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VALIDATION OF KEELVAYU NIVARANA CHOORANAM FOR ITS ACUTE AND CHRONIC ANTI INFLAMMATORY ACTIVITIES IN ANIMAL MODEL

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ABSTRACT

To validate *Keelvayu Nivarana Chooranam* (KVNC) for its acute and chronic anti inflammatory activities in animal model. Acute and Chronic anti inflammatory of KVNC were tested by Carrageenan induced rat paw oedema and Cotton pellet granuloma pouch method respectively. In acute anti inflammatory action of KVNC in doses of 100mg/kg and 200 mg/kg showed 80.13% and 81.33% inhibition of paw edema respectively. In chronic anti inflammatory action of KVNC in doses of 100mg/kg and 200 mg/kg showed 42.86%and 45.24%inhibition of paw edema respectively. From this study, *Keelvayu Nivarana Chooranam* (KVNC) revealed significant acute and chronic anti inflammatory activities. This result suggests that the study drug could be a drug of choice for treating all inflammatory conditions present in all type of arthritis.

KEYWORDS: *Anti inflammatory, Carrageenan, Keelvayu Nivarana Chooranam, Arthritis, Herbal drug.*

1. INTRODUCTION

Medicine is one of the greatest feats of mankind which brings health and happiness. It is very much important to note that the growth of medicine started based on the nature, the customs and the civilization of the respective peoples of the world.[1] The Siddha System of Medicine is one of the ancient systems in India. There are 32 types of Internal Medicines in Siddha Medicine. Among that *Chooranam* is one of the internal medicines which has been

prepared by purified raw drugs like medicinal plants. *Keelvayu Nivarana Chooranam* (KVNC) has four ingredients which include *Nannariverpattai Chooranam* (*Hemidesmus indicus*), *Parangipattai Chooranam (Smilax chinensis), Seemai Amukara Chooranam (Withania somnifera), Chittaraththai Chooranam (Alpinia officinarum)* and it's mentioned in Siddha literature for treating *Keelvatham.* (Arthritis). In Siddha, the term "Arthritis" is compared with *"Keelvayu". Keelvayu* is a disease caused due to the derangement of *Vadham* or *Vali* humour mainly.[2] Arthritis literally means joint inflammation. Although joint inflammation is a symptom or sign rather than a specific diagnosis, the term arthritis is often used to refer to any disorder that affects the joints. Arthritis affects 15% of Indian population (about 180 million people). There are several diseases where joint pain is primary, and is considered the main feature. Generally when a person has "arthritis" it means that they have one of these diseases, which include: Osteoarthritis, rheumatoid arthritis, gout and pseudo-gout, septic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and still's disease. Joint pain can also be a symptom of other diseases. These are diseases characterized by inflammation (signs include redness or heat, swelling, and symptoms such as pain)[3] Inflammation of muscles can affect people of all ages. To mitigate or reduce pain, over-the-counter (OTC) or prescription drugs such as non steroidal anti-inflammatory drugs (NSAID) or corticosteroids pain relievers are recommended by western medicine practitioners.[4] NSAIDs produces adverse effects in GIT (Peptic ulcer, bowel ulceration/ perforation, colitis, stomatitis, oseophagitis), Renal diseases (Acute renal failure, interstitial nephritis, hyponatraemia, Hyperkalaemia and anaemia.[5] The people are in need to have easily available medicines to cure many diseases with cost effective and no side effects. Siddha system of medicines dealing with various herbal plants and minerals with fewer side effects. The present study was carried out to validate the acute and chronic anti inflammatory potential of KVNC in animal model.

2. MATERIALS AND METHODS

2.1 Drug selection[6]

Keelvayu Nivarana Chooranam (KVNC) was taken as a compound drug from the literature, The Pharmacopoeia of Siddha Research Medicine. (Chapter 2-14)

2.2 Ingredients

Nannariverpattai Chooranam (Hemidesmus indicus) -116g

Parangipattai Chooranam (*Smilax chinensis*) -116 g

Seemai Amukara Chooranam (Withania somnifera) -116g

Chittaraththai Chooranam (Alpinia officinarum) -58g

2.3 Source of collection

All the raw drugs were bought from Ramasamy chetty country drug shop at Parry'scorner, Chennai, Tamilnadu, India.

