

Original Article

ANTI-INFLAMMATORY ACTIVITY OF SIDDHA POLYHERBAL FORMULATION *SEVVIYADHI CHOORANAM* ON CARRAGEENAN INDUCED PAW EDEMA IN WISTAR ALBINO RATS

SHAMSHALNIHA S.* , ANBU N.

Department of Post Graduate Maruthuvam, Government Siddha Medical College, Arumbakkam-600106, Chennai, India

*Corresponding author: Shamsalniha S.; *Email: nihaasiddha@gmail.com

Received: 12 Aug 2023, Revised and Accepted: 13 Sep 2023

ABSTRACT

Objective: The aim of the study was to explore the anti-inflammatory activity of Siddha polyherbal formulation *Sevviyadhi chooranam* in Carrageenan induced paw edema in wistar albino rats, and compared with the standard drug Indomethacin.

Methods: The Siddha polyherbal formulation *Sevviyadhi chooranam* indicated for sinusitis was prepared based on GMP (Good Clinical Practice) guidelines. Study procedure was approved by Institutional Animal Ethics Committee (IAEC). The experimental animals were measured for paw edema volume at 1, 2, 3, 4, 5 h using Plethysmometer (Model 7150 UGO Basile, Italy). Edema was expressed as mean increase in paw volume relative to control animals. And then, findings were compared with Indomethacin (Standard drug).

Results: The findings revealed that test drug *Sevviyadhi chooranam* at higher dosage 200 mg/kg (Group V) had equal effect on anti-inflammatory activity with percentage protection of 93.2% when compared with the standard drug Indomethacin at about 40 mg/kg (Group III) with percentage protection 93.2%. However, the test drug *Sevviyadhi chooranam* at a higher dosage 200 mg/kg (Group V) with a percentage protection 93.2% was highly effective when compared with lower dosage about 100 mg/kg (Group IV) with a percentage protection 27.12%. Hence, the study resulted that the Siddha polyherbal formulation *Sevviyadhi chooranam* has an optimistic anti-inflammatory activity with more therapeutic value.

Conclusion: The study concluded that the Siddha polyherbal formulation *Sevviyadhi chooranam* has a promising anti-inflammatory activity, probably due to the presence of biologically active phytochemicals. However, it is important to admit that there are some scientific evidences of the potential actions of these phytochemicals in anti-inflammatory activity.

Keywords: Siddha system, *Sevviyadhi Chooranam*, Sinusitis, Anti-inflammatory activity, Carrageenan, Wistar albino rats

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>) DOI: <https://dx.doi.org/10.22159/ijpps.2023v15i11.49131>. Journal homepage: <https://innovareacademics.in/journals/index.php/ijpps>.

INTRODUCTION

The Siddha system of medicine is the oldest traditional treatment system generated from Dravidian culture and it is flourished in the period of Indus Valley Civilization [1]. It is an ancient system that is practiced in Tamil Nadu in South India and other Tamil-speaking regions of the world. Siddha system of medicine focuses on addressing the root cause of the disease rather than treating the disease symptoms [2]. Herbal plants play an important role in preventing and treating of human diseases [3]. Herbal medicine derived from plant extracts are being increasingly utilized to treat a wide variety of clinical diseases, though little knowledge about their mode of action is available. There is a growing interest in the pharmacological evaluation of various plants used in Indian Traditional System of medicine" [4].

"Sinusitis is the inflammation of sinuses, which are air-filled cavities in the skull. It can be acute or chronic. Types of sinuses are maxillary, frontal, ethmoid and sphenoid. The maxillary sinuses are most commonly affected. Aetiology of sinusitis are both infectious and non-infectious. Infectious aetiology includes viral, bacterial and fungal. Non-infectious aetiology includes allergic rhinitis (with either mucosal or polyp obstruction), barotraumas (deep sea diving or air travel), exposure to chemical irritants [5].

