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Investigation of analgesic activity of *Ptersospermum canescens,* Roxb., (Sterculiaceae) extracts in experimental animals

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Abstract : Pain is an perception alone which does not require cortex. A lot of research is going on worldwide towards finding analgesic agents from the natural sources. The main aim of the present study was to investigate analgesic activity of petroleum ether, chloroform and methanol extracts (100 mg/kg, 200 mg/kg) of *Pterospermum canescens*, Roxb., (Sterculiaceae- leaf, stem and stem bark) andwas carried out by eddy's hot plate method using Indomethacin as standard (10 µg/kg). This present investigation revealsthat the methanol leaf and stem bark extracts were exhibited significant ($P < 0.05$) increase in animal reaction time to heat stimulus that at 200 mg/kg in experimental animals.
Key words : Pterospermum canescens, Analgesic activity**,** Brewer's yeast, Thermometer, Indomethacin.

Introduction

Plants are important and basic of preventive and curative healthcare system since immemorial. Disease is as old as mankind and use of indigenous herbal medicine is a very ancient art and an integral part of treatment [1]. According to WHO, nearly 75-80% of world population still depends on herbal medicines. Active constituents from plant sources directly used as therapeutic agent and phytoconstituents are also served as lead molecule for the synthesis of various drugs [2]. WHO noted that about 25% of modern medicines are derived from plant sources used traditionally and research on traditional medicinal herbal plant leads to discovery of 75% herbal drugs [3].

Pain is a complex unpleasant phenomenon composed of sensory experiences that includes time, space, intensity, emotion and motivation originating from damaged tissue or at abnormal condition.Nonsteroidal anti-

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inflammatory drugs (NSAIDs) reduce pain and edema by suppressing the formation of prostaglandins, by inhibiting the activity of the enzyme Cyclooxygenase (COX-1 and COX-2). However, prostaglandins are key mediators of several components of GI mucosal defense, so suppression of synthesis of prostaglandins (PGs) by NSAIDs greatly reduces the resistance of the mucosa to injury as well as interfering with repair processes. Selective COX-2 inhibitors were thought to be the solution to this conundrum as it is required that NSAIDs suppress prostaglandin synthesis at sites of inflammation, and not in the GI tract.

However, it is now clear that both COX-1 and COX-2 isoforms contribute to mucosal defense. Selective COX-2 inhibitors elicit less GI damage and bleeding than conventional NSAIDs, although the magnitude of this reduction continues to be contested in the literature. As widely reported in the lay-press, the selective COX-2 inhibitors also cause significant adverse effects in the renal and cardiovascular systems, possibly more serious than those caused by conventional NSAIDs. The market for NSAIDs is expanding rapidly because of an aging population in developed countries and the associated increase in the prevalence of diseases like arthritis. Use of aspirin is also increasing because of its utility in reducing the incidence of a number of common disorders including stroke, myocardial infarction, Alzheimer's disease and cancer [4].

However, their use is limited by their significant side effects upon the stomach and the kidney. Their side effects as well as their therapeutic actions are related to their ability to inhibit cyclooxygenase enzymes involved in the first step of the arachidonic acid cascade [5-6].In addition, the damaging effect of some NSAIDs upon the stomach and intestine is in part due to their acidic nature, as with indomethacin, ibuprofen, diclofenac, naproxene, aspirin,etc [7]. Although basic NSAIDs such as glafenine and floctafenine are expected to be devoid of the primary insult effect, their damaging effect upon the stomach and kidney is still prominent as they inhibit prostaglandin biosynthesis as strongly as indomethacin [8-9].

In the recent years, several novel approaches for reducing the GI toxicity of NSAIDs with promising results have been reported. These mainly involve structural modification of existing NSAIDs such that inhibition of COX is maintained, but other attributes are added that diminish GI (and other) toxicity, and in some cases boost efficacy and/or potency [1]. The mortality rate for NSAID induced GI bleeding is 5-10% in the world population.

