WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 8, 2056-2062. Research Article ISSN 2277– 7105

PHARMACOLOGICAL EVALUATION OF STEM BARK EXTRACT OF THESPESIA POPULNEA (MALVACEAE) FOR ANALGESIC ACTIVITY IN MICE

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Article Received on
06 June 2015,

Revised on 29 June 2015,
Accepted on 22 July 2015

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ABSTRACT

Objective: To determine the analgesic activity of stem bark extract of *Thespesea populnea* in Swiss albino mice. **Method**: For this study 60 Swiss albino mice of either sex were randomly selected and divided into 10 equal groups. Assessment of analgesic activity was done by using Hot plate method after administration 0.5ml gum acacia to Group 1, Pentazocine 25mg/kg to group 2, and group 3, 4 & 5 received 3, 10, and 30mg/kg stem bark extract of *Thespesea populnea* (TP) respectively. The latent period, jumping or licking response was noted. Acetic acid induced writhing was done in mice of groups 6 to 10 after administration of 0.5ml gum acacia to Group 6, Diclofenac sodium 10mg/kg to group 7 and group 8, 9 & 10 received 3, 10, 30mg/kg stem bark extract of TP respectively. The onset, duration& number of writhing in mice was noted. The results were analysed statistically.

Result: In hot plate method TP (30 mg/kg) the % increase in jumping response was more significant compared to standard drug pentazocine (25 mg/kg) and TP (30 mg/kg) gave the peak effect at 60 minutes whereas pentazocine showed a peak response at 180 minutes. In acetic acid induced writhing test, the % inhibition up to 20 minutes for the TP (30 mg/kg) was 68% and for diclofenac the % inhibition up to 20 minutes was 80%. **Conclusion**: *Thespesea populnea* had shown good analgesic effect in central as well as peripheral models.

KEY WORDS: *Thespesea populnea*, Hot plate method, Writhing test, Analgesic activity.

INTRODUCTION

Pain is a symptom which is always subjective.[1] Acute traumatic pain is unpleasant, emotional and sensory experience. Acute pain is usually short-term, lasting anything from a few seconds to a few hours, or a few days to a few weeks. Acute pain acts as a warning signal that alerts you to possible injury. Sometime acute pain will be more serious e.g. appendicitis and will require immediate medical attention to correct the problem and relieve the pain. Chronic pain was originally defined as pain that has lasted 6 months or longer. More recently it has been defined as pain that persists longer than the temporal course of natural healing, associated with a particular type of injury or disease process.[2] There are many causes for chronic pain and many reasons for sustaining chronic pain long after the original pain source has healed. Neuropathic pain can arise following injury of peripheral nerves, when damaged or neighbouring, undamaged nerve fibres are sensitized or fire ectopically. It is also characterized by mechanical and thermal hyperalgesia. In addition, patients and animals with neuropathy are sensitive to stimuli that do not evoke a pain behaviour under normal conditions, e.g., touching, cooling, or warming the affected site. Widely opioid analgesics and NSAID's are used for the management of pain. However these drugs pose serious side effects like: sedation, respiratory depression constipation, serious gastrointestinal tract reactions, bone marrow disturbances, liver disorders, dyspepsia, nausea and vomiting skin reactions, analgesic associated nephropathy etc.[3] In this regard, search for new, effective and low toxic compounds is desired. Plants form an important group of source from which new drugs can evolve. In ancient system of medicine many plants are prescribed for the alleviation of pain and inflammation. *Thespesia* is a genus of Malvaceae, it is found to possess[4] Infertility[5] antibacterial[6] anti-inflammatory, antioxidant, purgative and hepatoprotective activity.[7] Ground up bark is used to treat skin diseases (India), dysentery and haemorrhoids (Mauritius). In a study by Viswanathan et al, 2008 found that fractions of aqueous extract found to possess antidiarrheal activity by inhibiting the Prostaglandin biosynthesis. Hence, this study was designed to evaluate the analgesic activity of aqueous stem bark extract of *T.populnea* in Swiss albino mice.

