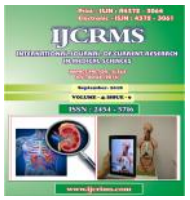
International Journal of Current Research in Medical Sciences
ISSN: 2454-5716
P-ISJN: A4372-3064, E -ISJN: A4372-3061
www.ijcrims.com



Original Research Article **Volume 4, Issue 9 -2018**

DOI: http://dx.doi.org/10.22192/ijcrms.2018.04.09.002

In-Vivo Evaluation of Analgesic and Anti-Inflammatory Potential of Siddha Drug *Sangu Chunnam* using Eddy's hotplate and Carageenan Induced Paw Oedema model in Rats

V. Indumathy*[1], A.Dhivyabharathi[2], N.Anbu[3], K.Kanakavalli[4]
[*1& 2] P.G.Scholar, Department of Maruthuvam, Government Siddha Medical College, Arumbakkam, Chennai 600106, Tamil Nadu, India.
[3]HOD,PG Department of Maruthuvam, Government Siddha Medical College, Arumbakkam, Chennai 600106, Tamil Nadu, India.
[4]Principal, Government Siddha Medical College, Arumbakkam, Chennai 600106, Tamil Nadu, India.
*Corresponding Author : **Dr.V.Indumathy,** P.G.Scholar,
Government Siddha Medical College, 6 Anna Arch Road, NSK Nagar, Arumbakkam, Chennai 600106, Tamil Nadu, India.

Abstract

Inflammation is the body's response against invading pathogens, which is typically characterized by redness, swelling, pain, and heat. Several reports have provided evidence that inflammation is involved in the pathogenesis of many diseases including aging, cancer, cardiovascular dysfunction, and other life-threatening and debilitating disorders. Conventional NSAID has potential of causing side effects such as hypertension, renal disorder, gastric irritation etc. There has been some concern over the use of modern cyclooxygenase -2 (COX-2) inhibitors ie rofecoxib and valdecoxib due to risk of cardiovascular and skin related toxicities. In the recent years, the use of traditional siddha remedies for the treatment of inflammatory disease has been gaining paramount importance. The main objective of the present research work is to evaluate the analgesic and anti-inflammatory activity of siddha preparation *Sangu Chunnam* (SC) in rats. Acute inflammation in rats was induced by carrageenan-induced rat paw edema and induction of pain was done using eddy's hotplate method. Results obtained from the study has revealed that treatment with SC at both the dose level of 100 and 200 mg/kg has shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 86.68 %. Similar results were observed in eddy's hotplate in which there was a significant increase in reaction time of rats treated with SC at the dose level of 100 and 200 mg/kg which reveals the analgesic potential of the drug SC. Further from the results it was concluded that siddha drug SC has analgesic and anti-inflammatory potential which may be due to the bioactive component present with in it and hence usage of these alternative traditional medicine offers good efficacy and reliable safety upon long term usage.

Keywords: Inflammation, Analgesic, Anti-inflammatory, Siddha remedies,*Sangu Chunnam*, Carrageenan,Eddy's hotplate.

1. Introduction

Inflammation is characterized by well-coordinated events in response to harmful stimuli, such as injury, infection, and irritants [1,2]. However, uncontrolled and chronic inflammation can lead to several diseases, such as autoimmune diseases, rheumatoid arthritis, asthma, and inflammatory bowel disease [3-7]. Non-steroidal anti-inflammatory drugs (NSAIDs) are potent synthetic drugs, widely used for the treatment of inflammatory diseases. Unfortunately, currently available NSAIDs have not been completely successful in clinical applications because of their serious side effects, such as gastric lesions, renal damage, bronchospasm, and cardiac abnormalities [8]. Therefore, there is a global search for new anti-inflammatory drugs as alternatives to NSAIDs.

