

# Evaluation of Analgesic Activity of Paroxetine in Adult Male Albino Rats in Comparison with Diclofenac

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**Abstract:** *Background:* Pain affects millions of people, leading to depression and anxiety. Paroxetine is the most potent inhibitor of serotonin re-uptake. The analgesic effect of Paroxetine has been shown both in animal models and human cases suffering from different type of chronic pain. *Objectives of the Study* To evaluate of analgesic activity of paroxetine in adult male albino rats in comparison with diclofenac. *Methodology:* The analgesic effect of graded doses of paroxetine (2.5mg/kg, 5mg/kg, 10mg/kg) was evaluated using Eddy's hot plate method and tail-flick method and compared with the standard analgesic diclofenac. The values obtained are expressed as mean±SEM. Statistical analysis of differences between groups was carried out using one-way analysis of variance (ANOVA). Probability (P) value of <0.05 was taken as the level of statistical significance. *Results:* Paroxetine showed statistically significant analgesic activity in comparison with control group and standard group (P < 0.05)

**Keywords:** Analgesic effect, Paroxetine, Diclofenac, Eddys hotplate, tailflick

## 1. Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage [1]. Analgesic medications are the first line of treatment in the pain management [2]. Over the course of human history pain has been treated by psychological technique, physical method (surgical intervention, electrical stimulant, pressure, cold, heat, counter irritant, acupuncture) and by drugs [3]. Severe pain due to cancer metastasis needs the use of strong analgesics like opioid drugs but addiction liability of opioid is a major drawback. In spite of vast number of drugs, search for new analgesics having better efficacy and minimal adverse effect are continuing throughout the world. Antidepressant and neuroleptic have been found to be useful in treating some type of acute and chronic pain [3]. In animals antidepressants that enhance 5HT neurotransmission augment stimulation produced analgesia [4]. Paroxetine is the most potent inhibitor of serotonin re-uptake among the SSRIs [5]. The analgesic effect of selective serotonin reuptake inhibitor (SSRI) has been shown both in animal models and human cases suffering from different type of chronic pain [6].

## 2. Materials and Methods

The study was carried out in the Institute of Pharmacology, Madurai medical college, Madurai after getting clearance from the Institutional Ethical Committee. (Ref no: 5953/E1/5/2015 dated 22/6/2015) 30 adult albino male rats weighing 150-250gm were obtained from central animal house, Madurai Medical college, Madurai. The animals had free access to food and water ad libitum. The animals were divided into five groups of 6 animals each. Group 1 serves as control, Group 2 serves as

standard and Group 3,4,5 serves as test Groups. Group 1 received Normal feed+water. Group 2 received Normal feed+water+ 10mg/kg Diclofenac ip. Group 3,4,5 received increasing doses of paroxetine (2.5mg/kg, 5mg/kg, 10mg/kg) intraperitoneally.

### Evaluation of Analgesic effect

- 1) Eddy's hot plate method:
- 2) Tail flick method

### Thermal stimulus by Eddy's hot plate method:

In this the rats will be placed on a hot plate which will be maintained at a temperature of  $55 \pm 0.5^{\circ}\text{C}$  throughout the test. A cut-off period of 15 sec will be considered as maximal latency to avoid injury to the paws. The time taken by the animals to lick the hind paw or jump away will be taken as the reaction time and is measured. Standard group (group II) received diclofenac sodium and the test group (Group III, IV, V) received graded doses of Paroxetine 2.5mg/kg, 5mg/kg, 10mg/kg. The reaction time of the rats was recorded at 30mins, 1, 2, 3 hour after drug administration. The mean of the observed values was considered for statistical analysis.

**Analgesiometer by tail flick method using radiant heat from electric sources:** Tail flick latencies (reaction time) of the animal will be assessed by the Analgesiometer. The strength of the current passing through the naked nichrome wire will be kept constant at 5 amps. The distance between the heat source & tail skin will be 1.5 cm. The site of application of the radiant heat in the tail will be maintained at 2.5 cm, measured from the root of the tail. The time taken by the animal to withdraw (flick) its tail from the hot wire will be noted and taken as the 'reaction time'. This tail flicking is considered as the end point of this test and time is measured. The cut-off time of 10 sec is planned to avoid

any tissue damage. Standard group (group II) received diclofenac sodium and the test group (Group III, IV, V) received graded doses of Paroxetine 2.5mg/kg, 5mg/kg, 10mg/kg. The reaction time of the rats was recorded at 30mins, 1, 2, 3 hours, after drug administration. The mean of the observed values was considered for statistical analysis.

**Statistical Methods:** The values obtained are expressed as mean ± SEM. Statistical analysis of differences between groups was carried out using one-way analysis of variance (ANOVA). Probability (P) value of <0.05 was taken as the level of statistical significance.

