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PHARMACOLOGICAL EVALUATION OF SCIATILON SOFT GEL CAPSULE FOR ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY

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Keywords:

Anti- inflammatory, carrageenan, analgesic, hot plate, Sciatilon Soft Gel Capsule, Experimental animals.

Abstract

Objectives: Aim of the present work was to investigate the anti-inflammatory and analgesic effects of Sciatilon Soft Gel Capsule.

Material and Methods. The anti-inflammatory of Sciatilon Soft Gel Capsule was assessed by using the carrageenan induced paw oedema in rats. The hot plate test was performed to assess analgesic effects Potential in mice.

Results: Among the doses Sciatilon Soft Gel Capsule (Sct) showed comparable activity with standard drug Indomethacine. Sct significantly ($p < 0.05$) reduced carrageenan induced paw oedema in a dose dependent manner. In hot plate method Sct 12mg/kg showed better analgesic activity than the other dose. POR showed comparable ulcer reducing potential ($p<0.01$) to that of standard drug Indomethacin (Ind)

Conclusions: The results of this study demonstrated that Sciatilon Soft Gel Capsule 12mg/kg possesses biological activity that is close to the standards taken for the treatment of peripheral painful or/and inflammatory conditions.

Introduction

Sciatica occurs due to lumbar disc herniation (LDH) in approximately 90 % of cases,[1] and is characterized by ipsilateral radiating leg pain[2] secondary to an inflammatory response from nerve root irritation[3]. The prevalence of sciatica ranges from 1.6 % in the general population to 43 % in specific working populations[4]. The annual incidence of sciatica in Western countries is estimated at 5 cases per 1,000 adults[5]. Although the natural history of sciatica is known to be favorable in most patients,[6] a sizable percentage (up to 30 %) report pain persisting for 1 year or more[7, 8]. Many randomized controlled trials (RCTs) comparing non-surgical treatment with surgery in LDH patients with sciatica have reported that between-group differences were not significant at long-term follow-up[9,10]. Though guidelines and experts agree that first-line treatment for sciatica should be conservative, they are divided regarding specific treatment modality[7]. Recently, more multidimensional approaches are being considered in conservative treatment, and are not limited to conventional treatment, but include complementary and alternative medicine (CAM)[11].

Plants have been used for therapeutic applications ever since man has been concerned about his health. For centuries, the world has depended on the useful possessions of plants as a source of medicines[12]. Ethnobotanical investigations done in the last few decades had discovered the analgesic properties of plants mentioned in the traditional information. Numerous herbal preparations are being suggested as analgesic in the traditional information. The exploration for new analgesic compounds from the enormous arrays of medicinal plant resources is growing. This is because such information may hold guarantee for the finding of new therapeutic agents capable of inhibiting, decreasing, or relieving pain[13]. Plants characterize a huge natural supply of valuable compounds that might achieve as lead for the expansion of novel drugs[14]. The exploration of the effectiveness of plant-based drugs used in the traditional medicine has been given great considerations because they are cheap and have little side effects, and, according to World Health Association (WHO), about 80% of the world population still relies chiefly on plant-based drugs[15].

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Sciatilon Soft Gel Capsule is an ethical proprietary products developed by Nagarjuna Herbal Concentrates Ltd. This product was developed as an affective herbal remedy for pain and swelling. Sciatilon Soft Gel capsule is used for the relieving lower back pain and pain associated with sciatica. The medicine was completely herbal combination processed in oil base. This method follows the principle of incorporating the efficacy of herbal ingredients through repeating the process (Avarthy). This method improves the efficacy in reduced dosage. Objective of the study is to ascertain the efficacy and dosage of Sciatilon Soft Gel Capsule through preclinical studies. For this we did anti-inflammatory property in carrageenan induced paw oedema in rats and analgesic property by using Eddy's hot plate method in Swiss albino mice.

Materials and Methods

2.1. Raw material collection

All the ingredients used for these medicines were collected from raw material store of Nagarjuna Herbal Concentrats Ltd, Thodupuzha, Kerala, India. The herbs were identified and authenticated at the herbarium of Pharmacognosy department, Nagarjuna Herbal Concentrats Ltd, Thodupuzha, Kerala, India. For Sciatilon 12 raw materials used for Kashayam(decoction) and 2 raw materials for Kalkam(Paste).

