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STUDY OF ANALGESIC ACTIVITY OF *MUCUNA PRURIENS* EXTRACT ON SWISS ALBINO MICE

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ABSTRACT

Mucuna pruriens, belonging to the family Fabaceae, has been used in traditional Ayurvedic Indian Medicine for various ailments. In the present study, we investigated the analgesic activity of the *Mucuna pruriens* extract was evaluated for its in-vivo analgesic activity by using the Eddy's Hot plate method in mice. Three doses of *Mucuna pruriens* (100, 200, 400 mg/kg, p.o.) and standard dose of tramadol (25 mg/kg, i.p.) were used for treatment. Swiss albino mice weighing between 20-30 g using oral feeding tube were evaluated for analgesic activity at different time interval such as 0, 30, 60, 90, 120 and 150 minutes against standard and control group. Results indicate that the extracts could possess analgesic activity.

KEYWORDS: *Mucuna pruriens*, Analgesic, Tramadol, Swiss albino mice.

INTRODUCTION

Pain is a frequent problem in any medical practice; it may be associated with advanced illness or minor conditions. Pain is the most common symptom. The causes may vary from minor ailments to life threatening conditions. The definition promulgated by 'International Association for the Study of Pain' (IASP) states, "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[1]

In pharmacotherapy a number of viable treatment options including traditional medicines are available, many involving combinations of medications with different mechanisms of

action.[2] Commonly used analgesic drugs are non-steroidal anti-inflammatory drugs (NSAIDs), opioids and antidepressants. NSAIDs are among the most widely used of all therapeutic classes of drugs because they are both analgesic and anti-inflammatory. The side-effects are primarily gastrointestinal (GI), haematological and renal and often related to COX inhibition, which greatly limits their use.[3] The opioids are commonly used for analgesia consists of morphine, hydromorphone, fentanyl, codeine, hydrocodone, methadone, mepiridine and sulfentanil. Opioid-induced side effects, particularly GI side effects, may be severe enough forcing the patients to decrease the doses or even discontinue therapy, resulting in inadequate pain control.[4]

Medicinal herbs have always been used as traditional primary healthcare agents, especially in developing countries. In last few years, rapid changes have been observed in popular use of herbal products for maintenance of health. Scientific interest in medicinal plants has burgeoned in recent times due to increased efficiency of new plant derived drugs and rising concerns about the side effects of allopathic medicines. Plants have been exemplary source of drugs since ages. In fact, many of the currently used modern medicine drugs have been derived either directly or indirectly from plant sources.[5] In one estimate large number of population is dependent on indigenous and traditional way of treatment (World Health Organization 1993). Few advantages of using medicinal plants are cost effectiveness, better tolerability, fewer side effects, less allergic, natural in composition, smoother action, rejuvenation function, maintaining balance and harmony in the body physiology.

Mucuna prurience, commonly known as a *Kapikacchu* is a plant of the Fabaceae family, typically found in tropical regions and used for various purposes in traditional medicine in several countries. *Mucuna prurience* is the popular drug in the Ayurvedic and Unani system of medicine. Number of studies have shown beneficial effects of *Mucuna pruriens* as aphrodiastic, anti-parkinsonism, hypoglycemic, antioxidant, antibacterial, antifungal, and anticancer agents.[6-12] However, there are only few studies of *Mucuna pruriens* in CNS effect. Studies pertaining to analgesic action of *M. prurience* are lacking so far. Therefore present study was planned with the objective to evaluate analgesic activity of *M. pruriens* using eddy's hot plate in swiss albino mice.

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology, King George's Medical University (KGMU), Lucknow. Prior permission was obtained from the Institutional Animal Ethics Committee (IAEC) for conducting the study.

Experimental animals

Adult healthy male Swiss Albino mice of similar physical constitution (in terms of age, body weight), weighing 20-30g had been used in study. Animals had been obtained from animal house of Indian Institute of Toxicology Research, Lucknow, which is certified by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) for breeding and housing of animals. The animals were housed in Institutional Animal facility under temperature, humidity and light and dark cycle-controlled environment [25 ± 2°C, 70%, 12 hrs. Cycle] and were given standard pellet diet and water *ad-libitum.* The maintenance of the animals and the experimental procedures were in accordance with the 'Guide for the Care and Use of Laboratory Animals' (Latest revision in 2011) and the guiding principles of IAEC which strictly adhered to the guidelines of CPCSEA.[13]