Macrophages play an important role in the inflammatory processes and produce inflammatory mediators, such as nitric oxide (NO) and prostaglandin E_2 (PGE_2), which are generated by activated inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2), respectively [9]. In addition, macrophages produce various cytokines, such as interleukin-1β (IL-1β), IL-6, and tumor necrosis factor-α (TNF-α), when activated by appropriate stimuli [10]. Activated macrophages thus play pivotal roles in inflammatory diseases via excess production of inflammatory mediators, such as NO and PGE_2, as well as pro-inflammatory cytokines, to promote the inflammatory response [11].

Many nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely prescribed therapeutics, mainly for the treatment of pain and inflammation. However, long-term clinical usage of NSAIDs is associated with significant side effects, such as gastrointestinal lesion, bleeding, and peptic ulcer [12]. Hence, as an alternative, ethnopharmacological remedies are getting an increased therapeutics market share due to their better action and fewer adverse effects.

In recent past a tremendous aggressive trust has been observed in natural origin as a prime source of healthcare. This fact significantly contributed in the development of modern medicine of natural origin. The uses of natural medicines are widespread and plants still present a large source of structurally novel phytocompounds that might serve as leads for the development of novel pharmaceutical agents for the prevention and treatment of diseases and ailments [13].

During the past 10 years, there has been a substantial resurgence of interests and pursuits of natural product drug discovery and development both in the public and private sectors. Explanation for this might include the increasingly sophisticated development process; the very real threat of the disappearance of the biodiversity essential for such research; and the persistence of old diseases and the emergence of new diseases that remain intractable to any known medicine or treatment [14].

Since ancient times, siddha system of traditional medicines have been used to treat various ailments including pain and inflammation. These are nature's herbal, minerals, herbomineral and polyherbal products which strengthen and enhance the body's own healing process and do not have adverse effects, if given in appropriate doses. The main aim of the present investigation is to evaluate the analgesic and anti-inflammatory potential of siddha drug sangu chunnam using Eddy's hotplate and carrageenan induced paw edema model in wistar rats.

2. Materials and Methods

2.1. Source of raw drugs:

The Required raw materials were procured from a well reputed indigenous drug shop from, Chennai, Tamil Nadu, India .All raw drugs were authenticated by respective authorities before utilizing the same for the preparing the formulation.

2.2. Ingredients

The siddha formulation *Sangu Chunnam* comprises of the following ingredients

Paalsangu - 2kg
Lemon juice - Quantity Sufficient

2.3. Formulation of Trial drug *Sangu Chunnam* [15]

A purified Paalsangu was grounded and powered filtered with a cloth.It was then grinded with lemon juice for 3 hours made into cakes and dried.Above processed material was kept inside a mud pot and was closed with lid.The mud pot was two times sealed with mud pasted cloth. The weight of the cow dung cakes should be 20 times the weight of the sealed mud pot. It was incinerated by cow dung cakes and cooled.T hen Chunnam was collected and kept in an air tight container. The Chunnam was tested by mixing the Chunnam in turmeric powder and it became reddish orange colour.

2.4.Animal

Healthy adult Wistar albino rats were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air. A 12 light / dark cycle were maintained .Room temperature was maintained between 22 $\pm$ 2^0 Cand relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water *ad libitum*. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of C.L.Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India.LI/04/CLBMCP/2017.

2.5.Carageenan Induced Paw Oedema [16,17]

Anti-inflammatory activity was measured using carrageenan-induced rat paw edema assay Edema was induced by subplantar injection of 100 µL of 1% freshly prepared solution of carrageenan in distilled water into the right-hind paws of each rat. Paw thickness were measured just before the carrageenan injection, that is, at “0 hour” and then at 1, 2, 3, 4, and 5^{th} hour after carrageenan injection. Increase in paw thickness was measured as the difference in paw thickness at “0 hour” and paw thickness at respective hours. The paw volume was measured using Plethysmometer (Model 7150 UGO Basile, Italy) Edema was expressed as the mean increase in paw volume relative to control animals. Percentage protection is calculated by the formulae: (T_2---$T_{1/}$ T_2) x 100 , T_1-- Normal control and T_2 -- Drug treated test

2.5.1.Grouping for Anti-Inflammatory Activity

For the experiment, the animals were divided into 5 groups with 6 animals in each group.