2.2. Method of preparation

The process is as per the preparation of Aavarthy (Repeating the process), a pottenciation process mentioned in the Ayurvedic classical texts. All the raw materials were cleaned, washed and dried. The raw materials used for preparing the Kashayam (decoction) were divided into different parts (as per the no. of averthies). The raw materials for Kalkam (Paste) are powdered and also divided into different parts (as per the no. of avarthees). From these, 3 parts were taken together for preparing the decoction for three Avarthees at a time. This was then added with 16 times of water and reduced to one fourth through boiling. On completion it was filtered and divided into three parts. One part of this kashayam along with Sesame oil and one part of Kalkam were boiled up to the proper consistency (Chalipakam). When the consistency is reached, milk is added up to thrice the quantity of oil and boiled again till it reaches the next consistency (Chikkanapakam). Then this allowed to settle the sediments and filtered. This process was repeated up to 21 times with the remaining materials in the same oil. The final product was filtered till all the residues were separated and used for the study.

2.3. Experimental animals

Female Wistar rats weighing 220-250 g and Female Swiss mice weighing 20-30g bred in Nagarjuna Herbal Concentrates Ltd., Thodupuzha, Kerala, India, were used in the present study. The animals were housed in polyacrylic cages (38 × 23 × 10 cm) with not more than 3 animals per cage and maintained under standard laboratory conditions with natural dark and light cycle. They were allowed free access to standard dry rat/mice diet and water *ad-libitum*. All animal for the experiments were approved by the Institutional Animal Ethics Committee, Nagarjuna Herbal Concentrates Ltd., and were maintained in accordance with the guidelines of the CPCSEA.

2.3.1. Anti-inflammatory activity

Female Wistar rats (120 - 170 g) kept at the laboratory Animal house of the Nagarjuna Herbal Concentrats Ltd. Idukki, Kerala, India were used. The animals were maintained under standard environmental conditions and had free access to standard diet and water. Anti-inflammatory activity was measured using carrageenan induced rat paw oedema assay[16]. 16 hour fasted rats were selected and classified into ten groups. Group I to serve as oedema control receiving 0.5% tween 20, Group II was treated with Sct (3mg/kg), Group III was treated with Sct (6mg/kg), Group IV was treated with Sct (12mg/kg), Group V was treated with Sct (24mg/kg), and the Group IV was treated with standard drug, Ind (10mg/kg). The initial paw volume was measured before inducing the oedema. The right hind paw of the rat was induced with oedema by injecting 0.1ml of 1% solution of Carrageenan in sterilized normal saline. The medicines were administered orally 30 min before the injection of Carrageenan. The paw volume was then measured at 60, 120, 180 and 240 minutes by the mercury displacement method using a Plethysmograph.

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2.3. 2. **Analgesic property**
Female Swiss albino mice (20 - 30 g) kept at the laboratory Animal house of the Nagarjuna Herbal Concentrats Ltd. Idukki, Kerala, India were used. The hot plate test was used to calculate analgesic activity by the method explained by Eddy and Leimbach[17] with minor modifications. Mice were retained on a hot plate having a stable temperature of 55 ± 1°C. The time taken for either paw licking or jumping was recorded. Each mouse was individually placed on the hot plate in order to find the animal's reaction to electrical heat-induced pain (licking of the forepaws and eventually jumping). Group I to serve as normal control receiving 0.5% tween 20, Group II was treated with Sct (3mg/kg), Group III was treated with Sct (6mg/kg), Group IV was treated with Sct (12mg/kg), Group V was treated with Sct (24mg/kg), and the Group IV was treated with standard drug, Ind (10mg/kg). The latency until mice showed first signs of discomfort (hind paw lifting, hind paw licking, or jumping) was recorded, before (baseline), and response was determined at 30, 60, and 90min after the treatment.

