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ANALGESIC ACTIVITY OF ETHANOLIC EXTRACT OF LEAVES OF *Nyctantes arbor-tristis* Linn.

B.Manikandan[1*], T.Komalavalli[2], A.Manoharan[3]

[1] PG Scholar, Department of *Pothu Maruthuvam,*

[2] Associate Professor, Department of *Pothu Maruthuvam,*

[3] Professor &Head, Department of *Pothu Maruthuvam,*

Govt. Siddha Medical College, Palayamkottai, Tirunelveli, Tamil Nadu, India.

*e-mail-id: drmani2gh@gmail.com

ABSTRACT

The medicine in the Siddha system is not an end by itself. It is only a means to keep and prolong to an extent the tenure of the soul in the body.[1] This noble Siddha medicine takes it role in curing chronic diseases and confronts, claims with the recent advance medicines now-a-days. The present study is concerned with Analgesic activity of ethanolic extract of leaves of *Nyctanthes arbor-tristis* Linn. (NEE) against experimental model of Eddy's hot plate method and heat conduction method in rats. The *Nyctanthes* leaves has been indicated for Back pain[2] in Siddha text 'Siddha Materia Medica (Medicinal Plant Division). Diclofenac sodium is used as a standard drug for these methods. *Nyctanthes arbor-tristis* Linn. leaves ethanolic extract (NEE) have shown propitious effect in reducing the thermal induced nociception at the dose of 300mg/kg significantly ($p<0.001$) in rats. The resultsproves that the ethanolic leaves extract of *Nyctanthes arbor-tristis* Linn. showed highest analgesic activity an another gift of nature to mankind.

Keywords

Analgesic, *Nyctanthes arbor-tristis* Linn. leaves Ethanolic extract (NEE), Diclofenac, Eddy's hot plate, Heat Conduction .

INTRODUCTION

Inflammation - The response of living tissue to injury, featuring widening of blood vessels with redness, heat, swelling and pain - the cardinal signs 'rubor', 'calor', 'tumor' and 'dolor' of the first century physician Celsus. Inflammation also involves loss of function and is the commonest of all the disease processes. Inflammation involves release of PROSTAGLADINS which strongly stimulate pain nerve endings.[3]

Pain [$P\bar{a}n$] a feeling of distress, suffering, or agony, caused by stimulation of specialized nerve endings. Its purpose is chiefly protective; it acts as a warning that tissues are being damaged and induce the sufferer to remove or withdraw from the source.[4]

Non-steroidal anti-inflammatory drugs are aspirin-type or non-narcotic or non-opioid analgesics. During inflammation arachidonic acid liberated from membrane phospholipids is converted to prostaglandis (PGs), catalyzed by the enzyme cyclo-oxygenase (CoX). These prostaglandins produce hyperalgesia they sensitize the nerve endings to pain caused by other mediators of inflammation like bradykinin and histamine.

NSAIDS inhibit the PG synthesis by inhibiting the enzyme cyclo-oxygenase.[5] Decreased prostaglandin production leads to less sensitization of nociceptic nerve endings to the inflammatory mediators, bradykinin and 6-hydroxy tryptamine (Rang *et al.*, 1995).[4]

Due to having adverse side effects, like gastric lesions, caused by NSAIDs and tolerance and dependence induced by opiates, the use of these drugs as analgesic agents have not been successful in all the cases. Therefore, analgesic drugs lacking those effects are being searched all over the world as alternatives to NSAIDs and opiates. During this process, the investigation of the efficacy of plant-based drugs used in the traditional medicine have been paid great attention because they are cheap, have little side effects and according to WHO still about 80% of the world population rely mainly on plant-based drugs (Kumara, 2001).[7]

Keeping this as a view, the present study is concerned to explore the analgestic study as such plant drug as described in Siddha text 'Siddha Materia Medica (Medicinal Plant Division)' indicated for Back pain[2], Rheumatic Complaints.[10]

MATERIALS AND METHODS

i) Trial Drug

Nyctanthes arbor-tristis Linn. is also called the "tree of sorrow", because the flowers lose their brightness during day time; the scientific name *arbor-tristis* also means "Sad tree".[8]