Carrageenan was used to induce paw edema volume in Wistar albino rats for the study. During past decade, carrageenan has become much used experimentally mainly for its ability to induce an acute inflammation [6]. Paw edema induced by carrageenan was described by Winter *et al.* [7]. Cardinal signs of inflammation such as edema, hyperalgesia and erythema develop immediately following sub-plantar injection of carrageenan into hind paw, as a result of the action of pro-inflammatory agents such as bradykinin, histamine, prostaglandins, thromboxane, reactive oxygen etc. that can be generated at the site of the insult by infiltrating cells [8-11].

Over 50 y ago, Indomethacin emerged as an extremely potent non-steroidal anti-inflammatory drug (NSAID) during massive effort to find effective anti-inflammatory and analgesic medications [12]. It is used as a potent antipyretic, analgesic and anti-inflammatory activity that has been effectively used in the management of mild to moderate pain since the mid-1960s [13]. Hence Indomethacin was used as a standard drug of the current study.

New drug development process must continue through several stages in order to make a medicine that is safe, effective and has approved all regulatory requirements [14]. The process of developing a novel drug is time-consuming and costly. To increase the chances of successfully completing a clinical trial leading to the approval of a new drug, the choice of appropriate preclinical models is of utmost importance. Identifying a safe, potent, and efficacious drug requires thorough preclinical testing, which evaluates aspects of pharmacodynamics, pharmacokinetics and toxicology in *in vitro* and *in vivo* settings. Nevertheless, merely a small fraction of investigational new drugs tested in clinical trials after passing pre-clinical evaluation eventually led to a marketed product. Hence, there is a need for optimizing current standard preclinical approaches to better mimic the complexity of human disease mechanisms [15].

The Siddha system of medicine contains many peculiar herbal, mineral and herbo-mineral combinations for the treatment and management of sinusitis. Among that one such distinct polyherbal formulation was *Sevviyadhi Chooranam* indicated for the treatment and management of sinusitis in Siddha literature "*Anupava Vaidhya Dheva Ragasiyam-Moondram paagam*" [16]. This polyherbal combination consists of 12 herbal drugs.

The present study was focused on the pharmacological evaluation of Siddha polyherbal formulation *Sevviyadhi chooranam* for its anti-inflammatory activity on Carrageenan-induced paw edema in Wistar albino rats. Hence, the objective of the study was to explore and

validate the formulation on its capability to reduce the inflammation induced by Carrageenan in Wistar albino rats.

MATERIALS AND METHODS

Study drug

Collection and authentication of drugs

The ingredients present in the formulation were acquired from an indigenous raw drug store. These raw drugs were verified and authenticated by the Botanist, Department of Medicinal Botany, Government Siddha Medical College, Chennai (Voucher number GSMC/MB 579-590).

Composition of *Sevviyadi chooranam*

The Siddha polyherbal formulation *Sevviyadi chooranam* consists of 12 herbal drugs as per Siddha literature "*Anupava Vaidhya Dheva Ragasiyam-Moondram paagam* (Pg. no-466)" [16] are as follows

1. *Piper nigrum* (black pepper root)-250g
2. *Zingiber officinale* (Dried ginger)-250g
3. *Piper longum* (Long pepper)-250g
4. *Abies spectabilis* (East Himalayan fir)-250g
5. *Cuminum cyminum* (Cumin)-250g
6. *Phyllanthus emblica* (Indian gooseberry)-250g
7. *Plumbago indica* (Indian leadwort)-250g
8. *Cinnamomum verum* (Cinnamon)-250g
9. *Cinnamomum tamala* (Indian bark)-250g
10. *Elettaria cardamomum* (Cardamom)-250g
11. *Piper nigrum* (black pepper)-250g
12. *Bambusa arundinaceae* (bamboo salt)-250g

Purification and preparation of sample

Purification of herbal drugs

Prior to preparation, all the herbal raw drugs of *Sevviyadi chooranam* were purified as per Siddha literature "*Sikittha Rathna Deepam Ennum Vaidhya Nool*" [17] as follows

- Black pepper root (*Sevviyam*)

Purified by peeling out the outer skin and sun-dried.