2.4. Data Analysis.
Data were analyzed using statistical software GraphPad Prism version 7. Two-way repeated measure ANOVA test used to assay the differences in volume of paw oedema in rats and increased latency response in pain was measured in mice. Data are shown as mean ± S.D. All data were considered significant at $P < 0.05$

Result

3.1. Carrageenan induced paw oedema in rats
Sct dose dependently reduced carrageenan induced paw oedema compared to control in rats at 240min. The activity was comparable with standard drug indomethacin. The percentage decrease in paw volume determines anti-inflammatory potential of the drug. The Sct (12 mg/kg) showed maximum inhibitory response in comparison to other doses 3 and 6mg/kg. Major variation in its effect was seen between 24, 3 and 6mg/ kg. The inhibitory activity of the Sct 12mg/kg and 24mg/kg with minor difference was seen between12 and 24mg. this was very close to indomethacine

3.2. Hot plate method
The different dose of Sct show comparable effect than indomethacin 10 mg/kg (Fig II). The results in Figure II shows that the treatment of mice increased the latency response in the hot plate test from 30 to 90 minutes. On the other hand, Sciatilon Soft gel capsules significantly influence the reaction time of the animals to the hot plate. The efficacy was dose depended, 17.26 and 15.32sec was the latency got at 12 and 24mg/kg respectively, but there was no much deference between in 12 and 24mg/kg. 12 and 24 mg/kg can be comparable with Indomethacine, which have optimum latency at the doses of 10mg/kg in 18.23minutes.

4. Discussion
The anti-inflammatory and analgesic activities of different dose of Sciatilon Soft Gel Capsule were investigated in the present study. The carrageenan test was selected because of its sensitivity in detecting orally active anti-inflammatory agents particularly in the acute phase of inflammation. The carrageenan-induced paw oedema model is used to screen the anti-inflammatory activity of a drug in the acute phase of inflammation. Oedema induced by carrageenan is believed to be biphasic[18,19]. First phase of action of carrageenan results from the concomitant release of mediators: histamine, serotonin and kinins those induces vascular permeability[20]. The second phase is correlated with leukotrienes. The oral administration of different dose of Sct suppresses inflammation during the second phase. The Sct (12 mg/kg) showed maximum inhibitory response in comparison to other doses 3 and 6mg/kg. The mechanism for testing analgesics was selected in such a way that both centrally and peripherally mediated effects could be investigated.

Three anti-nociceptive models hot plate models was used to evaluate the analgesic activity of Sct since tests of analgesic drugs commonly measure nociception and involves the reaction of animals to painful stimuli. The stimulus may be thermal (hot plate tests), chemical (acetic acid-induced writhing or formalin tests) or mechanical (tail or paw pressure tests) [21]. For this study we use hot plate tests. In hot plate model, the paws of mice are very sensitive to temperatures at 55 ± 1°C[22]. In this model, increase in pain reaction time (PRT) or latency period indicates the level of analgesia of drug [23]. The drugs showed a significant increase in Pain Reaction Time. When we campier the PRT

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the drugs in deferent doses 12 and 24mg/kg significantly increased the pain reaction time. Sciatilon shows a dose depended activity at a higher tetency of. In this model, sensory nerves sensitise the nociceptors and the involvement of endogenous substances such as prostaglandins are minimized[24]. From the results, though the medicines showed good analgesic actions in hot plate models.

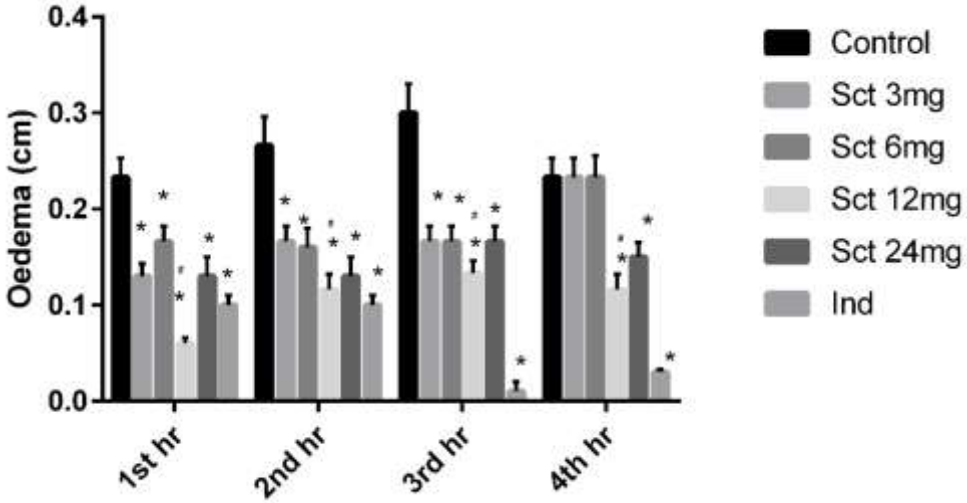

Figure I1: Anti-inflammatory effects of normal control, Indomethacine (10 mg/kg), and Sciatilon (3, 6, 12 and 24mg/kg b.wt.) on carrageenan induced paw oedema in rats. Data are presented as mean ± S.D. * indicates statically significant (p<0.05), compared to respective control. # indicates statically higher activity (p<0.05), compared to other doses of the same drug.