Drugs, Dosage and Treatment Groups

Mucuna pruriens (MP) seed extract was procured from Himalaya drug company, Bangalore, India. The standard drug tramadol (Biochem Pharmaceutical Industries Ltd.) was purchased from government authorized medical store. Total 30 mice were divided randomly into control and experimental groups (n=6). Group 1 received the Normal saline and served as the control group, group 2 received the standard drug tramadol (25mg/kg, i.p.), group 3, 4 and 5 received the test drug (MP) in doses of 100, 200 and 400 mg/kg, per-orally. Each of above mentioned drugs were dissolved / diluted in normal saline (vehicle) just before administration. The strength of solution was adjusted in such a way that 1 ml of solution contained the desired dose that was to be administered in an individual mouse.

Eddy's hot plate

The animals were allowed to habituate to laboratory surroundings prior to testing. In this model, prior to the experiment the hot plate was set for a temperature 55±1^{o}C. Then each mouse was gently placed on the hot plate, animals which showed paw licking or jump responses within 6-8sec were selected for the study. Each animal was tested before experiment for control reaction time (at 0 min). The animals were treated with respective drugs and reaction time was again measured at 30, 60, 90, 120 and 150 min after

administration of test/standard/control drug. The response time was noted as the time at which animals reacted to the pain stimulus either by jumping, withdrawal of the paws, paw licking, whichever appeared first. The cut off time for the reaction was 15 seconds to avoid damage to the paws.[14-16] The reaction time of all animals towards thermal heat was recorded. The mean reaction time for each treated group was determined and compared with that obtained for each group before treatment.

STASTISTICAL ANALYSIS

All result are expressed as mean ± SD. Data was analyzed using one way analysis of variance (ANOVA), to assess the comparability of the groups assigned to the treatment groups followed by Tukey's multiple comparison tests. P values <0.05 were considered significant.

RESULTS

The pain model, response to thermal stimulation by hot plate, was used for assessing the analgesic effects in mice. Table-1 Shows the response of all the groups of mice to thermal stimulation by hot plate method before administration of control, standard or test compound (0 minutes) and after administration of control, standard or test compound at different time interval (30min., 60min., 90min., 120min. and 150min.).

Table-1:- Comparison of response on hot plate at different time interval

Groups	Reaction time (seconds) at time interval (minutes) (Mean±SD)					
	0 min	**30 min**	**60 min**	**90 min**	**120 min**	**150 min**
Control	.40±2.07	7.30±2.33	6.64±2.36	6.59±2.36	6.63±1.73	6.42±2.19
Tramadol (25 mg/kg)	6.50±2.14	11.38±1.3*	14.99±1.37**	15.03±1.15**	12.68±1.53**	10.40±1.81*
Mucuna pruriens (100 mg/kg)	6.54±2.09	6.72±2.13	6.40±2.18	6.46±2.17	6.42±2.10	6.59±1.99
Mucuna pruriens (200 mg/kg)	6.35±2.15	7.32±2.62	11.48±2.60**	11.47±2.59**	10.11±2.13*	8.18±2.32
Mucuna pruriens (400 mg/kg)	5.93±2.06	7.07±1.86	11.79±1.94**	12.47±1.70**	10.17±1.87*	7.57±1.75
p-value	> .05	>.05	< .01##	< .01##	< .01##	< .05#

(p<.05) ## (p<.01) (ANOVA), * (p< .05), ** (p< .01), (Tukey's multiple comparison test).

As shown in table-1 the mean hot plate latency of all 5 groups, before administration of control, standard or test compound (0 minute) and after the 30 min. of drug administration, was compared using ANOVA which revealed similar mean hot plate latency among the groups (p >0.05) i.e. mean hot plate latency did not differ significantly among the groups. As it is clear from the above table, there is statistically significant difference in analgesia among

all the groups when compared with each other by ANOVA at 60 min., 90 min.,120 min. and 150 min.

The mean hot plate latency among all 5 groups, after administration control, standard or test compounds at 30 min, 60min, 90min and 120 min is maximum with standard Group followed by MPE 400 mg/kg.