Family	:	Oleaceae		
Vernacular Names	:	Sanskrit	-	*Sepha'lika*
		Hindi	-	*Harsingha'r,Har, Siha'ru*
		Bengali	-	*Sephalika*
		Marathi	-	*Pa'rtaka, Khurasli*
		Tamil	-	*Maja-pu*
		Telugu	-	*Poghada*
		Punjabi	-	*Paku'ra*[9]
		English	-	Night Jasmine
		Siddha	-	*Pavalamalli,Parijatham Parisatham*[2]
Habitat	:	Grows all over Bengal. It is cultivated in gardens for the sake of its flowers.		
Parts used	:	The leaves		
Collection and storage	:	The leaves are dried and kept in airtight place		
Chemical composition	:	The leaves contain an alkaloidal principle named Nyctanthine; they also contain an astringent principle, a resinous substance, colouring matter, sugar and a trace of an oily substance, similar to the oil of peppermint		
Physiological action	:	Anti-periodic, alternative, anti-bilious, expectorant, cholagogue, laxative, mild bitter tonic and anthelmintic		
Therapeutics	:	The decoction of leaves is used as an alternative in obstinate cases of sciatica and rheumatism. The fresh juice of the leaves is given with honey in chronic fever. The juice of the leaves 1 Oz is		

taken with a little honey in bilious fevers. The expressed juice of the leaves is given with a little sugar to children as a remedy for intestinal (Thread and round) worms.[9]

ii) Plant materials

Nyctanthes arbor-tristis Linn. fresh leaves of about 2 kgs were collected and they were authenticated by Department of Medicinal Botany of Government Siddha Medical College, Palayamkottai, Tirunelveli, Tami Nadu. Fresh leaves is cleaned to remove dust and impurities. Then, is made dry in shade. The dried leaves are made into coarse powder. About 500 gm of leaves powder of *Nyctanthes arbor-tristis* Linn. was subjected to extraction with ethanol 95%. After extraction, the solvent was distilled off and extracts were concentrated on water bath. Then the extract has been evaluated for analgesic activity.[11]

iii) Test animal

Wistar albino mice weighing 180-200gm of either sex were maintained under controlled conditions of light (12 Hrs) and temperature 25±1^{o}C in the animal house, one week prior to the experiment for acclimatization. Animals had access to food and water ad libitum. This experiment was performed according to ethical guidelines for the investigation of experiment pain in conscious animals (Reg. No.659/02/A CPCSEA) with IAEC approval No.1012/C06/CPCSEA-Corres-2008-2009.

iv) Chemical

Diclofenac sodium was used as a standard.

v) Eddy's hot plate method

The animals were divided into following six groups of 6 animals each.

Group-I: Treated as normal control received 0.9mg/dl of normal saline by using Intra-Gastric Catheter tube (IGC).

Group-II: Treated as standard control received 9mg/kg of diclofenac sodium intra peritonially.

Group-III: Treated as Test-I received 100mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) orally by using an Intra-Gastric Catheter tube (IGC).

Group-IV: Treated as Test-II received 150mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) orally by using an Intra-Gastric Catheter tube (IGC).

Group-V: Treated as Test-III received 300mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) orally by using an Intra-Gastric Catheter tube (IGC).

The animals were individually placed on the hot plate maintained at 55^{o}C, one hour after their respective treatments. The response time was noted as the time at which animals reacted the pain stimulus either by paw licking or jump response, which ever appeared first. The cut off time for the reaction was 15 seconds.

Statistics

Data are expressed as mean ±SEM; data analysed by one way ANOVA followed by Tukey Kramer multiple comparison test to determine the significance of the difference between the control group and rat treated with extracts.

- Values were considered significant at **P<0.01.

TABLE-1

ANALGESIC ACTIVITY OF *N.arbor-tristis* Linn. ETHANOLIC EXTRACT (NEE) AGAINST EDDY'S HOT PLATE METHOD ON ADULT ALBINO RATS

Groups	**Treatment**		**Response Time in seconds (Mean ±SEM) Eddy Hot Plate Method**
	Drug	**Dose**	
Group-I	Saline	0.9mg/dl	2.8±0.384
Group-II	Diclofenac	9mg/kg	9.84±0.356***
Group-III	Extract	100mg/kg	3.92±0.204^{NS}
Group-IV	Extract	150mg/kg	7.86±0.113**
Group-V	Extract	300mg/kg	10.12±0.326***

One way analysis if variance ANOVA: P value followed to be 0.001 is considered extremely significant NS-Not Significant. The data were expressed as mean ±SEM; Tukey Kramer multiple comparison test: $^{***}P<0.001$, $^{**}P<0.01$ (Extracts Vs Control).

v) Heat Conduction Method

The animals were divided into six groups of 6 animals each.