- Group-I (control) received 3% gum acacia 10 ml/kg p.o.
- Group-II (Carageenan) received 0.1ml of 1% w/v suspension of carrageenan S.C
- Group-III (standard) received Indomethacin 40 mg/kg p.o.
- Group-IV (Test-1) received SC 100mg/kg p.o.
- Group-V (Test-2) received SC 200mg/kg p.o.

2.6.Analgesic Activity by Eddy’s Hot Plate Method [18]

The hot plate assay method was employed for the purpose of preferential assessment of possible analgesic effects of test drug Sangu Chunnam. The analgesic drug, Pentazocine, was used for positive control group. In this experiment, four groups (n=6) of wister rats (200–250 g) were placed on a hot plate maintained at room temperature for 15 min. Food was withdrawn on the preceding night of the experiment. Group-1 normal control (0.5% CMC p.o.), and group-2 Pentazocine (30mg/kg, i.p.), whereas groups-3 and 4 animals received Sangu Chunnam (100and 200 mg/kg, p. o respectively). Each animal was then individually placed gently on Eddy’s hot plate at 55^oC. Latency to exhibit nociceptive responses such as licking paws or jumping off the hot plate, were determined 15, 30, 45 and 60 min after administration of the test drug or vehicle.

2.6.1.Grouping for Analgesic Activity

- Group-I (control) received 0.5 % CMC, p.o.
- Group-II received Pentazocine ,30mg/kg, i.p.
- Group-III (Test-1) received SC ,100mg/kg p.o.
- Group-IV (Test-2) received SC ,200mg/kg p.o.

3. Results

3.1.Effect of *Sangu Chunnam*on paw edema volume in carrageenan induced edematous rats

Result analysis of carrageenan induced paw edema reveals that treatment with SC at the dose of 100 and 200 mg/kg shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 86.68 %. As shown in tables 1 and 2.

Table 1: Effect of *Sangu Chunnam*on paw edema volume in carrageenan induced edematous rats

Group	Dose	Initial paw volume	Change in paw edema mm at different time intervals				
		0hr	1 hr	2hr	3hr	4hr	5hr
I	Control	1.20± 0.14	1.20±0.14	1.20±0.14	1.20±0.14	1.20±.14	1.20±0.14
II	Carrageenan	1.21± 0.17	1.91± 0.21	2.27± 0.02	2.37± 0.14	2.48± 0.1	2.62± 0.17
III	Indomethacin	1.01± 0.06	2.10± 0.26	1.56± 0.15	1.47± 0.05	1.34± 0.8	1.15± 0.16
IV	Low dose	1.34 ± 0.11	1.46± 0.32	1.52± 0.18	1.64± 0.22	1.53± 0.2	1.58± 0.24
V	High dose	1.24±0.42	1.98± 0.22	1.82± 0.23	1.66± 0.44	1.62± 0.1	1.20± 0.12

Table 2: Effect of *Sangu Chunnam*on percentage protection in carrageenan induced edematous rats

Group	Treatment	5 hr in mm	Difference in paw volume	Percentage protection
I	Control	1.20±0.14	0	100
II	Carrageenan	2.62 ± 0.17	1.41	15.62
III	Indomethacin,40mg/kg	1.15 ± 0.16	0.24	86.68
IV	SC 100 mg/kg	1.59 ± 0.32	0.15	31.42
V	SC 200 mg/kg	1.30 ± 0.12	0.08	65.45