2.4 Identification and Authentication of the drug

All the raw drugs were identified and authenticated by the *Gunapadam* experts in Government Siddha Medical College, Arumbakkam, Chennai – 106. The specimen sample of all the herbs have been preserved in PG *Gunapadam* department individually for future reference. RefNo: GSMC/PGGM/014-017/2014-2017

2.5 Purification of the drugs

All the drugs mentioned here were purified as per the Siddha literature.

i. *Nannariverpattai* were washed in the running tap water to remove the soil and impurities.

ii. *Parangipattai* was dried and powdered and then it was purified by *Pittaviyal* method (steam cooking in milk). A mud pot was taken and it was half filled by milk and half filled by pure water. The mouth of the pot was sealed by a cloth. This *chooranam* then placed over the cloth and the pot was heated. The same drug was later dried and powdered then sieved again.

iii. *Amukara* was dried and powdered and then it was purified by *Pittaviyal* method (steam cooking in milk). A mud pot was taken and it was half filled by milk and half filled by pure water. The mouth of the pot was sealed by a cloth. This *chooranam* then placed over the cloth and the pot was heated .The same drug was later dried and powdered then sieved again.

iv. *Chittaraththai* were washed in the running tap water to remove the soil and impurities.

2.6 Preparation of the trial drug–*Keelvayu nivarana chooranam*

2.6.1 Procedure

All the above purified ingredients were powdered in an iron mortar separately and it was sieved by a cotton cloth. Then these powders were mixed together and bottled up. It was labeled as *Keelvayu Nivarana Chooranam* (KVNC).

2.6.2 Purification of the *chooranam*: Steaming process (*Pittaviyal murai*)

The *Keelvayu Nivarana Chooranam* was purified by *pittaviyal* method (steam cooking in milk) as per Siddha classical literature. A mud pot was taken and it was half filled by milk and half filled by pure water. The mouth of the pot was sealed by a cloth. This chooranam then placed over the cloth and the pot was heated. After this process the drug was later dried and powdered then sieved again. It was used for the further study.

2.6.3 Storage of the drug

The prepared test drug was stored in a clean, air tight glass container. The contents were inspected frequently to avoid moisture and insects.

2.7 Evaluation of Acute Anti-inflammatory activity by Carrageenan induced rat paw oedema

The rats were divided into four groups containing six rats in each group.0.1smlof 1.0% carrageenan in normal saline (0.9% w/v NaCl) was injected to the sub plantar region of right hind paw. The trial drug KVNC was administered to the rats 1 h before carrageenan injection. Different groups were treated as follows:

Group I: Carrageenan (0.1 ml of 1.0% carrageenan/rat to the sub plantar region).

GroupII: Carrageenan+ Indomethacin (10 mg/kgb. w., p.o.)

Group III and IV: Carrageenan + KVNC (100 mg/kg and 200 mg/kg b. w., p.o.respectively).

The paw volume was measured initially and at 1, 2, 3 and 4 h after carrageenan injection, using Plethysmograph, inflammation was calculated for comparison.[7]

2.8 Evaluation of Chronic Anti-inflammatory activity by Cotton pellet granuloma pouch method

Chronic inflammation was induced by cotton pellet granuloma method. Rats were divided into four groups. Group I received saline solution. The reference drug indomethacin (10mg/kg) was used as a positive control (Group II). Group III and Group IVreceived oral doses of 100mg/kg and 200 mg/kg of KVNC respectively. Sterilized Cotton pellets 50 mg were implanted under light ether anesthesia in the axilla and groin region of each rat by making a small incision Drugs (KVNC 100, KVNC 200and Indomethacin) and saline (5ml/kg) for control group were administered orally to four groups of rats once daily for 7 consecutive days from the day of cotton pellet implantation. The 8th day, the animals were sacrificed and cotton pellets were removed and dried in an oven at 600C for24 hours.

They were then weighed. The granuloma formation was calculated as a measure of increment in the dry weight of the pellet. The percentage of inhibition of granuloma was calculated using the following formula. P = (1 - Wt /Wc) × 100, where, Wt – Dry weight of the cotton in test animals and Wc - Dry weight of the cotton in control animals.