- Dried ginger (*Chukku*)

A part of the dried ginger was treated and bleached with 2 parts of limestone solution (kal sunnambu) for 3 h, washed, dried and the external scale leaf was peeled off.

- Long pepper (*Thippili*)

Soaked and treated in leaf juice of *P. indica* for 24 min and sun-dried.

- East Himalayan Fir (*Thalisapathiri*)

Purified by washing and sun-dried.

- Cumin (*Seeragam*)

Soil and dust particles were removed and dried in sunlight.

- Indian gooseberry (*Nellivattal*)

Boiled in cow milk and then seeds were removed and sun dried.

- Indian leadwort (*Chithiramoolam*)

Outer bark was removed, powdered and boiled with steaming method in cow milk and dried.

- Cinnamon (*Lavangapattai*)

Unwanted dust particles were removed and dried under sunlight.

- Indian bark (*Lavangapathiri*)

Cleaned and dried under sunlight

- Cardamom (*Elakkai*)

Unwanted soil and dust were removed and sun-dried

- Black pepper (*Milagu*)

Soaked and treated with buttermilk (sour) for 3 h and dried under sunlight.

- Bamboo salt (*Moongiluppu*)

Dissolved in clear water and dried under sunlight to obtain the salt precipitate.

Sample preparation

The polyherbal Siddha formulation *Sevviyadi Chooranam* was prepared as per Siddha literature "*Anupava Vaidhya Dheva Ragasiyam-Moondram Paagam* (Pg. no 466)" [16]

- After purification, all the ingredients were grounded individually in an iron mortar by using a pestle and sieved with the sieving cloth.

- And then all the grounded ingredients were mixed together and stored in an airtight container.

Ethical approval

Before the initiation of preclinical evaluation, ethical approval for the study procedure was obtained from Institutional Animal Ethics Committee (IAEC) at Department of Pharmacy, C. L. Baid Metha college of Pharmacy, Thorapakkam, Chennai-600092. All the study procedure were performed as per the guidelines and ethical principles of ethics committee for experimentation using animals under proper care and control. (IAEC NO. 9/31/PO/Re/S/01/CPCSEA/dated 06/04/2022)

Experimental animals

Selection of experimental animals

For study the healthy, young adult Wistar albino female rats were taken. They were nulliparous, non-pregnant about 6-8 w old with weight of about 150-200 gm, the weight of the animals fell in the mean interval of +20% of mean weight. Female rats were chosen because of their sensitivity to the treatment [18]. Experimental animals were obtained from Mass biotech, Chennai.

Housing and feeding conditions of experimental animals

Animals involved in the experiment were housed in polypropylene cages, with husk bedding. The temperature maintained was about 22 °C+3 °C and relative humidity about 50-60%. In 24 h, 12 h of light cycle and 12 h of dark cycle were maintained. Conventional laboratory feeds were fed with an unlimited supply of drinking water. Prior to the administration of drugs, acclimatization was done followed by a veterinary examination of all the experimental animals. And then, all the experimental animals were kept as group caged with proper study procedure.

Preparation of experimental animals

For an experiment, the animals were randomly selected and kept in individual cages marked with picric acid for identification 7 d before to inducing inflammation. The animals were divided into 5 groups (each group contains 6 animals). They were grouped as follows

❖ Group I (Control)-received 3% of gum acacia 10 ml/kg per oral administration.

❖ Group II (Carrageenan)-received 0.1 ml of 1% w/v suspension of Carrageenan (Subcutaneous injection)

❖ Group III (Standard)-received Indomethacin 40 mg/kg per oral administration.

❖ Group IV (Low dose)-received *Sevviyadi Chooranam* 100 mg/kg per oral administration.