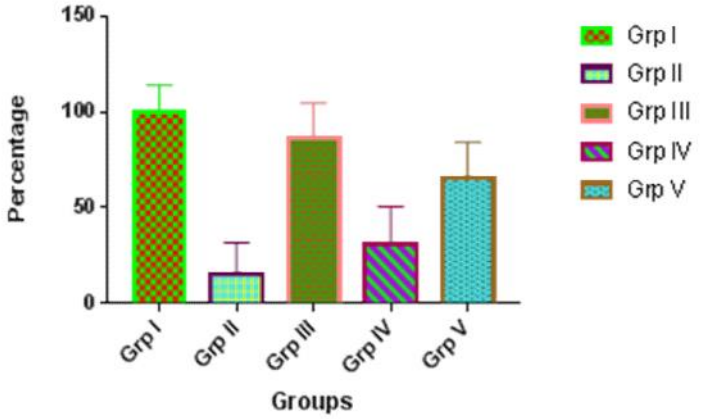


Figure 1: Percentage protection of SC and standard drug in carrageenan induced edematous rats

3.2.Effect of *Sangu Chunnam*on Eddy's Hot plate induces pain in rats

Results were clearly justifies that treatment with SC at the dose of 100 and 200 mg/kg offers greater protection against thermal induced pain in experimental animal which were reflected by significant increase in the latency reaction time of SC treated rats when compare to control rats.

Table 3: Effect of *Sangu Chunnam*on Eddy's Hot plate induces pain in rats

Groups	Dose	15 mins	30 mins	45 mins	60 mins
	mg/kg	Latency Reaction time			
Control	10	2.2±.0.2	2.1±0.4	2.4±0.6	1.9±0.2
Pentazocine	30	4.5±0.2	7.2±0.4	7.9±0.6	9.6±0.6
***Sangu Chunnam* (SC)**	100	2.64±1.6	3.98±1.8	4.94±1.6	5.96±2.6
***Sangu Chunnam* (SC)**	200	4.3±0.8	6.7±0.4	6.9±0.2	7.7±0.6
Statistical analysis one way ANOVA followed by Dunnett t-test with n = 6 per group					

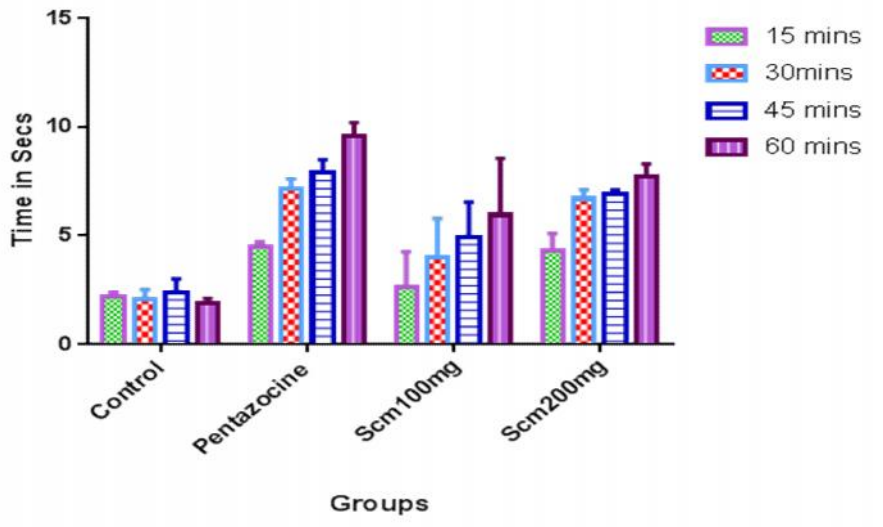


Figure 2: Latency reaction time on SC and standard drug treated animal in Eddy's Hot plate