With this background, this study was conducted with an objective of evaluation of the antipyretic activity of *Pterospermum canescens,* Roxb., in Wistar albino rats. The genus *Pterospermum* Schreb., (Sterculiaceae) represents of about 40 species in the world, of which 12 species were reported from India [10] and 8 species has been reported from TamilNadu [11] and is also available in the dry evergreen forests of SriHarikotta Island, Nellore District, Andrapradesh [12] as well as in Coramantal coast [13].

An ethnomedicinal plant species *Pterospermum canescens* Roxb., (Syn. *Pterospermum suberifolium* Lam.) locally known as *Sempulavu* was distributed in all districts of TamilNadu. Ethnomedicinally, the leaves are used for the treatment of headache [14], fractured bones [15] small pox [16], has antimicrobial [17-18], anti-inflammatory [19] and antipyretic properties [20]. The plant has been reported to contain β- amyrin, betulin, kaempferol, lupeol, quercetin, scopoletin and β-sitostero [21] and α-sitosterol, 3, 7, 11, 15- tetramethyl-2-hexa decane-1-ol, ricinoleic acid, vitamin-E, phytol, α-tocopherol, diethyl phthalate, squalene, benzhydrazide-3-mthoxy-N2-(4-henylcyclo hexylideno, benzoic acid, 4- heptyl-4-cyanophenyl ester and n-hexa decanoic acid [22]. After the scrutiny of literatures, it was confirmed that so far no other work has been carried out on this plant. Hence, the present study aims to develop an analgesic lead of therapeutic interest from this selected ethnomedicinal plant.

Materials and Methods

Plant material

The plant material (leaf, stem and stem bark) of *Pterospermum canescens* Roxb., were collected from the Kalapet vicinity of Pondicherry and the collected plant material was botanically identified and confirmed by the Plant Taxonomist Dr.A.C.Tangavelou and the herbarium specimen (KPJ 42) was prepared and deposited at the department for future reference. The leaf, stem and stem bark were separately dried in shade.

Preparation of extracts

The collected plant material (leaf, stem, stem bark) were chopped into small pieces, shade dried and coarsely powdered by using a pulverizerand then pass it through a 40 mesh size sieve. Then, the powder materials were subjected to successive solvent extraction with organic solvents of increasing polarity such as petroleum ether, chloroform and methanol by continuous hot percolation method using soxhlet apparatus[23-24]. The solvents were then evaporated to dryness under reduced pressure in a rotary evaporator at 40˚- 45˚C. The concentrated extracts of leaf, stem and stem bark were separately aliquoted in amber-coloured bottles and kept in dessicator for further use. The resulted extracts were used for screening of analgesic activity.

Animals

Wistar albino rats (180 – 230 g) were used for analgesic studies. They were kept in polypropylene cages at 25˚±2˚C, with relative humidity 45-55% under 12 h light and dark cycles. All the animals were acclimatized to the laboratory conditions for a week before use. They were fed with standard animal feed (Kamadhenu agencies, Bangalore, India) and water *ad libitum.* The experimental protocols were carried out at C.L. Baid Metha College of Pharmacy, Thoarpakkam, Chennai (IAEC/ 34/ 22/ CLBMCP/ 2011, dated on 7/2/2011) approved by the Institutional Animal Ethics Committee.

Antipyretic activity Induction of pyrexia

Eddy's hot plate method [25]

Analgesic activity of *Pterospermum canescens* Roxb., was studied by eddy's hot plate method. Wistar albino rats were divided into eight groups of four animals each and they were fasted overnight, during the experiment free access of water *ad libitum.* Group I served as control (0.9% Normal saline with 3% Tween, 2 ml/kg), Group II, III (PETL, PETH - 100, 200 mg/kg); Group IV, V (CHL, CHH - 100, 200 mg/kg) and Group VI, VII (MEL, MEH - 100, 200 mg/kg) are administered with petroleum ether, chloroform and methanol extracts of *Pterospermum canescens*, Roxb., (leaf, stem, stem bark) respectively and Group VIII served as standard (Indomethacin, 10 mg/kg, orally).