❖ Group V (High dose)-received *Sevviyadi Chooranam* 200 mg/kg per oral administration

Induction of paw edema volume

The study was performed at C. L. Baid Metha College of Pharmacy, Chennai. After the preparation of animals, all the drugs were administered orally and the volume of the medicaments were kept constant at 10 ml/kg body weight of the experimental animals. Thus, Group I received 3% of gum acacia orally, Group II received 0.1 ml of 1% w/v suspension of Carrageenan injected subcutaneously, Group III received the standard drug Indomethacin 40 mg/kg orally, Group IV received low dose (100 mg/kg) of test drug Sevviyadhi chooranam orally and Group V received high dose (200 mg/kg) of Sevviyadhi chooranam orally. After 1 h of dosing, 0.1 ml of 1% w/v suspension of carrageenan was injected into the sub-plantar region of the left hind paw to all the groups involved in the study. Then the paw edema volume was measured in 1, 2, 3, 4 and 5 h using a Plethysmometer (Model 7150 UGO Basile, Italy). Edema was expressed as the mean increase in paw volume relative to control animals. Anti-inflammatory activity was measured as the percentage reduction in edema level when drug was relative to control [19].

Analysis of reduction in paw edema volume

After injection of carrageenan to the subcutaneous region of left hind paw, the paw edema volume was analyzed for the experimental animals. The paw volume was measured up to the tibiotarsal articulation measured at 0, 1, 2, 3, 4, 5 h and denoted as mean+SEM. The percentage protection of test drug Sevviyadhi chooranam was calculated by formulae $(T_2 - T_1 / T_2) \times 100$, Where T1 denotes normal control and T2 denotes drug used for test.

Statistical analysis

The observations were statistically analyzed using One-way ANOVA followed by Dunnett's test. The study drug was statistically significant ($p < 0.05$) when compared with the standard drug.

RESULTS

The paw edema volume of experimental animals at different time intervals were indicated in table 1 and the percentage protection of test drug Sevviyadhi chooranam were described in table 2 and fig. 3

Table 1: Paw edema volume at different time intervals

Group	Dose	Initial paw volume						P-value
		0 h	1h	2h	3h	4h	5h	
I	Control	1.20+1.14	1.20+1.14	1.20+1.14	1.20+1.14	1.20+1.14	1.20+1.14	0.00**
II	Carrageenan	1.23+2.18	1.96+2.12	2.31+1.11	2.40+1.16	2.49+0.28	2.68+1.23	1.29
III	Indomethacin	1.33+1.14	2.25+1.26	1.89+1.14	1.54+1.25	1.34+1.23	1.27+2.12	0.03*
IV	Low dose	1.46+1.23	1.68+1.12	1.78+2.22	1.69+1.28	1.61+1.13	1.59+2.24	0.95
V	High dose	1.33+1.32	1.68+1.33	1.73+2.21	1.65+1.34	1.56+1.42	1.27+3.31	0.03*

Paw edema volume measurements denoted as Mean+SEM; n=6 rats, *p value is less than 0.05 ($p < 0.05$), **p value < 0.01; statistically analyzed through One way ANOVA test followed by Dunnett's test.

Table 2: Percentage protection of sevviyadhi chooranam

Group	Dose	Initial paw volume	Paw volume in 5 h	Difference in paw volume in ml	Percentage protection
I	Control	1.20+1.14	1.20+1.14	00	100
II	Carrageenan	1.23+2.18	2.68+1.23	1.45	-43.21
III	Indomethacin	1.33+1.14	1.27+2.12	0.06	93.21
IV	Low dose	1.46+1.23	1.59+2.24	0.13	27.12
V	High dose	1.33+1.32	1.27+3.31	0.06	93.2

Paw edema volume measurements denoted as mean+SEM; n=6 rats.