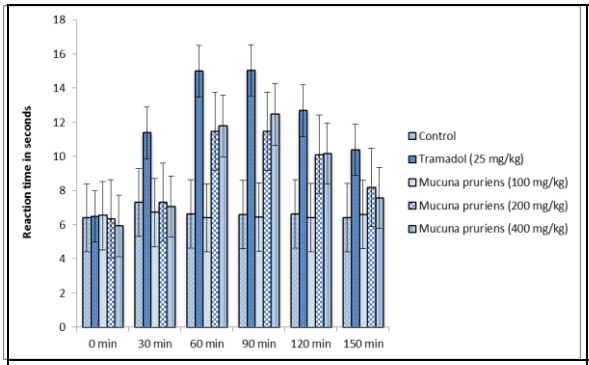

Fig 1:-Comparison of response between all treatment groups at different time interval on hot plate

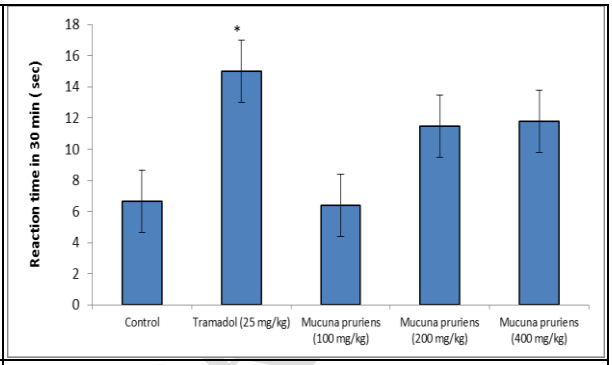

Fig 2:- Comparison of reaction time after 30 min of drug administration

* (p<.05), ** (p<.01), (Tukey's multiple comparison test)

After 30 min of drug administration, when compared with control group, latency time is significant (p< .05) in Standard group (tramadol) while it is insignificant (p> .05) in all the test groups (Table-1, Fig 1 & 2).