4. Discussion

Inflammation is the first response of the immunological defense system to microbial infections, burns, allergens, mechanical injuries and other noxious stimuli [19]. Inflammation is involved in the pathogenesis of many diseases, such as diabetes, cardiovascular, neurodegenerative, cancer and other life-threatening diseases [20]. Inflammation is a complex series of cascade reactions, including enzyme activation, release of chemical mediators, effusion of fluids, cell migration, and tissue damage and repair [21]. During the inflammatory process, macrophages play a crucial role. Macrophages activated by stimuli produce inflammatory mediators such as nitric oxide (NO) and prostaglandin E_2 (PGE_2), and various cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-10 (IL-10) and tumor necrosis factor-α (TNF-α) [22,23]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the main available potent synthetic drugs in the treatment of inflammatory diseases. However, the use of NSAIDs as anti-inflammatory agents has not been successful in their clinical use because of the serious adverse side effects such as gastric lesions and reappearance of symptoms after discontinuation [24]. Therefore, there is a worldwide search for new anti-inflammatory drugs as an alternative to conventional analgesics and anti-inflammatory agents.

NSAIDs are among the most widely used drugs in the treatment of inflammatory diseases. Their main pharmacological effects come from inhibiting the enzymatic activity of COX. NSAIDs, commonly used as positive control anti-inflammatory agents, showed potent anti-inflammatory effects on xylene-induced ear and carrageenan-induced mouse paw edema model [25,26]. Unfortunately, the use of NSAIDs is limited by gastrointestinal adverse effects and about 20% of regular users of NSAIDs will develop duodenum or gastric ulcer [27,28].

Acute carrageenan-induced inflammation is characterized by distinct phases and a number of mediators are involved in the inflammatory response of carrageenan. The initial phase observed around (0-1 h) is attributed to the release of histamine, serotonin, bradykinin and substance p, whilst the delayed phase (after 1 h) is mainly sustained by the migration of polymorphonuclear (PMN) cells to the inflammatory site which produce several pro-inflammatory mediators [30,31].Result analysis of carrageenan induced paw edema reveals that treatment with SC at the dose of 100 and 200 mg/kg shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 86.68 %.

The hot plate test is commonly used to test central-mediated anti-nociceptive effects and analgesic effect. The cyclooxygenase pathway promotes inflammatory pain via conversion of AA to PGE2 by COX-2, an important inflammatory mediator [32]. In this study, SC at the dose of 100 and 200 mg/kg significantly increased latency time (during about 60 min in hot plate test), indicative of an anti-nociceptive effect. The experimental results have suggested that SC at both the dose level inhibited inflammation because of disruption of prostaglandin synthesis.

5. Conclusion

In conclusion, the results of the current study suggested that the siddha drug *Sangu Chunnam* Possessed significant anti-inflammatory activity in carrageenan-induced rat paw edema, which is comparable to indomethacin. The anti-inflammatory mechanism of SC may be related to the reduction of inflammatory cytokines that could result in percentage inhibition offered by SC towards induction of inflammation by carrageenan .Furthermore, the protective effect of SC in eddy's hot plate suggested that analgesic potential of the formulation. This current findings provide new perspectives on the therapeutic use *Sangu Chunnam* in the management of inflammatory diseases.

Acknowledgements

I wish to acknowledge my thanks to The Noble research solutions, Chennai, Tamil Nadu, India for their technical assistance in publishing this research work.