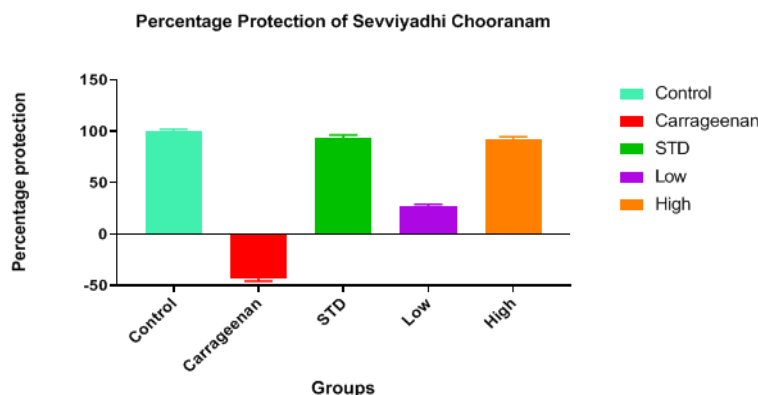


Fig. 3: Percentage protection of sevviyadhi chooranam, [N= 6 rats, Percentage protection in control = 100%, Carrageenan = -43.21%, Standard (Indomethacin) = 93.21%, Low dose (Sevviyadhi chooranam) = 27.12%, High dose (Sevviyadhi chooranam) = 93.2%]

DISCUSSION

Carrageenan-induced rat paw edema is used widely as a working model of inflammation in the search for new anti-inflammatory drug [20]. From the results obtained, the test drug at the lower dose of 100 mg/kg have mild inhibition on inflammation induced by carrageenan when compared to standard drug with percentage

protection of 27.12% at 5th h. However, at higher dose, the test drug sevviyadhi chooranam had equal effect on reducing inflammation with percentage protection of 93.2%, when compared with standard drug Indomethacin contains the percentage protection of 93.21% at 5th h. This ensured an anti-inflammatory activity of Siddha polyherbal formulation Sevviyadhi chooranam in Carrageenan induced paw edema volume in Wistar albino rats.

The development of edema in the paw of the rat after the injection of carrageenan is due to release of histamine, serotonin and prostaglandin [21]. Thus, the anti-inflammatory effect of *sevviyadi chooranam* may be due to the presence of many phytochemicals in its ingredients. Many prior studies were published regarding the anti-inflammatory activity of individual drugs in *sevviyadi chooranam*. In *P. nigrum*, piperine possesses inhibition of prostaglandin release mediated anti-inflammatory properties [22]. The small and long varieties of *Pippali* (*P. longum*) produced considerable suppression of edema formation against carrageenan-induced paw edema in rats [23]. The unique ability of *Z. officinale* to inhibit the synthesis of PGE₂ and TXB₂, and to lower serum cholesterol levels is clinically important, because its daily intake for a prolonged period will neither lead to side-effects nor to complications as normally occurs with non-steroidal anti-inflammatory drugs [24].

The copper oxide nano Particles in *Abies spectabilis* (AS-CuONPs) is effective against different stimuli induced nociception and it act as a potent anti-inflammatory agent without rendering any side effects [25]. The aqueous extracts of *C. cuminum* seeds show predominantly anti-inflammatory activity [26]. The anti-inflammatory and analgesic activities of the standardized water extract from the fruit of *P. emblica* seem to be similar to NSAIDs [27]. *P. zeylanica* extract showed significant action against carrageenan-induced rat paw edema in a dose-dependent manner [28]. The cinnamon extract from *C. verum*, its active compounds trans-cinnamaldehyde and p-cymene or combinations increase potency of central active compounds opening up novel treatment strategy for diverse inflammatory diseases [29]. *C. tamala* possesses anti-inflammatory activity and has therapeutic potential for the treatment of inflammatory diseases [30]. *E. cardamom* extracts have a therapeutic potential against periodontal infections through their anti-bacterial and anti-inflammatory properties [31]. Sarijang is a bamboo salt soy sauce which has been demonstrated to exert anti-inflammatory and anti-tumour activity [32]. The phytochemicals present in herbal drugs of *sevviyadi chooranam* individually contains anti-inflammatory property by its inhibitory effects in histamine, prostaglandin and serotonin. These scientific evidences acquired from research articles further ensured the anti-inflammatory activity of the Siddha polyherbal formulation *Sevviyadi chooranam*.

