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A COMPARATIVE STUDY OF ANALGESIC EFFECT OF TINOSPORA CORDIFOLIA WITH PIROXICAM IN ALBINO RATS, USING DIGITAL ANALGESIOMETER

[1]Lakshmi Deepika P*, [2]Dr. Supriya Priyambada, [3]Dr. Jagadeesh P, [4]Hanumanth N

[1]Tutor, Dept. of Pharmacology, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutapalli, Krishna Dist, Andhra Pradesh, India.

[2]Asso. Professor, Dept. of Pharmacology, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutapalli, Krishna Dist, Andhra Pradesh, India.

[3]Asst Professor, Dept. of Pharmacology, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutapalli, Krishna Dist, Andhra Pradesh, India.

[4]Lecturer in Statistics, Dept. of Community Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutapalli, Krishna Dist, Andhra Pradesh, India.

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***Correspondence for Author**
Lakshmi Deepika P
Tutor, Dept. of Pharmacology, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutapalli, Krishna Dist, Andhra Pradesh, India.

ABSTRACT

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is frequently classified as physiologic or acute pain and pathologic or chronic pain, which includes inflammatory pain and neuropathic pain. Acute pain typically has a sudden onset and recedes during the healing process. Acute pain can be considered as 'good pain' as it serves an important protective mechanism like withdrawal reflex. Chronic pain can be considered as 'bad pain' because it persists long after recovery from an injury and is often refractory to common analgesic agents.Analgesics are the drugs which possess significant pain relieving properties by acting in the CNS or on the peripheral pain receptors without significantly affecting consciousness. Piroxicamis an NSAID (non-steroidal anti-inflammatory drug) that is commonly used for the relief of symptoms of osteoarthritis and rheumatoid arthritis, primary dysmenorrhea, postoperative pain and act as an analgesic, especially where there is an inflammation component.Tinosporacordifolia

(Guduchi) is a large, glabrous, perennial, deciduous, climbing shrub of weak and fleshy stem found throughout India.Tinosporacordifolia (T. cordifolia, Menispermaceae) belongs to a group of medicinal plants that grows in the tropical and subtropical regions of India. It has both analgesic and anti-inflammatory activity.The main aimof this study is tocompare the analgesic effect of Tinosporacordifolia with a standard analgesic drug Piroxicam. **Objectives:** To study the analgesic effect of Tinosporacordifolia, To compare the analgesic effect of Tinosporacordifolia with a standard analgesic drug Piroxicam. **Materials & Methods:** A Randomized controlled trail was conducted in the Dept. of Pharmacology, Dr Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation (Dr.PSIMS), Chinoutapalli, Krishna District, Andhra Pradesh with the institutional ethical committee clearance. Total rats were divided into 3 groups consisting of 6 rats in each group. First group of rats (control group) were treated with 0.2 ml normal saline. Second group were considered as standard group and treated with Piroxicam (standard drug) at dose of 0.33mg/kg. Third group were considered as test group and treated with Tinosporacordifolia(test) at dose of 100mg/kg which is the standard analgesic dose **Conclusion:**The result showed that Tinosporacordifoliais having analgesic property, and it is less when compared to Piroxicam. However the above preclinical experiments only give us an idea about the analgesic effect of Tinosporacordifolia&Piroxicam but large scale clinical trials are necessary for final assessment.

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[1,2] Pain is frequently classified as physiologic or acute pain and pathologic or chronic pain, which includes inflammatory pain and neuropathic pain. Acute pain typically has a sudden onset and recedes during the healing process. Acute pain can be considered as ‘good pain’ as it serves an important protective mechanism like withdrawal reflex. Chronic pain can be considered as ‘bad pain’ because it persists long after recovery from an injury and is often refractory to common analgesic agents. Analgesics are the drugs which possess significant pain relieving properties by acting in the CNS or on the peripheral pain receptors without significantly affecting consciousness.

Tinosporacordifolia (Guduchi) is a large, glabrous, perennial, deciduous, climbing shrub of weak and fleshy stem found throughout India and belongs to the family Menispermaceae. It

belongs to a group of medicinal plants that grows in the tropical and subtropical regions of India. It is a large glabrous climber with succulent corky stem, sub-deltoid cordate leaves, branches sending down, and pendulous fleshy roots.[3] It is known for its immuno modulatory, antioxidant and antibacterial properties.[4][5][6]

According to the International Journal of Ayurveda Research, April (2010). Tinosporacordifolia is a widely used plant in folk and Ayurvedic systems of medicine. It is available as 250 mg capsules.Tinosporacordifolia is reported to possess antispasmodic, anti-inflammatory, antiallergic, antipyretic, antileprotic and anti-diabetic properties.[7,8] It is generally prescribed in general debility, diabetes, fever, jaundice, skin diseases, rheumatism, urinary diseases, dyspepsia, gout, gonorrhoea and leucorrhoea[9] The chemical constituents reported from this shrub belong to different classes, such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides.According to "Siddalingappa C.M. Internationaljournal of Basic Medical Sciences (2011)Tinosporacordifolia has both analgesic and anti-inflammatory activity.[10]

