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Effectiveness of *Tinospora cordifolia* in comparison to tramadol for analgesic activity in albino rats

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ABSTRACT

Background: Pain and pyrexia are the warning signals, primarily protective in nature, that cause discomfort and suffering and may even be unbearable and incapacitating. The modern drugs (such as opioids, NSAIDs, and corticosteroids) currently used for the management of pain, fever, and inflammatory conditions, present with many known adverse effects. *Tinospora cordifolia* known as Giloe or guduchi, widely used in folk medicine due to its property to cure several diseases. **Aims and Objectives:** The present study was undertaken to explore the analgesic activity of water-soluble extract of *T. cordifolia* in albino rats in experimentally induced pain. **Materials and Methods**: The present study was done in the Department of Pharmacology, Gandhi Medical College, Secunderabad. Albino rats were used to study the analgesic activity of *T. cordifolia* aqueous extract at the dose of 300 mg/kg and 1 g/kg and tramadol 50 mg/kg per orally. Eddy's hot plate was used for the antinociceptive study. **Results**: In Eddy's hot plate, an increase in reaction time was observed with peak effect at 90 min. Results were close to the standard drug tramadol. **Conclusion**: Aqueous extract of *T. cordifolia* was effective in model of pain suggesting its possible action by central and peripheral mechanisms, and in higher doses, it was found to be effective like that of tramadol.

Key words: Analgesic; Anti-inflammatory; Aqueous extract; Albino rats; *Tinospora cordifolia*

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INTRODUCTION

Pain and pyrexia are the warning signals, primarily protective in nature, that cause discomfort and suffering and may even be unbearable and incapacitating, these are the most important symptoms that bring the patient to the physician.[1] The international association of study of pain definition states "pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[2] Pain is a major symptom in many medical conditions and significantly interferes with a person's quality of life and general functioning.[3]

The modern drugs (opioids, NSAIDs, and corticosteroids) currently used for the management of pain, fever, and inflammatory conditions, present with many known adverse effects. Moreover, synthetic drugs are expensive, and many medicinal herbs have been used as therapy for the relief of pain without much adverse effects.[4] There are over 400 different tribal and other ethnic groups in India. Each tribal group has its own tradition, folk language, beliefs, and knowledge about the use of natural resources as medicines.[5]

Tinospora cordifolia or Guduchi is a member of *Menispermaceae* family. It is also known as Giloe, Gurchi (Hindi), and Amrta (Sanskrit). It is found almost everywhere in India and, even up to 1000 feet height in Himalayas. Its habitat ranges across a wide region in India spreading from Kumaon

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Mountains to Kanyakumari.[6] *T. cordifolia* is widely used in veterinary folk medicine/ayurvedic system of medicine for its general tonic, anti-spasmodic, anti-inflammatory, anti-arthritic, hepatoprotective, anti-allergic, and anti-diabetic properties. The plant is used in ayurvedic medicine as "Rasayanas" to improve the immune system and the body resistance against infections. It is also known by the name magical herb due to its property to cure several diseases.

Hence, the present study was undertaken to explore the analgesic activity of water-soluble extract of *T. cordifolia* in albino rats in experimentally induced pain.[7]

Aims and objectives

The aim of the study was to evaluate the effectiveness of *T. cordifolia* in comparison to tramadol for analgesic activity in albino rats.

MATERIALS AND METHODS

T. cordifolia (guduchi) powder was taken from Patanjali store. The powder of guduchi was mixed with 5 mL of distilled water and was used for 2 days only. The preparation was used in two forms 300 mg/kg and 1 gm/kg. Tramadol tablet was crushed and diluted with 5 ml of water and sample was prepared. The study was conducted in albino rats of either sex (150–200 g) after taking approval from the Institutional Animal Ethical Committee with Reg No:428/GO/Re/S/2001/CPCSEA. The animals were provided the ideal conditions according to the CPCSEA norms. The food was withdrawn 12 h before and during the experimental period.

Eighteen animals (n=18) were used for each set of experiment and animal were divided into three groups with six animals in each group of experiment.

GROUP 1 was given *T. cordifolia* extract 300 mg/kg orally,[8] Group 2 was given *T. cordifolia* extract 1 g/kg orally, and Group 3 was given tramadol dose 50 mg/kg orally.[9] Analgesic activity was noted at 30, 60, 90, 120, and 150 min. The pain was produced by Eddy's hot plate.