CONCLUSION

From the results and discussion, the Siddha polyherbal formulation *Sevviyadi chooranam* has potent anti-inflammatory activity without any adverse effects. This activity mainly due to the presence of phytochemicals of herbal drugs present in *Sevviyadi chooranam* which has an inhibitory action over pro-inflammatory agents such as prostaglandins, serotonin and thromboxanes. By this the current study concluded and ensured the anti-inflammatory activity of the Siddha polyherbal formulation *Sevviyadi chooranam*. Hence, it will be a promising drug of choice for the management and treatment of sinusitis and various other inflammatory diseases.

ACKNOWLEDGEMENT

This publication is a part of the MD program in Government Siddha Medical College, Arumbakkam, Chennai-106 of The Tamil Nadu Dr. MGR Medical University, Guindy, Chennai, Tamil Nadu.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Dr. S. Shamshalniha has designed, conducted the study and wrote the manuscript, Dr. N. Anbu reviewed and approved the manuscript.

CONFLICT OF INTERESTS

Authors have declared no competing interests exist.

REFERENCES

1. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and other Indian system of

medicines. *J Ethnopharmacol.* 2006;103(1):25-35. doi: 10.1016/j.jep.2005.09.024, PMID 16271286.

2. Lalitha N. Protecting traditional knowledge in Siddha system of medicine. India: NISCHAIR-CSIR; 2013.

3. Shakya AK. Medicinal plants: future source of new drugs. *Int J Herb Med.* 2016;4(4):59-64.

4. Ratheesh M, Helen A. Anti-inflammatory activity of *Ruta graveolans* linn on carrageenan induced paw edema in Wistar male rats. *Afr J Biotechnol.* May 16 2007;6(10):1209-11.

5. Kapser F. Harrison's principle of internal medicine. 20th ed; 2015. p. 209.

6. Di Rosa M. Biological properties of carrageenan. *J Pharm Pharmacol.* 2011;24(2):89-102. doi: 10.1111/j.2042-7158.1972.tb08940.x.

7. Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs. *Proc Soc Exp Biol Med.* 1962;111:544-7. doi: 10.3181/00379727-111-27849, PMID 14001233.

8. 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(1):15-29. doi: 10.1002/path.1711040103, PMID 4398139.

9. Di Rosa M, Willoughby DA. Screens for anti-inflammatory drugs. *J Pharm Pharmacol.* 1971;23(4):297-8. doi: 10.1111/j.2042-7158.1971.tb08661.x, PMID 4102520.

10. Salvemini D, Wang ZQ, Bourdon DM, Stern MK, Currie MG, Manning PT. Evidence of peroxynitrite involvement in the carrageenan-induced rat paw edema. *Eur J Pharmacol.* 1996;303(3):217-20. doi: 10.1016/0014-2999(96)00140-9, PMID 8813572.

11. Guay J, Bateman K, Gordon R, Mancini J, Riendeau D. Carrageenan-induced paw edema in rat elicits a predominant prostaglandin E2 (PGE2) response in the central nervous system associated with the induction of microsomal PGE2 synthase-1. *J Biol Chem.* 2004;279(23):24866-72. doi: 10.1074/jbc.M403106200, PMID 15044444.

12. Lucas S. The pharmacology of indomethacin. *Headache.* 2016;56(2):436-46. doi: 10.1111/head.12769, PMID 26865183.

13. Nalamachu S, Wortmann R. Role of indomethacin in acute pain and inflammation management: a review of the literature. *Postgrad Med.* 2014;126(4):92-7. doi: 10.3810/pgm.2014.07.2787, PMID 25141247.

14. Deore AB, Dhurane JR, Wagh R, Sonawane R. The stages of drug discovery and development process. *Asian J Pharm Res Dev.* 2019;7(6):62-7. doi: 10.22270/ajprd.v7i6.616.

15. Honek J. Preclinical research in drug development. *Med Writing.* 2017 Dec 1;26:5-8.

16. Seetharamanpillai. Anupava Vaidhya Dheva Ragasiyam-Moondram Paagam; 1931. p. 466.

17. Kannusampillai C. Sikittha Rathna Deepam Ennum Vaidhya Nool; 1931.

18. Lalitha P, Sripathi SK, Jayanthi P. Acute toxicity study of extracts of *Eichhornia crassipes* (Mart.). *Solms. Asian J Pharm Clin Res.* 2012;5(4):59-61.