MATERIALS AND METHODS

For this study 30 healthy Swiss albino mice of either sex weighing 20-25gm, were procured from the Central animal house of the Institute and were kept in the Pharmacology experimental laboratory for about 10 days. They were maintained at room temperature (25±2^{o}C) under standard 12:12 hr. L: D cycle, fed on germinating grams and water ad

libitum. All the drugs were administered via intragastric route except pentazocine which was administered via i.p. route. Hot plate method was conducted to mice of group 1 to 5, and acetic acid induced writhing test was conducted to mice of group 6 to 10. The study protocol was approved by the Institutional animal ethics committee.

Plan of study

Groups– Hot plate method	Drug	Dose	Groups- Acetic acid induced writhing test
1	2% gum acacia	0.5ml	6
2	Pentazocine/ Diclofenac	25mg/kg / 10mg/kg	7
3	Stem bark extract of TP	3mg/kg	8
4	Stem bark extract of TP	10mg/kg	9
5	Stem bark extract of TP	30mg/kg	10

Hot Plate method[8]

Assessment of analgesic activity by Hot plate method was conducted after administration of 0.5ml distilled water to Group 1, Pentazocine 25mg/kg to group 2, and group 3, 4 & 5 received 3, 10, and 30mg/kg stem bark extract of *Thespesea populnea(*TP) respectively. Hot plate was maintained at 55± 1^0 C temperature. The mouse was placed individually on the hot plate and the latency time for the response of licking or jumping occurred was recorded with the help of a stop watch, at an interval of 60, 120, and 180 minutes following administration of the standard and the test compound. The cut off time was 15seconds.

Acetic Acid Induced Writhing test[9]

Acetic acid induced writhing was done in mice of groups 6 to 10 after administration of 0.5ml gum acacia to Group 6, Diclofenac sodium 10mg/kg to group 7 and group 8, 9 & 10 received 3, 10, 30mg/kg stem bark extract of TP respectively. After one hour of drug administration 1% w/v acetic acid (0.1ml/10g) was injected intraperitoneally. The onset, duration, number of writhing movement, and % protection against acetic acid induced writhing was noted.

Statistical analysis

The results were analyzed statistically by Paired T test and One-way ANOVA followed by Dunnett's test using SPSS16.0 software. The data were expressed as mean ±standard error mean (SEM) and $P < 0.05$ was considered significant.

RESULTS

Hot Plate method

In hot plate method, the onset of licking or jumping response in vehicle treated group did not significantly change over a period of three hours. Pentazocine (25mg/kg) showed significant analgesic activity at 60, 120, and 180 minutes compared to placebo. TP (3mg/kg) had shown significant analgesic effect at 3 hours only. Whereas TP (10mg/kg) produced significant effect at 120 and 180 minutes compared to control. TP (30mg/kg) showed significant effect at 180 minutes. The latency of licking or jumping response with TP (10 mg/kg) was more significant compared to standard drug pentazocine (25 mg/kg).These observations suggest that TP has produced more analgesia compared to pentazocine (Table 1).

Table 1: Effect of drugs on hot plate method in Swiss albino mice

Treatment	Latency time (sec) at the end of		
	1 hour	2 hours	3 hours
Gum acacia 0.5ml	7.4 ± 0.89	7.8 ± 0.67	6.00 ± 0.5
Pentazocine(25mg/kg)	12.33 ± 0.71*	11.67 ± 1.31*	13.5 ± 0.56**
TP (3 mg/kg)	7.00 ± 0.5	10.2 ± 0.73	10.2 ± 0.73
TP (10 mg/kg)	10.2 ± 0.73	13.2 ± 0.67**	14.2 ± 0.53**
TP (30 mg/kg)	8.6 ± 1.70	8.6 ± 1.70	11.4 ± 1.43**

Values are expressed as mean ± SEM. ***P*<0.01 compared with control group using one-way ANOVA followed by Dunnett's test.