Analgesic activity Eddy's hot plate method

Rats weighing 100–200 g were used and placed on the hot plate, which consists of electrically heated surface. Temperature of the hot plate was maintained at 55°C. Responses such as jumping, withdrawal of the paws, and licking of the paws were observed. The time period (latency period) when animals were placed and until responses occur was recorded by the stopwatch, and latency period was recorded before and after 30, 60, 90, 120, and 150 min of administration for each animal by administering respective study medication, i.e., standard drug (tramadol) and test drug (Guduchi powder) in the study groups. The observations were tabulated and analyzed.

Statistical analysis

The recorded observations were analyzed by applying one-way ANOVA (GraphPad prism version 9) test where ever needed and $P<0.05$ was considered statistically significant.

RESULTS

Eighteen animals (n=18) were used for each set of experiment and animal were divided in three groups with six animals in each group of experiment, study groups:

- Group 1 was given *T. cordifolia* extract 300 mg/kg orally
- Group 2 was given *T. cordifolia* extract 1 g/kg orally
- Group 3 was given tramadol dose 50 mg/kg orally.[9]

Observations from these three study groups tabulated as distribution of latency time (in seconds) of drugs according to their dosages had been showed in Figure 1 and mean latency time had been showed in Table 1.

Figure 1 shows that 300 mg/kg of tinospora extract at 0 min showed 2–4 s, at 30 min 8–9 s, at 60 min 11–12 s, at 90 min 14–15 s, at 120 min 12–13 s, and at 150 min 9–10 s.

1 g/kg of tinospora extract at 0 min showed 4–6 s, at 60 min 10–11 s, at 60 min 13–15 s, at 90 min 16–17 s, at 120 min 14–15 s, and at 150 min 11–12 s.

Tramadol dose 50 mg/kg at 0 min showed 5–6 s, at 30 min 11–13 s, at 60 min 14–15 s, at 90 min 17–18 s, at 120 min 15–16 s, and at 150 min 12–13 s.

The above table shows the mean latency time of three study groups.

T. cordifolia (300 mg/kg) at 0 min is 3.5±0.55, *T. cordifolia* (1 g/kg) at 0 min is 4.5±0.55, and Tramadol dose

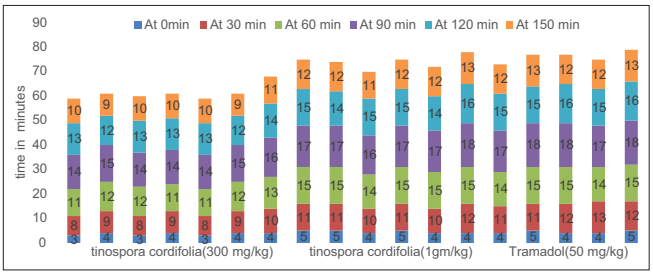

Figure 1: Distribution of latency time (in seconds) of three study groups with respective dosages. The above Figure 1 shows distribution of latency time in three study groups with respective drugs and it dosages, 1 g/kg of tinospora extract had been showed almost similar to that the response produced by Tramadol with the dose of 50 mg/kg.

Table 1: Mean latency time of drugs

Drug	At 0 min	At 30 min	At 60 min	At 90 min	At 120 min	At 150 min
Tinospora cordifolia (300 mg/kg)	3.5±0.55	8.5±0.55	11.5±0.55	14.3±0.52	12.7±0.52	9.7±0.52
Tinospora cordifolia (1 g/kg)	4.5±0.55	10.5±0.55	14.5±0.84	16.7±0.52	14.5±0.55	11.7±0.52
Tramadol (50 mg/kg)	4.3±0.52	11.8±0.75	14.7±0.52	17.7±0.52	15.5±0.55	12.5±0.55
P-value	0.012	<0.001	<0.001	<0.001	<0.001	<0.001

(50 mg/kg) at 0 min is 4.3±0.52, their values (Mean±SD) were compared by one-way ANOVA and was found to be significant (P=0.012).

