guideline 420 fixed dose methods study showed that extract was safe at a dose of 2000 mg /kg body weight. The alcoholic extract of *P. aculeata Linn. leaves at a dose* of 200 mg/kg body weight has shown significant analgesic, antipyretic and anti-inflammatory activity as compared to aqueous extract. The analgesic activity of leaves of *Parkinsonia aculeata Linn.* was studied for its central activity. The result of hot plate indicated that the total alcoholic extract shows a significant increase ($P<0.01$) in reaction time at 3 and 4 hours comparable to the reference drug Pentazocin but lesser ($P<0.05$) at 2 hr. Aspirin leads to a relief from inflammatory pain by suppressing the formation of pain inducing substances in the peripheral tissues, prostaglandins and bradykinin were suggested to play an important role in the pain process[20]. Therefore it is likely that *Parkinsonia aculeata Linn.* leaves might suppress the formation of these substances. It has been widely accepted that Carrageenin-induced paw oedema model is applied for the evaluation of the antioedemal effect of drugs. Recent investigation demonstrated that Carrageenin oedema is effectively decreased by lipooxygenase inhibitors. In the present study, total alcoholic extract significantly inhibited Carrageenin-induced paw oedemaas compared; it may be due to possible inhibition of lipooxygenase pathway although such assumption obviously requires confirmation by further detailed experimentation[21]. The total alcoholic extract of P. aculeata L leaves at the a dose of 200 mg/kg body weight has shown significant ($p<0.01$) antipyretic activity as compared to aqueous extract, it has shown significant fall in body temperature up to 4h

following its admistraction. The antipyretic activity stared as early as 1h and the effect was maintain for 4h.The response was comparable to that antipyretic activity of paracetamol a standard antipyretic drug. But aqueous extract did not showed significant activity as compared total alcoholic extract.

A drug with anti-inflammatory activity usually exhibit anti-pyretic and analgesic properties. The best examples would be the nonsteroidal anti-inflammatory drugs, which possess all three activities[22]. Inflammation is a defensive reaction of the local microcirculation to tissue injury arising from cell damages due to mechanical trauma, chemical, physical and thermal injury, antigen antibody reactions and infections. The signs and symptoms of inflammation include redness, swelling, heat, pain and loss of function of the affected area. Pain is an unpleasant sensation that is a consequence of complex neurochemical processes in the central and peripheral nervous systems. Non-steroidal anti-inflammatory drugs (NSAIDS) and opioids are used in management of mild to moderate and severe pains respectively. These drugs have serious limitations due to their side effects. Most of the drugs used presently for the management of pain and inflammation possess some side and toxic effects. It is therefore, inevitable to search for new, less toxic and more effective anti-inflammatory and analgesic agents[23]. Fever may due to infection or one of the sequels of tissue damage, inflammation, graft rejection, or other disease states. Antipyretic are agent which reduce the elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained. In fever this set point elevates and a drug like paracetamol does not influence body temperature when it is elevated by the factors such as exercise or increase in ambient temperature. Yeast-induced fever is called pathogenic fever. Its etiology includes production of prostaglandins which set the thermoregulation center at a lower temperature[24]. In the present study, total alcoholic extract significantly inhibited Carrageenin-induced paw oedemaas compared to aqueous extract. The tail immersion and hot plate test reveal that this plant has high analgesic activity. This is because some form of error may be introduced with the animal handing while the test is being elicited. Both test show highest degree of analgesia in alcoholic extract compared to aqueous extract. Alcoholic extract of bark possesses a significant antipyretic effect in yeast provoked elevation of body temperature in rats as compared to aqueous extract but its effect less than that of paracetamol (standard drug). The result clearly indicate that the total alcoholic extract of *Parkinsonia aculeata Linn.* bark in context of analgesic, antipyretic and anti-inflammatory activity. The detailed study is required in order to identify the actual active constituent from this drug.