### 3. Results

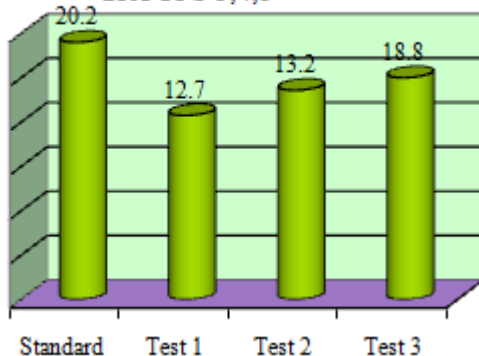
Analgesic activity of paroxetine in tail flick response in rats

**Table 1**

Groups	30min	1hr	2hr	3hr
Group I CONTROL	9.5±0.42	10.5±0.25	11.2±0.48	12.5±0.42
Group II	11.9±0.40 *	12.2±0.35 *	16.2±0.87 *	20.2±0.70 *
Group III	11.6±0.49	10.9±0.38	11.4±0.61	12.7±0.66
Group IV	10.7±0.91	11.5±0.35	12.2±0.79	13.2±0.54
Group V	11.2±0.65	11.8±0.33	15.3±0.66 *	18.8±0.54 *

\* P < 0.05

**AT '3' HR - STANDARD VS TEST GROUPS 3,4,5**



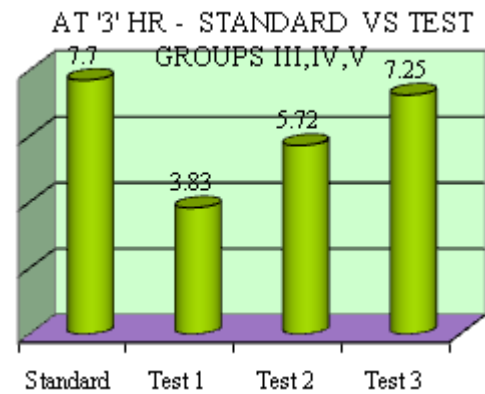
In Tail flick test, Paroxetine showed significant elevation in pain threshold in comparison to control, as represented in **Table 1** and Group V showed statistically significant analgesic activity (P < 0.05) as compared to control. The results also demonstrated that analgesic activity produced by Paroxetine was comparable to that of standard group that received Diclofenac.

Analgesic Effect of Paroxetine in Eddys Hot Plate

**Table 2**

Groups	30min	1hr	2hr	3hr
Group I	3.91±0.03	3.89±0.02	3.85±0.04	3.86±0.02
Group II	3.94 ± 0.05	7.74±0.20	8.66±0.19 *	7.70±0.32
Group III	3.89±0.04	4.13±0.11	4.25±0.14	3.83±0.16
Group IV	3.91±0.06	5.22±0.09 *	6.30±0.16*	5.72±0.17 *
Group V	3.84±0.05	6.04±0.36 *	7.42±0.16 *	7.25±0.08 *

\* P < 0.05



In hot-plate test, Paroxetine showed significant elevation in pain threshold in comparison to control, as represented in **Table 2** and indicated statistically significant analgesic activity (P < 0.05) as compared to control at doses 5 and 10 mg/kg.

In these pain models, treatment with paroxetine produced dose dependent analgesia and increased mean reaction time. The analgesic effect was observed within 30 min. in diclofenac and all paroxetine groups; however, it was maintained for 120 min. in all groups. The results also demonstrated that analgesic activity produced by Paroxetine was comparable to that of standard Diclofenac.

### 4. Discussion

In this present study analgesic effect of paroxetine selective serotonin reuptake inhibitor (SSRI) was evaluated using albino rats by tail flick and eddys hot plate method and it is found to be statistically significant.

Serotonin and norepinephrine are the neurotransmitters in diffused noxious inhibitory control probably at spinal and supraspinal level. Reuptake inhibition will enhance / prolong the effect of released biogenic amines. This might be the possible mechanism of action of paroxetine as an analgesic. Studies suggested that, the involvement of serotonergic mechanisms and serotonin receptors in analgesic effect induced by a SSRI drug, paroxetine [8]. Paroxetine provided analgesic effect for patients with refractory chronic pain. Depression is the most common emotional disturbance in patients suffering from chronic pain [9]. The analgesic properties of psychotropic drugs were reported shortly after their introduction into psychiatric practice [2]. Traditional tricyclic antidepressants have numerous undesirable side effects hence, the selective serotonin reuptake inhibitors (SSRIs), with a favorable side effect profile, are preferred [10].

This study proves that Paroxetine has antinociceptive effect and it can be used to treat pain associated with depression instead of using additional antinociceptive agent, or we can use in patients having pain likely to develop depression due to non-reduction in pain. Further studies are however necessary to explore mechanism(s) of action in depth.

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