T. cordifolia (300 mg/kg) at 30 min is 8.5±0.55, *T. cordifolia* (1 g/kg) at 30 min is 10.5±0.55, and tramadol dose (50 mg/kg) at 60 min is 11.8±0.75; their values (Mean±SD) were compared by one-way ANOVA and were found to be significant (P=0.001).

T. cordifolia (300 mg/kg) at 60 min is 11.5±0.55, *T. cordifolia* (1 g/kg) at 60 min is 14.5±0.85, and tramadol dose (50 mg/kg) at 60 min is 14.3±0.52; their values (Mean±SD) were compared by one-way ANOVA and were found to be significant (P=0.001).

T. cordifolia (300 mg/kg) at 90 min is 14.3±0.52, *T. cordifolia* (1 g/kg) at 90 min is 16.7±0.52 and tramadol dose (50 mg/kg) at 90 min is 17.7±0.52; their values (Mean±SD) were compared by one-way ANOVA and were found to be significant (P=0.001).

T. cordifolia (300 mg/kg) at 120 min is 12.7±0.52, *T. cordifolia* (1 g/kg) at 120 min is 14.5±0.55, and tramadol dose (50 mg/kg) at 120 min is 15.5±0.55; their values (Mean±SD) were compared by one-way ANOVA and were found to be significant (P=0.001).

T. cordifolia (300 mg/kg) at 150 min is 9.7±0.52, *T. cordifolia* (1 g/kg) at 150 min is 11.7±0.52, and Tramadol dose (50 mg/kg) at 150 min is 12.5±0.55; their values (Mean±SD) were compared by one-way ANOVA and were found to be significant (P=0.001).

DISCUSSION

The hot plate method measures the complex response to a non-inflammatory, acute nociceptive input and is one of the models used for studying central nociceptive activity.

The group of rats receiving *T. cordifolia* extract showed statistically significant difference with the standard drug tramadol at 60 min (P<0.01), 90 min (P<0.01) similarly at 120 min and 150 min, respectively. The hot plate method is selective for the drugs acting centrally.

T. cordifolia showed less significant effect and less potent in test group when compared to standard group aspirin in the study conducted.[7]

Findings of our study also in accordance with results of Hossain et al., which showed a significant increase in pain threshold in hot plate with tramadol as a standard drug.[8]

Although it is not the scope of the study to elucidate the mechanism of action of this extract, based on the previous studies, the probable mechanism of action of this extract as analgesic, but it is possible that the extract act on opioid receptor. It also potentiated analgesic effect of morphine so its activity might involve opioid receptors.[9]

Antioxidant and calcium-attenuating actions of aqueous and alcoholic extract of *T. cordifolia* are contributing for attenuating sciatica pain associated with sciatic nerve root ligation.

Petroleum ether extract of *T. cordifolia* found to increase the levels of monoamines such as noradrenaline, serotonin, and dopamine which may be responsible for its antinociceptive activity.[10]

T. cordifolia contains alkaloids, glycosides, flavonoids, steroids, and terpenoids in the aerial part of the plant. Hence, the observed analgesic activity may be attributed to any of these phytoconstituents. There are also reports of analgesic activity of flavonoid which is mediated by inhibiting the production of prostaglandins.[11]

Prostaglandins sensitize the peripheral nerve endings. Moreover, substances such as bradykinin and Substance P (potent mediators of pain) are released during inflammation. Anti-inflammatory agents such as NSAIDs are used as analgesics and decrease pain by decreasing various mediators of inflammation especially PG.[12]

As it was mentioned in the current available literature, the activity of *T. cordifolia* can be attributed to various phytoconstituents, namely, protoberberine alkaloids, terpenoids, glycosides, and polysaccharides. It can be developed as potent analgesic agent in the future.

Limitations of the study

More sample size is required. More dosage forms need to be analysed with respective intervals.

CONCLUSION

The current study results state that *T. cordifolia* in higher doses was found to be effective like that of tramadol and can be used in routine clinical practice as analgesic and anti-inflammatory. It is easily available and has no chances of causing drug dependence.

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Authors Contribution:
SGA- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis; **SS-** Concept, design, clinical protocol, manuscript preparation and submission of article, editing, and design of study, statistical analysis and interpretation; **BE-** Coordination and manuscript revision; **PRO-** Data collection, prepared first draft of manuscript; **SE-** Literature survey and preparation of figures.

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