Table 1: Effect of pentazocine, alcoholic extract, and aqueous extract of leaves of *Parkinsonia aculeata* on eddy's hot plate test in mice

S.No	Treatment	Reaction time in seconds				
		0 min	30 min.	60 min	9o min	120 min
1.	Control	2.83±0.3073	3.66±0.3333	3.66±0.3333	3.00±0.2582	3.00±0.2582
2.	Pentazocine (5 mg/kg. s.c)	2.83±0.3073	3.66±0.2108	5.5±0.2236**	6.65±0.3333**	7.5±0.4282**
3.	PALAL (200 mg/kg, p.o)	2.83±0.1667	3.33±0.3333	3.66±0.2108	4.83±0.3073**	5.5±0.2236**
4.	PALAQ (200 mg/kg, p.o)	2.83±0.1667	3.33±0.3333	3.16±0.1667	4.83±0.3073*	5.33±0.2108**

The results were analyzed by ANOVA followed by Dunnet's test (p-value ≤0.05 was taken as significant).

Table 2: Effect of acetyl salicylic acid, alcoholic extract, and aqueous extract of leaves of P*arkinsonia aculeata* on tail immersion test in rats

S. No.	Treatment	Response Time In Seconds						
		0.0 min	30min	1st hr.	2nd hr.	3rd hr	4th hr.	6th hr.
1	Control	2.83±0.1667	2.88±0.1667	3.00±0.2582	3.00±0.2582	3.00±0.2582	3.16±0.3073	3.16±0.1667
2	Aspirin (640mg/kg, p.o)	3.16±0.3073	3.33±0.2108	3.83±0.3073	5.66±0.3333**	6.83±0.3073**	7.67±0.2108**	8.00±0.2582**
3	PALAL (200mg/kg, p.o)	3.00±0.2582	3.00±0.2582	3.5±0.2236	4.00±0.2582	4.50±0.3416**	6.17±0.3073**	6.33±0.3333**
4	PALAQ (200mg/kg, p.o)	3.00±0.2582	2.66±0.2108	3.33±0.2108	3.5±0.2263	4.00±0.2582*	4.83±0.3073**	4.83±0.3073**

The results were analyzed by ANOVA followed by Dunnet's test (p-value ≤0.05 was taken as significant).

Table 3: Effect of paracetamol, alcoholic and aqueous extracts of leaves of *Parkinsonia aculeata* on yeast-induced pyrexia

S.NO.	Treatment	Initial temp (°C)	Temp. after 19 hr yeast admn.(°C)	Temp at different hr after treatment (°C)			
				20 hr	21 hr	22 hr	23 hr
1	Control	37.18±0.0945	39.16±0.0667	37.30±0.5574	39.45±0.6708	39.51±0.0654	39.56±0.0843
2	Paracetamol 150 mg/b.w	37.33±0.0894	39.38±0.600	38085±0.7188	38.18±0.1887	37.51±0.07949**	37.51±0.600**
3	PALAL 200mg/b.w	37.6±0.0577	39.65±0.0428	38.46±0.0494	38.38±0.0497	38.21±0.4014*	38.13±0.1145**
4	PALAQ 200mg/b.w	37.53±0.0714	39.51±0.0703	38.58±0.1138	38.35±0.1025	38.16±0.0706	38.11±0.1483*

The results were analyzed by ANOVA followed by Dunnet's test (p-value ≤0.05 was taken as significant)

Table 4: Effect of aspirin, alcoholic extract, and aqueous extract of leaves of *Parkinsonia aculeata* on paw edema in carrageenan paw edema model in rat

S.No	Treatment	(Paw size) Change in volume (ml) at h				
		0 Hr.	1 Hr.	2 Hr.	3 Hr.	4 Hr.
1.	Control	0.84±0.0160	1.02±0.0275	1.16±0.0518	1.19±0.0393	1.21±0.0339
2.	Aspirin 150 mg/b.w	0.77±0.0315	0.74±0.0049	0.70±0.0079**	0.69±0.0060**	0.64±0.0085**
3.	PALAL 200 mg/b.w	0.79±0.0122	0.82±0.0140	0.83±0.0130	0.86±0.0107	0.84±0.0080**
4.	PALAQ 200 mg/b.w	0.77±0.0231	0.81±0.0168	0.83±0.0137	0.85±0.0144	0.84±0.0121*

The results were analyzed by ANOVA followed by Dunnet's test (p-value ≤0.05 was taken as significant)

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