Piroxicam[11] is an NSAID (non-steroidal anti-inflammatory drug) that is commonly used for the relief of symptoms of osteoarthritis and rheumatoid, primary dysmenorrhea (menstrual pains), postoperative pain and act as an analgesic (a medication given to reduce pain without resulting in loss of consciousness), especially where there is an inflammation component. The World Health Organization (WHO) includes piroxicam in its "Essential Drugs List"; a list of minimal medical needs for a basic health care system.

So, the main aim of this study is to compare the analgesic effect of Tinosporacordifolia with standard drug like Piroxicam (Oxicam derivative).

Objectives

1. To study the analgesic effect of Tinosporacordifolia.
2. To compare the analgesic effect of Tinosporacordifolia with a standard analgesic drug Piroxicam.

MATERIALS AND METHODS

A Randomized controlled trail was conducted in the Dept. of Pharmacology, Dr Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation (Dr.PSIMS), Chinoutapalli, Krishna District, Andhra Pradesh with the institutional ethical committee

clearance. Male albino wistar rats weighing between 200-250 gms were selected for the study and Total rats were randomly divided into 3 groups consisting of 6 rats in each group. First group of rats (control group) were treated with 0.2 ml normal saline (control). Second group were considered as standard group and were treated with Piroxicam (standard drug) at dose of 0.33mg/kg. Third group were considered as test group and treated with Tinosporacordifolia(test) at dose of 100mg/kg which is the standard analgesic dose.

Tail flick time was taken as the reaction time. Normal reaction time was noted for 5 times in each animal before starting the experiment. Average of all the 5 readings were taken as mean reaction time at 0 minutes. After recording of normal reaction time, normal saline was administered (orally) to control group, Piroxicam was administered (orally) to standard group of animals, Tinosporacordifoliawas administered (orally) to test group. For the above mentioned drugs, reaction time was recorded after administration to their respective groups at 30 minutes, 60 minutes and 90 minutes. All recordings were tabulated separately.

EQUIPMENTS

Digital analgesiometer(INCO), Insulin syringes, Measuring jar, Glass beaker, Animal weighing balance, Motor & pestle, Spirit, Cotton, Stop watch.

Chemicals & Solutions

Tinosporacordifolia, Piroxicam, Double distilled water, Normal saline.

Animals: Male Albino rats weighing about 200-250gm.

Instrument Description: Digital Analgesiometer is the instrument meant for studying the analgesic effect of pain by observing the flicking of tail due to heat. It is provided with an arrangement for holding the tail of the rat. A wire is connected between two terminals through which heat is generated. The instrument is also provided with a metallic rat carrier for proper holding of rat. This also facilitates easy positioning of the tail of rat in the groove provided for holding the tail above the heater wire. Analgesiometer operates on 220/230V, 50HZ.

The Tail Flick Method[12]

- The tail flick procedure was originally described by D'amor&smith[13] (1941) for testing analgesics in both rats and mice.

- Male albino rats are selected for the experiments. Animals are weighed with the help of weighing machine. The animals weighing 250gms on average are selected for the experiment.
- The animals were divided into 3 groups. First group is control; second group is standard(Piroxicam), third group is test (Tinosporacordifolia).
- Each group contains 6 animals. For identification each group was marked with different colors. A portion of the tail is darkened, using ink, at approximately 3 cm from the tip of the tail.
- Control group of animals were marked with black ink, standard group of animals were marked with blue ink and Test group of animals were marked with red ink.
- Prior to the experiment all animals normal reaction time for heat on analgesiometer was tested for at least 5 times and reaction was tabulated.
- The timer in the analgesiometer will automatically record the tail flick latency. The instrument was operated at 2.5 amps current throughout the experiment.
- The rat is inserted in the metallic rat holder and the tail of the rat is taken out from the slit provided in the rat holder.
- The tail of the rat is positioned in the groove provided.
- The mains plug is inserted into the mains socket for powering the analgesiometer.
- The set current knob is rotated anti-clock wise fully.
- The instrument is switched ON with the help of switch marked with mains on the front panel. Mains ON indicator starts glowing.
- Current meter will start indicating current in the meter.
- Now the desired level is set by observing the color of the wire connected between the two terminals below the tail of the rat. It shall be near to red hot.
- The flicking of the tail of the rat is observed and the time taken for flicking of the tail after heat is applied is noted.
- A cut off period of 20 seconds is observed to prevent damage to tail. Any animal failing to withdraw its tail within cut off period is rejected from the study.
- At least 3-5 reading were taken for each rat at a gap of 5 min to the normal behavior of the animal.
- First group (Control) will be treated with 0.2ml of Normal saline orally; Second group (Standard) will be treated with 2mg/kg of Piroxicam orally. Third group will be treated with the test drug Tinosporacordifolia of 100mg/kg dose orally.