Group-I: Treated as normal control given 0.9% saline by IGC.

Group-II: Treated as standard and were injected Diclofenac sodium (9mg/kg) intra-peritonially.

Group-III: Treated with 100mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) on the day of this experiment by orally by using an Intra-Gastric Catheter tube (IGC).

Group-IV: Treated with 150mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) on the day of this experiment by orally by using an Intra-Gastric Catheter tube (IGC).

Group-V: Treated with 300mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) on the day of this experiment by orally by using an Intra-Gastric Catheter tube (IGC).

After one hour, the tip of tail was dipped upto 5cm into hot water maintained at 58^{o}C. The response time was noted as the sudden withdrawal of the tail from the hot water. Cut off time of 10 seconds was maintained to avoid damage to the tail for all groups. The time required for flicking of the tail, was recorded, to assess response to noxious stimulus (Kulkarni, 1999) and re-modelling in all groups.

Statistics

Data are expressed as mean ±SEM; data analysed by one way ANOVA followed by Tukey Kramer multiple comparison test to determine the significance of the difference between the control group and rat treated with extracts.

- Values were considered significant at $^{**}P<0.01$.

TABLE-2

ANALGESIC ACTIVITY OF *N.arbor-tristis*Linn.ETHANOLIC EXTRACT (NEE) AGAINST HEAT CONDUCTION METHOD ON THE ADULT ALBINO RATS

Groups	Treatment		Response Time in seconds (Mean ±SEM) Heat Conduction Method
	Drug	Dose	
Group-I	Saline	0.9mg/dl	1.918.±0.413
Group-II	Diclofenac	9mg/kg	9.106±0.236***
Group-III	Extract	100mg/kg	3.113±0.139*
Group-IV	Extract	150mg/kg	6.936±0.338**
Group-V	Extract	300mg/kg	7.318±0.124***

One way analysis if variance ANOVA: P value found to be 0.001 is considered extremely significant NS-Not Significant. The data were expressed as mean ±SEM; Tukey Kramer multiple comparison test: ***P<0.001, **P<0.01 (Extracts Vs Control).

RESULTS AND DISCUSSION

The table valuesshows that analgesic activity of *N.arbor-tristis* Linn. ethanolic extract (NEE) at a dose of 100mg/kg, 150mg/kg and 300mg/kg by Eddy's hot plate and heat conduction method. The result reveals that dose of 300 mg/kg of *N.arbor-tristis* Linn. ethanolic extract (NEE) possess significant analgesic activity at P<0.001.

Effect of ethanolic extract of *Nyctanthes arbor-tristis* Linn. and Diclofenac sodium against Eddy's hot plate method are shown in Table-1. Oral administration of the ethanolic extract at doses 150 and 300 mg/kg shows significant response (Table-1). Ethanolic extract at dose 300 mg/kg showed maximum analgesic effect in hot plate test in rat with response time of 10.12 sec. Diclofenac at dose 9 mg/kg, significantly increase pain latency with response time of 9.8 sec. (Table-1).

Effects of ethanolic extract of *N.arbor-tristis*Linn. and diclofenac against heat conduction method are shown in Table-2. NEE at 150, 300 mg/kg significantly inhibit the withdrawal of the tail from hot water. The maximum inhibition of thermal response at the

dose of 300 mg with response time of 7.3 secs. So, ethanolic extract of *Nyctanthes arbor-tristis* Linn. exerts its pain-relieving effect in a dose dependent manner respectively in rats.

The hot plate method and heat conduction 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 (Sabina *et al.,* 2009).[7] It is an established fact that any agent that causes a prolongation of the pain latency using this test must be acting centrally (Ibironke and Ajiboye, 2007).[7]Therefore, the ethanolic extracts of plant must have a central activity. Again, narcotic analgesics inhibit both peripheral and central mechanism of pain, while NSAIDs inhibit only peripheral pain (Elisabetsky *et al.,* 1995; Pal *et al.,* 1999).[7]The plant extract of *N.arbor-tristis* Linn. exhibited both types of pain inhibition. The analgesic effect of the plant in both model suggests that they have been acting through central and peripheral mechanism (Sabina *et al.,*2009).[7] Thus, proving therapeutics uses described earlier.

CONCLUSION

In conclusion, we can confirm that the *Nyctanthes arbor-tristis* Linn. ethanolic extract at the dose of 300 mg/kg has got both central and peripheral analgesic properties through Eddy's hot plate and heat conduction method with the level of significance at $P<0.001$.

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