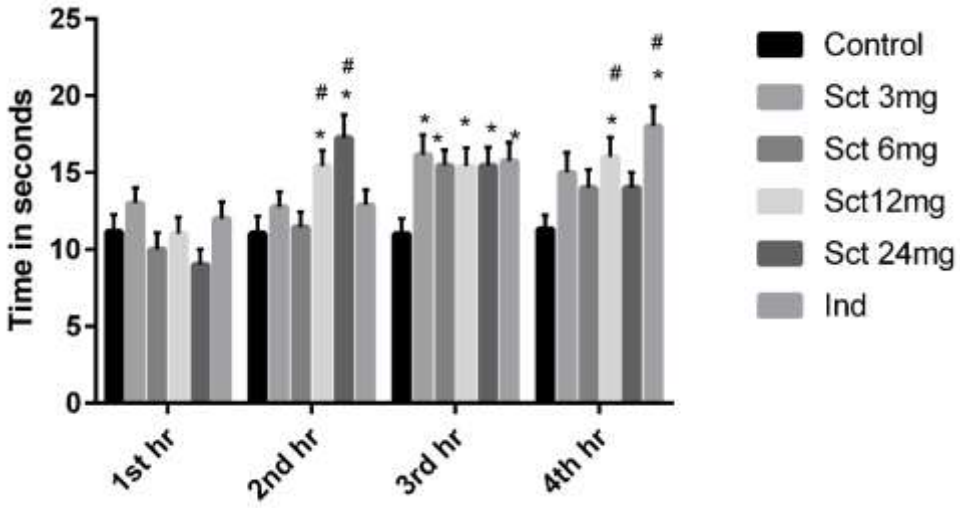

Figure I1: Analgesic effects of normal control, Indomethacine (10 mg/kg), and Sciatilon (3, 6, 12 and 24mg/kg b.wt.) on the results of the hot plate test in mice. Data are presented as mean ± S.D. * indicates statically significant (p<0.05), compared to respective control. # indicates statically higher activity (p<0.05), compared to other doses of the same drug.