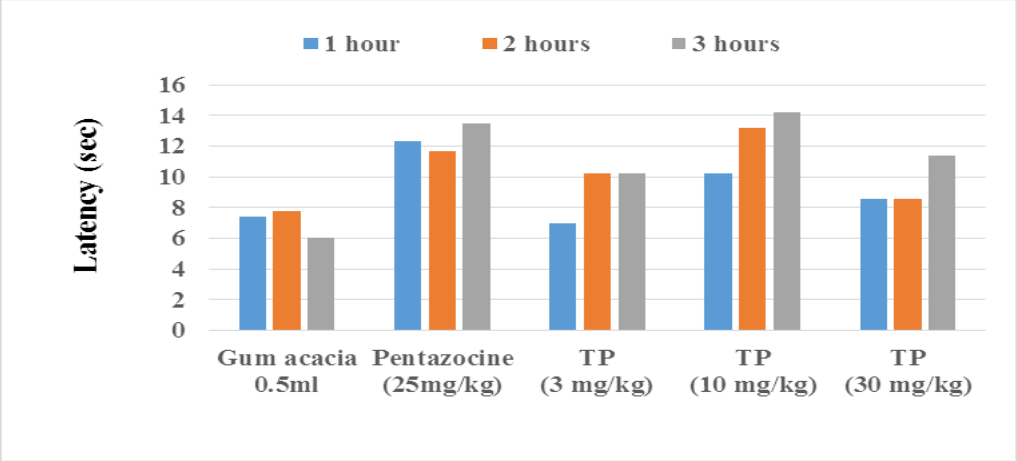

Figure 1: Effect of drugs on hot plate method in Swiss albino mice

Acetic Acid Induced Writhing test

In Acetic acid induced writhing, number of writhes were observed over a period of 20 minutes. Vehicle treated group did not show significant change in the number of writhes over a period of 20 minutes. Diclofenac (10mg/kg) showed significant reduction in the number of

writhing compared to placebo. The plant extract at a dose of TP (3mg/kg), TP (10mg/kg) and TP (30mg/kg) produced dose dependant reduction in the acetic acid induced writhing test in Swiss albino mice. The potency of the compound TP was found to be lesser than diclofenac sodium (Table 2).

Table 2: Effect of drugs on Acetic acid induced writhing test in Swiss albino mice

Treatment	No of writhing (Counts/20min)	% inhibition
Gum acacia 0.5ml	69.5 ± 6.75	----
Diclofenac (10mg/kg)	13.33 ± 2.24**	80.81
TP (3 mg/kg)	41.5 ± 8.32**	40.29
TP (10 mg/kg)	33.83 ± 4.17**	51.32
TP (30 mg/kg)	22.17 ± 3.89**	68.10

Values are expressed as mean ± SEM. ***P*<0.01 compared with control group using one-way ANOVA followed by Dunnett's test.