In eddy's hot plate method, the basal reaction time of all the animals of control, standard and test groups were recorded by putting them on hot plate maintained at 55.5°C. Fore paw licking or jumping response was taken as the index of reaction of heat. Thereafter, all the groups were treated with the respective drug substances. The response time was noted as the time at which animals were reacted to the pain stimulus either by paw licking or jumping response, whichever appeared first. Analgesics increase the reaction time. It evaluates thermal pain refluxes due to footpad contact with a heated surface [26]. The cut off time for the reaction was 15 seconds. Post treatment reaction time of each animal was recorded at 30 minutes interval for 120 minutes and the percentage increase or decrease in reaction time (as an index of analgesia) at each time interval was calculated.

% increase in reaction time= $\frac{Rt}{}$ 1Rc

Where, Rt = reaction time of treated group Rc = reaction time of control group

Statistical analysis

Data were expressed as mean ± SEM and were analyzed statistically by one way ANOVA procedures followed by using Dunnett's test. A difference was considered significant as $P < 0.05$[27-28].

Results and Discussions

Leaf

In hot plate method, standard group of animals were exhibited significant ($P < 0.05$), increase in the animal reaction time to heat stimulus when compared with control group of animals. Methanol leaf extract (200 mg/kg) was exhibited significant ($P < 0.05$), increase in the animal reaction time to heat stimulus when compared with control group of animals. Petroleum ether (100, 200 mg/kg), chloroform (100, 200 mg/kg) and

methanol (100 mg/kg) leaf extracts didn't show significant, but increase in the animal reaction time to heat stimulus when compared with the control group of animals (Fig. 1; Table 1).

Stem

In this method, standard group of animals were exhibited significant ($P < 0.05$), increase in the animal reaction time to heat stimulus when compared with control group of animals. Petroleum ether, chloroform and methanol (100, 200 mg/kg) stem extracts didn't show significant, but increase in the animal reaction time to heat stimulus when compared with control group of animals (Fig. 2; Table 2).

Stem bark

In this method, standard group of animals were exhibited significant ($P < 0.05$), increase in the animal reaction time to heat stimulus when compared with control group of animals. Methanol stem bark extract (200 mg/kg) was exhibited significant ($P < 0.05$), increase in the animal reaction time to heat stimulus when compared with control group of animals. Petroleum ether (100, 200 mg/kg), chloroform (100, 200 mg/kg) and methanol (100 mg/kg) stem bark extracts didn't show significant, but increase in the animal reaction time to heat stimulus when compared with the control group of animals (Fig. 3; Table 3).

In this present study, extracts tested at administered doses showed dose-dependent analgesic activity. In methanol leaf and stem bark extracts were exhibited significant ($P < 0.05$) increase in animal reaction time to heat stimulus at 200 mg/kg in experimental animals,while the other extracts of leaves, stem and stem bark did not show significant.

Table No.1. Analgesic activity of leaf extracts

Treatment	**Basal reaction time in seconds**				
0 min	30 min	60 min	90 min	120 min	
Control	2.50 ± 0.22	3.00 ± 0.00	2.83 ± 0.16	2.83 ± 0.30	2.66 ± 0.21
PETL	2.50 ± 0.22	3.67 ± 0.21	3.33 ± 0.21	3.50 ± 0.22	4.33 ± 0.21
PETH	2.83 ± 0.17	3.67 ± 0.21	4.00 ± 0.26	5.17 ± 0.31	5.50 ± 0.22
CHL	2.67 ± 0.21	3.50 ± 0.22	3.67 ± 0.21	4.00 ± 0.37	4.00 ± 0.45
CHH	3.17 ± 0.17	3.50 ± 0.22	3.50 ± 0.22	4.67 ± 0.21	5.17 ± 0.40
MEL	2.67 ± 0.33	4.00 ± 0.26	4.50 ± 0.22	5.17 ± 0.31	5.33 ± 0.33
MEH	3.17 ± 0.17	4.17 ± 0.17*	4.67 ± 0.21*	5.00 ± 0.37*	5.67 ± 0.21*
STD	2.83 ± 0.17	3.33 ± 0.33*	5.17 ± 0.31*	6.00 ± 0.26*	6.33 ± 0.33*