3. RESULTS AND DISCUSSION

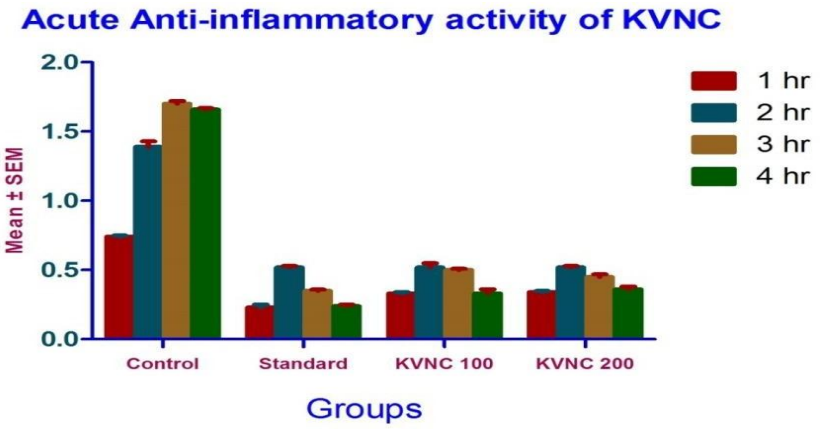
3.1 Carrageenan induced rat paw oedema

Acute anti-inflammatory activity of KVNC was observed in all groups after 1, 2, 3 and 4 h of being injected with carrageenan injection. % of inhibition was noted. Group II standard drug shows 85.55%. Group III Carrageenan +KVNC (100mg/kg) shows 80.13% Group IV Carrageenan +KVNC (200mg/kg) shows 81.33%. Group III & IV exhibited highly significant inhibition of paw oedema which is closely to Group II standard drug % of inhibition.

Table 1: Results of the acute anti-inflammatory activity of KVNC.

Groups	Treatment	1h	2h	3h	4h	% of Inhibition
Group I (Control)	Carrageenan (1%w/v)	0.74± 0.01	1.39± 0.04	1.70± 0.02	1.66± 0.01	–
Group II (Standard)	Carrageenan+ Indomethacin (10mg/kg)	0.23± 0.01	0.52± 0.01	0.35± 0.01	0.24± 0.01***	85.55%
GroupIII	Carrageenan +KVNC (100mg/kg)	0.33± 0.01	0.52± 0.01	0.50± 0.01	0.33± 0.01***	80.13%
GroupIV	Carrageenan +KVNC (200mg/kg)	0.34± 0.01	0.52± 0.01	0.45± 0.01	0.36± 0.01***	81.33%

*Values are mean ± SEM (n=6) (Dunnett'test).***p<0.001when compared to control*



Graph 1: Acute Anti-inflammatory activity of KVNC.

The carrageenan-induced hind paw oedema model in rats is known to be the acute inflammatory model sensitive to cyclooxygenase (COX) inhibitors and has been used to evaluate the effect of non steroidal anti-inflammatory agents (NSAID), which primarily inhibit the cyclooxygenase involved in prostaglandin (PG) synthesis. In case of the time course of oedema development in carrageenan induced paw edema model in rats is generally two phases are found. The first phase, which occurs between 0 to 2.5 h of injection of the phlogistic agent, has been attributed to the release of histamine or serotonin. The edema volume reaches to its maximum approximately 3 h post treatment and then begin to decline. The second phase of inflammatory reaction which is measured at 3h is caused by the release of bradykinin, protease, prostaglandin and lysosome.[8] Therefore, it can be inferred that the inhibitory effect of the extract on the carrageenan induced inflammation could be due to the inhibition of enzyme cyclooxygenase leading to inhibition of prostaglandin synthesis. Thus, the results of the present study demonstrate that the *Keelvayu Nivarana Chooranam* exhibited acute anti-inflammatory activity in the tested models which was found to be the most effective at higher concentrations employed.