19. Duffy JC, Dearden JC, Rostron C. Design, synthesis and biological testing of a novel series of anti-inflammatory drugs. *J Pharm Pharmacol.* 2001;53(11):1505-14. doi: 10.1211/0022357011778043, PMID 11732753.

20. Ratheesh M, Helen A. Anti-inflammatory activity of *Ruta graveolens* Linn on carrageenan-induced paw edema in Wistar male rats. *Afr J Biotechnol.* 2007 May;6(10):1209-11.

21. Vinegar R, Schreiber W, Hugo R. Biphasic development of carrageenin edema in rats. *J Pharmacol Exp Ther.* 1969;166(1):96-103. PMID 5776026.

22. Tasleem F, Azhar I, Ali SN, Perveen S, Mahmood ZA. Analgesic and anti-inflammatory activity of *P. nigrum* L. *Asian Pacific Journal of Tropical Medicine* 2014;7 Suppl 1:S461-S468.

23. Kumari M, Ashok BK, Ravishankar B, Pandya TN, Acharya R. Anti-inflammatory activity of two varieties of *Pippali* (*Piper longum* Linn.). *Ayu.* 2012 April-June;33(2):307-10. doi: 10.4103/0974-8520.105258, PMID 23559810.

24. Thomson M, Al-Qattan KK, Al-Sawan SM, Alnaqeeb MA, Khan I, Ali M. The use of ginger (*Zingiber officinale* Rosc.) as a potential

- anti-inflammatory and antithrombotic agent. Prostaglandins Leukot Essent Fatty Acids. 2002;67(6):475-8. doi: 10.1054/plef.2002.0441, PMID 12468270.
25. Liu H, Zheng S, Xiong HF, Alwahibi MS, Niu X. Biosynthesis of copperoxide nanoparticles using *Abies spectabilis* plant extract and analyzing its antinociceptive and anti-inflammatory potency in various mice models. Arab J Chem. 2020;13(9):6995-7006. doi: 10.1016/j.arabjc.2020.07.006.
 26. Bhat SP, Rizvi W, Kumar A. Effect of *Cuminum cyminum* L. seed extracts on pain and inflammation. J Nat Rem. 2014;14(2):186-92.
 27. Jaijoy K, Soonthornchareonnon N, Panthong A, Sirerawatawong S. Anti-inflammatory and analgesic activities of the water extract from the fruit of *Phyllanthus emblica* Linn. Int J Appl Res Nat Prod. 2010 Jun-July;3(2):28-35.
 28. Subramaniyan V, Paramasivam V. Potential anti-inflammatory activity of *Plumbago zeylanica*. Asian J Pharm Clin Res. 2017;10(10). doi: 10.22159/ajpcr.2017.v10i10.20357.
 29. Schink A, Naumoska K, Kitanovski Z, Kampf CJ, Frohlich Nowoisky J, Thines E. Anti-inflammatory effects of cinnamon extract and identification of active compounds influencing the TLR2 and TLR4 signaling pathways. Food Funct. 2018;9(11):5950-64. doi: 10.1039/c8fo01286e, PMID 30379176.
 30. Gambhire MN, Juvekar AR, Wankhede SS. Anti-inflammatory activity of aqueous extract of *Cinnamomum tamala* leaves by *in vivo* and *in vitro* methods. J Pharm Res. 2009;2(9):1521-4.
 31. Souissi M, Azelmat J, Chaieb K, Grenier D. Antibacterial and anti-inflammatory activities of cardamom (*Elettaria cardamomum*) extracts: potential therapeutic benefits for periodontal infections. Anaerobe. 2020;61:102089. doi: 10.1016/j.anaerobe.2019.102089, PMID 31430531.
 32. Sangeetha R, Diea YKT. The amazing bamboo: a review on its medicinal and pharmacological potential. Indian J Nutr. 2015;2(1).