Values shown are mean ± SEM (n= 6). * $P < 0.05$ experimental groups were compared with control

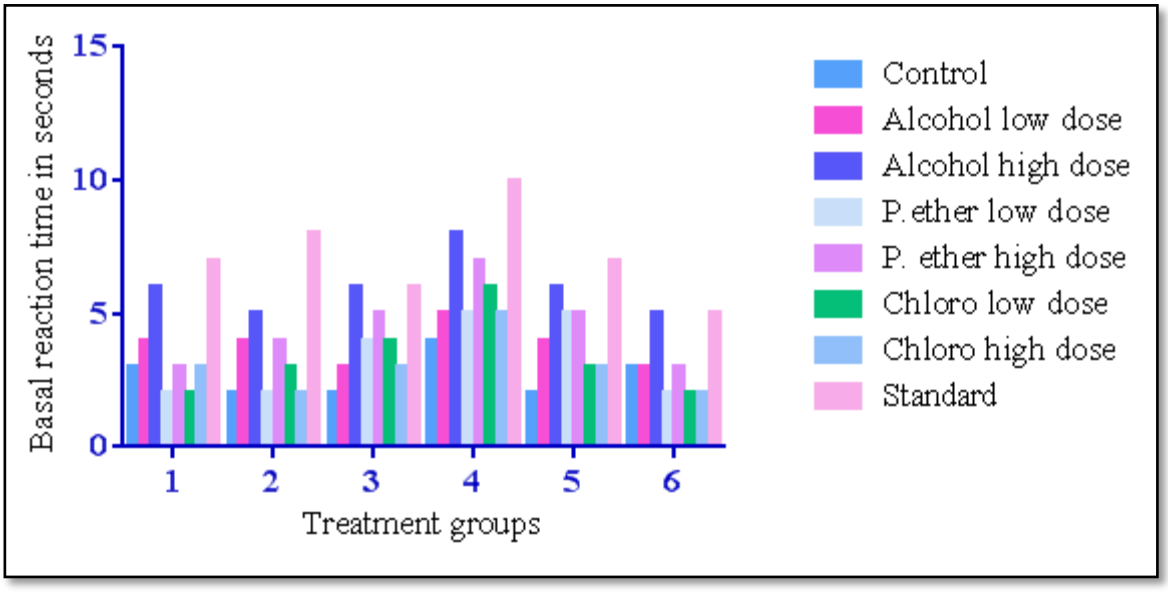

Figure No.1. Analgesic activity of leaf extracts

Table No.2. Analgesic activity of stem extracts

Treatment			**Basal reaction time in seconds**		
0 min	30 min	60 min	90 min	120 min	
Control	2.50 ± 0.22	3.00 ± 0.00	2.83 ± 0.16	2.83 ± 0.30	2.66 ± 0.21
PETL	2.00 ± 0.00	2.67 ± 0.21	2.83 ± 0.17	3.50 ± 0.22	3.67 ± 0.21
PETH	2.33 ± 0.21	3.00 ± 0.00	3.33 ± 0.33	4.83 ± 0.40	5.17 ± 0.31
CHL	2.17 ± 0.47	2.50 ± 0.34	2.83 ± 0.31	3.67 ± 0.21	4.17 ± 0.31
CHH	2.00 ± 0.00	2.83 ± 0.17	3.00 ± 0.26	4.17 ± 0.31	4.83 ± 0.40
MEL	2.67 ± 0.33	3.33 ± 0.21	3.33 ± 0.21	3.83 ± 0.31	4.17 ± 0.31
MEH	2.50 ± 0.34	3.00 ± 0.36	3.50 ± 0.22	4.16 ± 0.40	4.67 ± 0.21
STD	2.83 ± 0.17	3.33 ± 0.33*	5.17 ± 0.31*	6.00 ± 0.26*	6.33 ± 0.33*