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REFERENCES

1. Valat J. P., Genevay S., Marty M., Rozenberg S. and Koes B. "Sciatica", Best Pract Res Clin Rheumatol. , 2010,vol. 24, pp. 241–52.
2. Mens J., Chavannes A., Koes B., Lubbers W., Ostelo R. and Spinnewijn W.b"NHG-guideline lumbosacral syndrome", Huisarts Wet., 2005, vol. 48, pp. 171–8.
3. Patrick D. L., Deyo R. A., Atlas S. J., Singer D. E., Chapin A., Keller R. B., "Assessingbhealth-related quality of life in patients with sciatica", Spine (Phila Pa 1976).b1995, vol. 20, pp.1899–908.
4. Konstantinou K. and Dunn K. M., "Sciatica: review of epidemiological studies and prevalence estimates", Spine (Phila Pa 1976). 2008, vol. 33, pp. 2464–72.
5. Cherkin D. C., Deyo R. A., Loeser J. D., Bush T. and Waddell G., "An international comparison of back surgery rates", Spine (Phila Pa 1976), 1994, vol.19, pp. 1201–6.
6. Legrand E., Bouvard B., Audran M., Fournier D. and Valat J. P., "Spine Section of the French Society for Rheumatology. Sciatica from disk herniation: medical treatment or surgery?", Joint Bone Spine, 2007, vol. 74 pp. 530–5.
7. Vroomen P. C., de Krom M. C., Slofstra P. D. and Knottnerus J. A., "Conservative treatment of sciatica: a systematic review", J Spinal Disord, 2000, vol. 13 pp. 463–9.
8. Weber H., Holme I. and Amlie E., "The natural course of acute sciatica with nerve root symptoms in a double-blind placebo-controlled trial evaluating the deffect of piroxicam", Spine (Phila Pa 1976). 1993, vol. 18, pp. 1433–8.
9. Peul W. C., van den Hout W. B., Brand R., Thomeer R. T. and Koes B. W., "Leiden-ThenHague Spine Intervention Prognostic Study Group. Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial", BMJ, 2008, vol. 336, pp. 1355–8.
10. Weber H., "Lumbar disc herniation. A controlled, prospective study with tennyears of observation", Spine (Phila Pa 1976). 1983, vol. 8, pp. 131–40.
11. Oken B. S., "Complementary therapies in neurology", New York & London: Parthenon Publishing Group, 2005.
12. Brunelli B. and Gorson K. C., "The use of complementary and alternative medicines by patients with peripheral neuropathy", J Neurol Sci. 2004, vol. 218, pp. 59–66.
13. Vittalrao A. M., Shanbhag T., Kumari K. M., Bairy K. L., and Shenoy S., "Evaluation of antiinflammatory and analgesicactivities of alcoholic extract of *Kaempferia galanga* in rats," Indian Journal of Physiology and Pharmacology, 2011, vol. 55, no. 3, pp. 13–24.
14. Kakoti B. B., Pradhan P., Borah S., Mahato K. and Kumar M., "Analgesic and anti-inflammatory activities of the methanolic stem bark extract of *Nyctanthes arbor-tristis* Linn.," BioMed Research International, 2013, vol. 2013, Article ID 826295, pp. 6 .
15. Anilkumar M., "Ethnomedicinal plants as anti-inflammatory and analgesic agents," in Ethnomedicine: A Source of Complementary Therapeutics, Research Signpost, India, 2010, pp. 267–293,.
16. Chorousus G. P., Katzung B. G., Masters S. B. and Trevor A. J., "Basic and clinical pharmacology", eds. Adrenocorticosteroids and Adrenocortical Antagonists, 12th ed. New York, NY: McGraw-Hill, 2012, pp. 697e711.
17. Eddy N. B. and Leimbach D., "Synthetic analgesics. II. Dithienylbutenyl-and dithienylbutylamines", J of Pharm and Exp Ther, 1953, vol. 107, no. 3, pp. 385– 393.
18. Shashidhara S., Bhandarkar A. V. and Deepak M., "Comparative evaluation of successive extracts of leaf and stem bark of Albizzia lebbeck for mast cell stabilization activity". Fitoterapia, 2008, vol. 79, pp. 301e302.
19. Tripathi R. M., Sen P. C. and Das P. K., "Further studies on the mechanism of the antianaphylactic action of Albizzia lebbeck, an Indian indigenous drug", J Ethnopharmacol, 1979, vol. 1, pp. 397e400.
20. Nurul I. M., Mizuguchi H. and Shahriar M., "Albizzia lebbeck suppresses histamine signalling by the inhibition of hisamine H1 receptor and histidine decarboxylase gene transcriptions", Int Immunopharmacol, 2011, vol. 11, pp. 1766e1772.

September 2016; 3(9) ISSN: ISSN: 2349-5340
DOI: 10.5281/zenodo.154359 Impact Factor: 3.052

21. Franzotti E. M., Santos C. V. F., Rodrigues H. M. S., Mourao R. H. V., Andrade M. R., *et al*. "Anti-inflammatory, analgesic and acute toxicity of *Sida cordiforlia* L", J Ethnopharmacol, 2000, vol. 72, pp. 273–277.
22. George K. A., Eric W., David D. O. and George A. K., "Antinociceptive Effects of *Newboulia Laveis* (P.Beauv) Stem Bark Extract in Rat Model", Pharmacog Mag, 2009, vol. 17, pp. 49–54.
23. Ranadran K. and Basinath L., "A critical Analysis of the Experimental Evaluation of Nociceptive reactions in Animals", Pharm Research. 1986, vol.3, pp. 253–270.
24. Bachlav R. S., Gulecha V. S. and Upasani C. D., "Analgesic and Anti-inflammatory Activity of *Argyreia Speciosa* roots", Indian J Pharmacol., 2009, vol.41 no. 4 pp. 158–161