- Tail flick latency was recorded for 3 groups of animals after 30 mins, 60 mins and 90 mins after administration of drugs. Imposing a cutoff time at each test time period.
- The results were tabulated.

RESULTS AND DISCUSSION

Table 1: Comparison of mean reaction time of Normal Saline, Piroxicam and Tinospora at 0 minutes, 30 minutes, 60 minutes and 90 minutes by using ANOVA test

Time (min)	Drug	Mean	SD	F-value	Inference
At 0	Normal saline	7.63	0.46	12.18	p>0.01 Not Significant
	Piroxicam	7.47	0.21		
	Tinospora	7.23	0.30		
At 30	Normal saline	7.50	0.55	36.85	p<0.01 Highly Significant
	Piroxicam	11.50	1.05		
	Tinospora	8.67	0.82		
At 60	Normal saline	7.17	0.75	57.26	p<0.01 Highly Significant
	Piroxicam	13.00	1.27		
	Tinospora	10.83	0.75		
At 90	Normal saline	7.50	0.55	145.09	p<0.01 Highly Significant
	Piroxicam	14.83	0.98		
	Tinospora	13.17	0.75		

HS- Highly Significant; S- Significant; NS- Not Significant.

Mean reaction time at the beginning was not significant among three groups (control, standard and test) and it was highly significant at the time of 30, 60 and 90 min.

Table 2: Comparison of mean reaction time between two drugs at 30 minutes, 60 minutes and 90 minutes by using Tukey test

Time	Comparison between the Drugs		p-value	Inference
At 30	Normal	Piroxicam	.000	HS
		Tinospora	.068	NS
	Piroxicam	Tinospora	.000	HS
At 60	Normal	Piroxicam	.000	HS
		Tinospora	.000	HS
	Piroxicam	Tinospora	.004	HS
At 90	Normal	Piroxicam	.000	HS
		Tinospora	.000	HS
	Piroxicam	Tinospora	.006	HS

HS- Highly Significant; S- Significant; NS- Not Significant

Mean reaction time was not significant between Normal and Tinospora group at 30 min and it was highly significant between the drugs (control vs standard, control vs test and test vs standard) at 60 and 90 minutes of time.

Table 3: Pair wise comparison of mean reaction time of Normal Saline, Piroxicam and Tinosporaat 0 to 30 min, 30 to 60 min and 60 to 90 minutes by using paired t-test

Drug	Comparison between time (min)	Paired t-value	p-value	Inference
Normal	At 0 to 30	0.674	0.53	NS
	At 30 to 60	0.791	0.465	NS
	At 60 to 90	-0.791	0.465	NS
Piroxicam	At 0 to 30	-8.656	<0.01	HS
	At 30 to 60	-3.503	<0.01	HS
	At 60 to 90	-5.966	<0.01	HS
Tinospora	At 0 to 30	-9.087	<0.01	HS
	At 30 to 60	-13	<0.01	HS
	At 60 to 90	-11.068	<0.01	HS

HS- Highly Significant; S- Significant; NS- Not Significant.

Mean reaction time was not significant at time intervals (0 min – 30 min, 30 min – 60 min and 60 min – 90 min) by the normal saline. Where as in standard and test groups it was highly significant.

SUMMARY AND CONCLUSION

This study was carried out to compare the analgesic activity of Tinosporacordifolia with Piroxicamon rats by using digital analgesiometer. Male Wistar Albino rats (approx. 250gms) were selected for the study and were divided into control, standard, and test groups. Six rats were taken in each group.

First group of rats were considered as controls and treated with 0.2 ml normal saline. Second group were considered as standard and treated with Piroxicam, third group were considered as test and treated with Tinosporacordifolia. Analgesic property was assessed by using dose of each drug (Piroxicam-0.33mg &Tinospora cordifolia-100mg) per kg body weight on digital analgesiometer. The time required for the rat to flick its tail was considered as reaction time.

In comparison between standard and test drugs, it was found that mean reaction time gradually increased after 30 minutes, 60 minutes and 90 minutes of administration of both the drugs. But better results were observed with standard drug than with test group of drug.

Tinosporacordifoliais having analgesic property and it is less when compared to Piroxicam. However the above preclinical experiments only give us an idea about the analgesic effect of Tinosporacordifolia&Piroxicam but large scale clinical trials are necessary for final assessment.

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