6. References

1. Ryu H.W., Lee S.U., Lee S., Song H.H., Son T.H., Kim Y.U., Yuk H.J., Ro H., Lee C.K., Hong S.T., et al. 3-methoxy-catalposide inhibited inflammatory effects in lipopolysaccharide-stimulated RAW264.7 macrophages. Cytokine. 2017;91:57–64.
2. Kim K.N., Ko Y.J., Kang M.C., Yang H.M., Roh S.W., Oda T., Jeon Y.J., Jung W.K., Heo S.J., Yoon W.J., et al. Anti-inflammatory effects of trans-1,3-diphenyl-2,3-epoxypropane-1-one mediated by suppression of inflammatory mediators in LPS-stimulated RAW 264.7 macrophages. Food Chem. Toxicol. 2013;53:371–375.
3. Flavell R.A. The relationship of inflammation and initiation of autoimmune disease: Role of TNF super family members. Curr. Top. Microbiol. Immunol. 2002;266:1–9.
4. Christodoulou C., Choy E.H. Joint inflammation and cytokine inhibition in rheumatoid arthritis. Exp. Med. 2006;6:13–19.
5. Bousquet J., Jeffery P.K., Busse W.W., Johnson M., Vignola A.M. Asthma: From bronchoconstriction to airways inflammation and remodeling. Am. J. Respir. Crit. Care Med. 2000;161:1720–1745.
6. Danese S., Grisham M., Hodge J., Telliez J.B. JAK inhibition using tofacitinib for inflammatory bowel disease treatment: A hub for multiple inflammatory cytokines. Am. J. Physiol. Gastrointest. Liver Physiol. 2016;310:G155–G162.
7. Manrique-Moreno M., Heinbockel L., Suwalsky M., Garidel P., Brandenburg K. Biophysical study of the non-steroidal anti-inflammatory drugs (NSAID) ibuprofen, naproxen and diclofenac with phosphatidylserine bilayer membranes. Biochim. Biophys. Acta. 2016;1858:2123–2131.
8. Ha Y.M., Chung S.W., Kim J.M., Kim D.H., Kim J.Y., Lee E.K., Lee J., Kim Y.J., Yoo M.A., Jeong K.S., et al. Molecular activation of NF-κB, pro-inflammatory mediators, and signal pathways in γ-irradiated mice. Biotechnol. Lett. 2010;32:373–378.
9. MacMicking J., Xie Q.W., Nathan C. Nitric oxide and macrophage function. Annu. Rev. Immunol. 1997;15:323–350. doi: 10.1146/annurev.immunol.15.1.323.
10. Korhonen R., Lahti A., Kankaanranta H., Moilanen E. Nitric oxide production and signaling in inflammation. Curr. Drug Targets Inflamm. Allergy. 2005;4:471–479.
11. Ha Y.M., Chung S.W., Kim J.M., Kim D.H., Kim J.Y., Lee E.K., Lee J., Kim Y.J., Yoo M.A., Jeong K.S., et al. Molecular activation of NF-κB, pro-inflammatory mediators, and signal pathways in γ-irradiated mice. Biotechnol. Lett. 2010;32:373–378.
12. Bink A., Kucharíková S., Neirinck B., Vleugels J., Van Dijck P., Cammue B. P. A., Thevissen K. The nonsteroidal antiinflammatory drug diclofenac potentiates the in vivo activity of caspofungin against Candida albicans biofilms. Journal of Infectious Diseases. 2012;206(11):1790–1797.
13. Shah A. S., Alagawadi K. R. Anti-inflammatory, analgesic and antipyretic properties of Thespesia populnea Soland ex. Correa seed extracts and its fractions in animal models. Journal of Ethnopharmacology. 2011;137(3):1504–1509.
14. Soejarto DD: Biodiversity prospecting and benefit sharing perspective from the field. J Ethnopharmacol1996;51:1–15
15. Anuboga Vaidhiya Navaneetham - part 1 (Pg.no.93) by Abdula Shahib
16. C. A. Winter, E. A. Risley, and G. W. Nuss, “Carrageenan-induced edema in the hind paw of rat as an assay for anti-inflammatory activity,” Proceedings of the Society for Experimental Biology and Medicine, vol. 111, pp. 544–547, 1962. View at Google Scholar
17. O. O. Adeyemi, S. O. Okpo, and O. O. Ogunti, “Analgesic and anti-inflammatory effects of the aqueous extract of leaves of Persea americana Mill (Lauraceae),” Fitoterapia, vol. 73, no. 5, pp. 375–380, 2002.View at Publisher • View at Google Scholar • View at Scopus
18. Eddy NB, Leimbach DJ. Synthetic analgesics: II Dithienyl butenyl and Dithienyl butylamine. J Pharmacol Exp Ther. 1953;107:38593.