Values shown are mean ± SEM (n= 6). * P < 0.05 experimental groups were compared with control

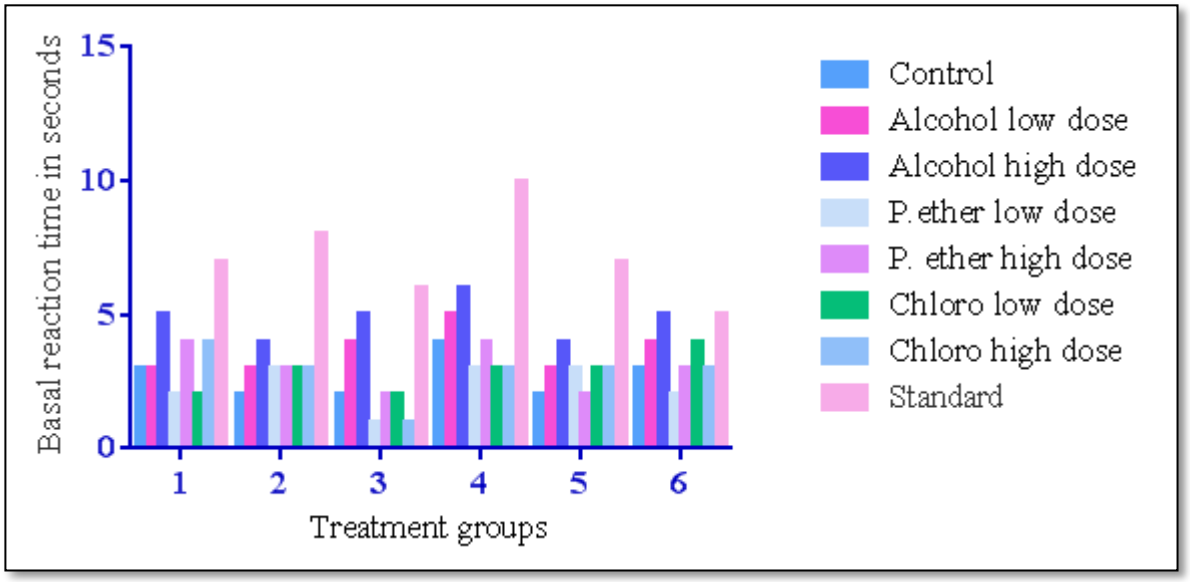

Figure No.2. Analgesic activity of stem extracts

Table No.3. Analgesic activity of stem bark extracts

Treatment			**Basal reaction time in seconds**		
0 min	30 min	60 min	90 min	120 min	
Control	2.50 ± 0.22	3.00 ± 0.00	2.83 ± 0.16	2.83 ± 0.30	2.66 ± 0.21
PETL	2.33 ± 0.22	3.00 ± 0.26	3.50 ± 0.22	3.50 ± 0.43	3.33 ± 0.21
PETH	3.00 ± 0.26	3.66 ± 0.21	3.83 ± 0.31	6.00 ± 0.37	6.17 ± 0.31
CHL	1.66 ± 0.42	2.83 ± 0.17	3.50 ± 0.43	4.17 ± 0.31	4.00 ± 0.63
CHH	1.83 ± 0.48	2.50 ± 0.22	3.50 ± 0.22	4.50 ± 0.22	4.67 ± 0.42
MEL	2.50 ± 0.22	3.33 ± 0.21	4.00 ± 0.26	4.17 ± 0.17	5.17 ± 0.31
MEH	4.00 ± 0.37	4.33 ± 0.21*	4.33 ± 0.66*	4.83 ± 0.48*	5.67 ± 0.21*
STD	2.83 ± 0.17	3.33 ± 0.33*	5.17 ± 0.31*	6.00 ± 0.26*	6.33 ± 0.33*

Values shown are mean ± SEM (n= 6). * P < 0.05 experimental groups were compared with control