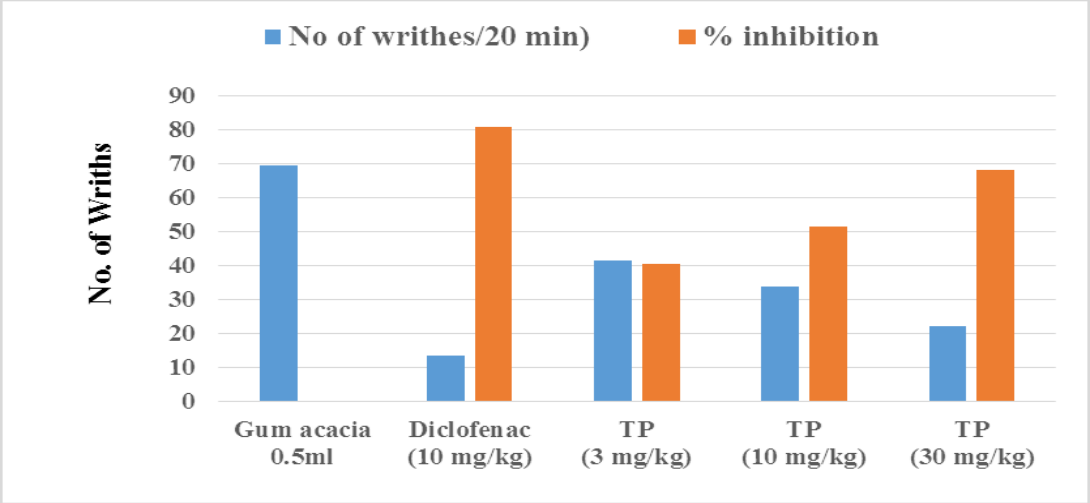

Figure 2: Effect of drugs on Acetic acid induced writhing test in Swiss albino mice

DISCUSSION

From the present investigation it was clear that, *Thespesea Populnea (TP)* produces analgesic activity in both the models, namely, hot plate method, and acetic acid induced writhing test in Swiss albino mice in a dose dependent manner. In hot plate method, the onset of licking in vehicle treated group did not significantly change over a period of three hours. These results suggest that the temperature used for the test method (55 ± 1^0 C) did not produce any injury to the paw of the mice. The vehicle is inert pharmacologically. It is very well established that reflex latency reaction to thermal stimulation of non-inflamed / non injured paws such as classical hot plate test is suitable for measuring anti nociceptive effects of centrally acting

analgesics. But this test is largely insensitive to non-steroidal anti-inflammatory agents. The % increase in the latency of the licking response in mice in the hot plate method for the standard drug pentazocine and test drug TP (3 mg/kg; 10mg/kg and 30 mg/kg) were calculated. TP (3mg/kg), TP (10mg/kg) and TP (30mg/kg) had shown significant analgesic effect in a dose dependent manner. It is observed that the test drug at 10 mg/kg has attained peak effect of 136% at 180 minutes, whereas pentazocine attained peak effect of 125% at 180 minutes. These observations suggest that TP has produced more analgesia compared to pentazocine, and this effect may be due to central analgesic activity.

In the acetic acid induced writhing test in mice the injection of acetic acid 1% w/v acetic acid (0.1ml/10gm) intraperitonially produced writhing behaviour in mice. Acetic acid causes inflammatory pain by inducing capillary permeability,[10] and liberating endogenous substances that excite pain nerve endings[11] NSAIDs can inhibit COX in peripheral tissues and, therefore, interfere with the mechanism of transduction of primary afferent nociceptors.[12] Treatment with TP (3mg/kg; 10mg/kg and 30mg/kg) significantly reduced number of writhing's produced by acetic acid, by 40% at 3mg/kg dose, 51% at 10mg/kg dose, and 68% at 30mg/kg dose compared to 80% at 10mg/kg of diclofenac. Hence it is possible that TP may be able to inhibit writhing by inhibiting the release of endogenous substance, responsible for pain. These actions suggest that TP might produce peripheral analgesic effect. It has been observed that the TP at a dose of 30mg/kg showed more efficacy compared to the standard drug. Diclofenac (10 mg/kg) in inhibiting the licking response which may be interpreted as inhibition of early phase inflammatory pain. These results suggest that TP can inhibit supraspinal and spinal mediated neurogenic pain and peripherally mediated inflammatory pain. It is shown that TP induces analgesia both peripherally and centrally in mice in hot plate test, and acetic acid induced writhing test in a dose dependent manner.

CONCLUSION

Thespesea *populnea* (TP) 10mg/kg) has shown more significant analgesia than pentazocine (25mg/kg) in hot plate method. TP has shown significant analgesia in acetic acid induced writhing model, compared to Placebo and less significant effect compared to diclofenac. From the study it can be safely concluded that the test drug TP produces analgesia centrally as well as peripherally. Further studies at the molecular level may be necessary to confirm the above findings.

ACKNOWLEDEMENTS

The Authors are thankful to Dr. K. Nandha kumar, Ph.D., for his valuable guidance and to Dr. M. Rajesh, M.D., for reviewing this manuscript.

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