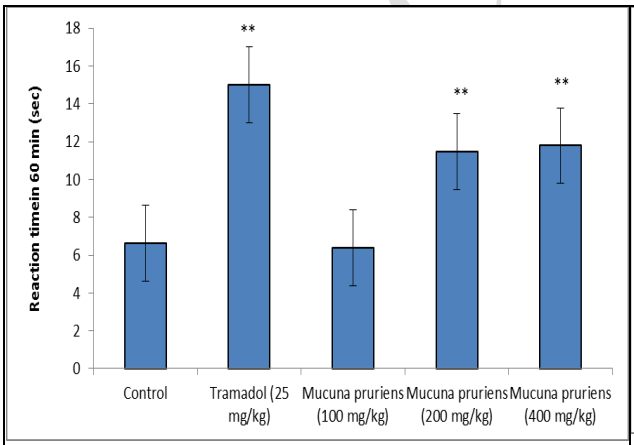

Fig 3:- Comparison of reaction time after 60 min of drug administration

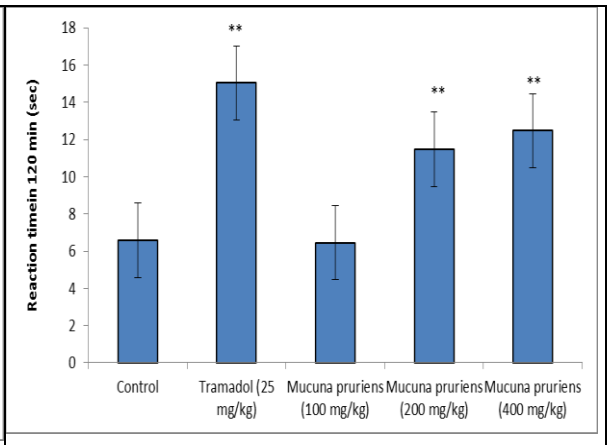

Fig 4:- Comparison of reaction time after 90 min of drug administration

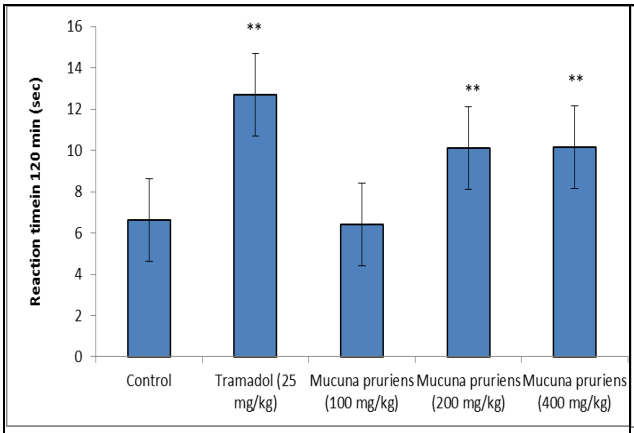

Fig 5:- Comparison of reaction time after 120 min of drug administration

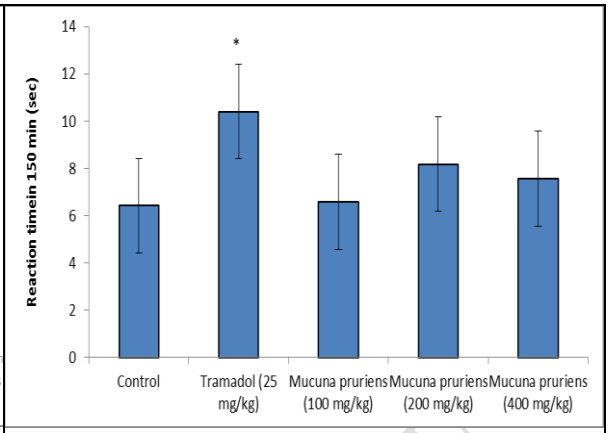

Fig 6:- Comparison of reaction time after 150 min of drug administration

* (p<.05), ** (p<.01), (Tukey's multiple comparison test)

After 60, 90 and 120 min of drug administration, when compared with control group, latency time is insignificant (p> .05) in group III (MPE 100mg/kgbw) while it is significant (< .05) in all other groups (Table-1, Fig 3, 4 & 5).

After 150 min of drug administration, when compared with control group, latency time is significant (p< .05) only in Standard group (tramadol) while it is insignificant (p> .05) with all doses of MP (Table-1, Fig 1 & 6).

DISCUSION

Presently therapeutics has many allopathic pharmacological measures for treatment of pain. But the adverse effects and cost, limits their uses. Hence there is justifiable need to search for agents which are relatively safe, cheap, easily available, natural in origin and potent. Plants have been exemplary source of drugs since ages. In fact, many of the currently used so called allopathic drugs have been derived either directly or indirectly from plant sources. In one estimate large number of population is dependent on indigenous and traditional way of treatment (World Health Organization 1993).

Analgesic activity was assessed by Eddy's hot plate. *Papaver somniferum* from which morphine was isolated is one of the best known plant to be used as analgesic. It is regarded as the prototype of opiate analgesic drugs. Many other herbs having analgesic potentials are being used in indigenous system of medicines.

The present study was conducted to evaluate the anti-nociceptive activity of commercially available crude extracts of herbs *Mucuna pruriens.* Eddy's hot plate test was used for

evaluation of analgesic activity of the compounds. The paws of mice are sensitive to heat temperatures which are not damaging the skin. The responses are in the form of jumping, withdrawal of the paws and licking of the paws. Pain induced by thermal stimulus of the hotplate is a sensitive and specific method used to demonstrate the involvement of central mechanism nociception. The central analgesic drug, *Tramadol* was taken as the standard and *Normal saline* as the control in the study. Tramadol-induced antinociception is mediated by opioid (mu) and nonopioid (inhibition of monoamine uptake) mechanisms.

In present study results showed significant ($p < 0.05$) increase in latency to thermal simulation in hot plate at the two doses of *Mucuna pruriens* extract i.e. 200 mg/kg p.o. as well as 400 mg/kg p.o. Percentage increase was more at 400mg/kg dose followed by 200mg/kgbw. Tramadol has shown greater increase in response time as compared to *test* groups. The ability of the any drug to prolong the reaction latency to the thermally-induced pain in mice by the hot plate suggests central analgesic activity.[17]

Mucuna pruriens and *Aegle maemelos s extracts contain* certain alkaloids which may be responsible for its central analgesic action.[18] In study by Bala *et al* it was found that the standardized extract of *Mucuna pruriens* at the doses of 200 and 400 mg/kgbw elicited a significant anti-inflamatory activity.[19] Lauk et al showed the analgesic and anti-pyretic effect of *Mucuna pruriens* in their study.[20] From the results it could be concluded that the extracts exhibit anti-nociceptive activity by both central as well as peripheral mechanisms. Present study was done to evaluate the analgesic effects of *Mucuna prurience*, results may favor use of *Mucuna pruriens* as analgesic drug. However more studies on animals and clinical trials are required to categories this extracts as therapeutic drugs for the relief of pain.

CONCLUSION

Keeping in view the result obtained in the present study, the following conclusion may be drawn regarding the potential effectiveness of *Mucuna pruriens* in pain. But, details of the complete mechanism have yet not been explored. Therefore, further experiments are required to elucidate the exact mechanism of action. Also more specific and longer duration animal and human studies are required to further substantiate the finding of the present study.

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