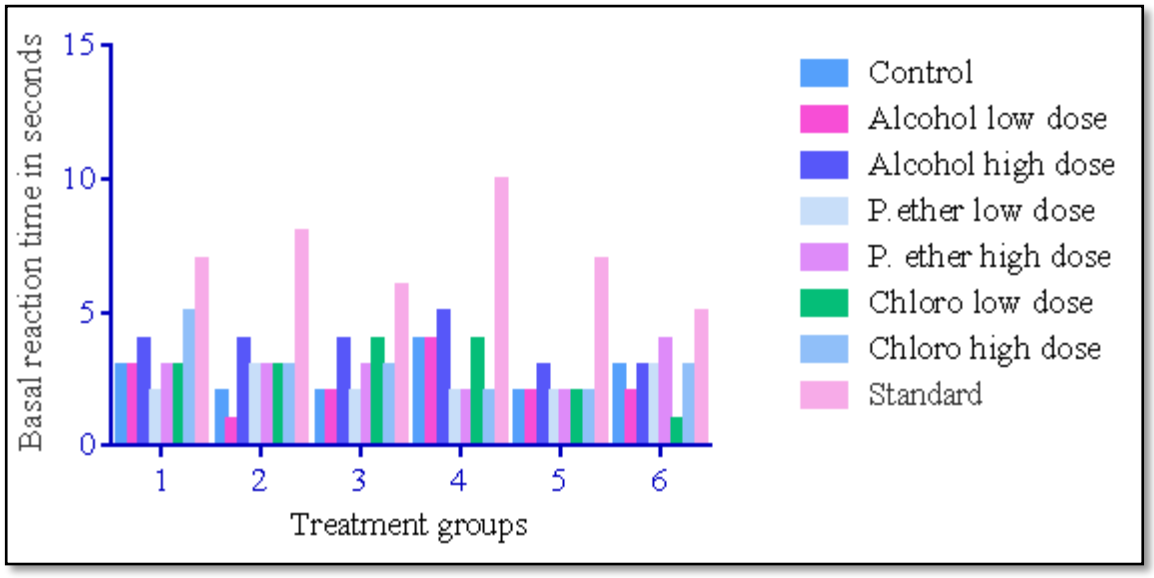

Figure No.3. Analgesic activity of stem bark extracts

This may be attributed the presence of various classes of phytoconstituents such as alkaloids, flavonoids, phenolic compounds, steroids, carbohydrates and tannins present in the methanol extracts and these phytoconstituents have been reported to produce analgesic effect. A significant increase in the reaction time for acute pain models (hot plate method) indicated the analgesic effect by methanol leaf and stem bark extract which reveals the involvement of central mechanism in analgesic action. The observation that both plants increased pain threshold of animals could be due to inhibition of sensitization of pain receptors by prostaglandins at the inflammation site. After administration of acetic acid several mediators such as cytokines, eicosanoids and arachidonic acid are liberated from membrane after phospolipase A2 activity leading to production of prostaglandins and leukotrienes. The analgesic activity of the ethanol and aqueous extracts of *Pterospermum daemia* and *Carissa carandas* may be due to inhibition of phospolipase A2 or even blocking cyclooxygenase (COX-1 and/or COX-2) [29].

Hot plat method measures the complex response to a non-inflammatory, acute nociceptive input and is one of the models normally used for studying central nociceptive activity [30]. It is an established fact that any agent that causes a prolongation of hot plate latency using this test must be acting centrally [31]. The petroleum ether, chloroform and methanol extracts of the plants produced longer latency time than the control group in the hot plate test in a dose related manner due to that it must have a central activity. Again, narcotic analgesics inhibit both peripheral and central mechanism of pain, while NSAIDs inhibit only peripheral pain [32-33].

Results of the study demonstrated that petroleum ether, chloroform and methanol extracts of *P. canescens* leaf exerts potential analgesic effect in experimental animal models, which support the claims by traditional medicine practitioners. On the basis of the results, it can be used as a good source of analgesic drugs. However, pharmacodynamic studies should be undertaken to establish the mechanism of action of the plant extracts contributing in nociception. Phytochemical investigation is also proposed in order to isolate the active fraction and eventually the pure compound.

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