19. Lawrence T., Willoughby D.A., Gilroy D.W. Anti-inflammatory lipid mediators and insights into the resolution of inflammation. Nat. Rev. Immunol. 2002;2:787–795.
20. Kuncha M., Boyapati S., Vegi G.M.N., Sistla R., Banda N., Akkinepally R.R., Prakash V.D. Anti-inflammatory potential of thienopyridines as possible alternative to NSAIDs. Eur. J. Pharmacol. 2012;678:48–54.
21. Yang J.H., Li S.C., Xie C.F., Ye H.Y., Tang H., Chen L.J., Peng A.H. Anti-inflammatory activity of ethyl acetate fraction of the seeds of *Brucea Javanica*. J. Ethnopharmacol. 2013; 147:442–446.
22. Posadas I., Terencio M.C., Guillen I., Ferrandiz M.L., Coloma J., Paya M., Alcaraz M.J. Co-regulation between cyclo-oxygenase-2 and inducible nitric oxide synthase expression in the time-course of murine inflammation. Naunyn Schmiedeberg Arch. Pharmacol. 2000;361:98–106.
23. Zhang C.X., Dai Z.R., Cai Q.X. Anti-inflammatory and anti-nociceptive activities of *Sipunculus nudus L.* extract. J. Ethnopharmacol. 2011;137:1177–1182.
24. Lin D.L., Chang H.C., Huang S.H. Characterization of allegedly musk-containing medicinal products in Taiwan. J. Forensic Sci. 2001;49:1187–1193.
25. Sadeghi H., Hajhashemi V., Minaiyan M., Movahedian A., Talebi A. Further studies on anti-inflammatory activity of maprotiline in carrageenan-induced paw edema in rat. Int. Immunopharmacol. 2013;15:505–510.
26. Liao J.C., Tsai J.C., Peng W.H., Chiu Y.J., Sung P.J., Tsuzoki M., Kuo Y.H. Anti-inflammatory activity of *N*-(3-florophenyl) ethylcaffeamide in mice. Int. J. Mol. Sci. 2013;14:15199–15211.
27. Hosseinzadeh A., Khoshdet M., Ghorbani M. Antinociceptive, anti-inflammatory effects and acute toxicity of aqueous and ethanolic extracts of *Myrtus communis* L. Aerial Parts in mice. J. Acupunct. Meridian Stud. 2011;4:242–247.
28. Wallace J.L. Nonsteroidal anti-inflammatroy drugs and gastroenteropathy: The second hundred years. Gastroenterology. 1997; 112:1000–1016.
29. Wallace J.L. Pathogenesis of NSAID-induced gastroduodenal mucosal injury. Best Pract. Res. Clin. Endocrinol. Metab. 2001;15:691–703.
30. Di Rosa M, Giroud JP, Willoughby DA. Studies on the mediators of the acute inflammatory response induced in rats in different sites by carrageenan and turpentine. J. Pathol. 1971;104:15–29.
31. Gilligan JP, Lovato SJ, Erion MD, Jeng AY. Modulation of carrageenan-induced hind paw edema by substance P. Inflammation. 1994; 18:285–292
32. Ricciotti E., FitzGerald G. A. Prostaglandins and inflammation. Arterioscler. Thromb. Vasc. Biol. 2011;31: 986–1000.

Access this Article in Online

Website: www.ijcrims.com

Subject: Siddha Medicine

Quick Response Code

How to cite this article:
V. Indumathy, A.Dhivyabharathi, N.Anbu, K.Kanakavalli. (2018). *In-Vivo* Evaluation of Analgesic and Anti-Inflammatory Potential of Siddha Drug *Sangu Chunnam* using Eddy's hotplate and Carageenan Induced Paw Oedema model in Rats. Int. J. Curr. Res. Med. Sci. 4(9): 10-17.
DOI: http://dx.doi.org/10.22192/ijcrms.2018.04.09.002