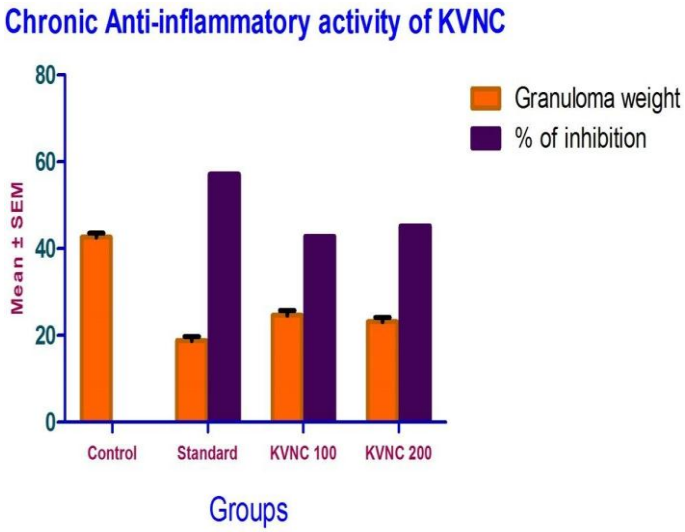
3.2 Cotton pellet granuloma pouch method

The percentage of inhibition of granuloma in Cotton pellet granuloma pouch method is shown in table. From this result it was observed that both doses of *Keelvayu Nivarana Chooranam* (KVNC100mg and KVNC200mg) significantly inhibited granuloma weight ($P<0.05$ and $P < 0.01$ respectively) when compared to the control group. The percentage of inhibition of KVNC100mg and KVNC200mg were 42.86% and 45.24% respectively which indicated the dose dependent activity of *Keelvayu Nivarana Chooranam*. KVNC 200mg exhibited percentage of inhibition more than KVNC *100 mg* and slightly less than the reference drug Indomethacin (10mg/kg) which produced 57.15% of inhibition.

Table 2: Results of the Chronic Anti-inflammatory activity of KVNC.

S. No.	Treatment	Dose(mg/kg)	Granuloma Weight (mg)%	% of Inhibition
1.	Control	5ml/kg	42.66±0.88	--
2.	Indomethacin	10mg/kg	18.83±0.94***	57.15%
3.	KVNC	100mg/kg	24.66±1.14***	42.86%
4.	KVNC	200mg/kg	23.16±1.01***	45.24%

*Values expressed in mean±SEM (Dunnett'test),***P<0.001comparedtocontrol.*



Graph 2: Chronic Anti-inflammatory activity of KVNC.

3.3 Statistical data

Statistical Data were presented as mean ± S.E.M. Statistical differences between control and treated groups were tested by one way ANOVA followed by dunnett's test.

4. CONCLUSION

The present results suggest that *Keelvayu Nivarana Chooranam* confirming its anti inflammatory activity. These results have also recommended that anti-inflammatory action may due to the phyto constituents in the drug. Further clinical studies are required to elucidate the mechanisms for treating Osteoarthritis, Rheumatoid arthritis and other inflammatory conditions.

5. REFERENCES

1. Dr. G. Ganapathy, Siddha Medicine Vol 1: History, Published by: Tamil Valarchi Kazhagam, University building, Chepauk, Chennai, 2010; 05: 25.
2. Siddha treatment for Rheumatoid Arthritis, Agasthiyar Guru Siddha Hospital, Available at: http://siddham.in/siddha-treatment-rheumatoid-arthritis
3. B M Gupta Arthritis Research in India: A Sciento metric Assessment of Publications Output during 2007-16. SF J Orthopedic Rheumatol, 2017; 1: 1.
4. Pranporn Kuropakornpong, Arunporn Itharat, Sumalee Panthong, Seewaboon Sireeratawong, and Buncha Ooraikul ; *In Vitro* and *In Vivo* Anti-Inflammatory Activities of Benjakul: A Potential Medicinal Product from Thai Traditional Medicine, Volume 2020 https://doi.org/10.1155/2020/9760948
5. Rheumatology - Medical Journal of Dr. DY Patil University S Deshpande - 0241 Parkes,

M.W., and J.T. Pickens. Conditions influencing the inhibition of analgesic drugs of the response to intraperitoneal injections of phenylbenzoquine in mice. Br. J. Pharmacol, 1965; 25: 81-87.

6. The Pharmacopoeia of Siddha Research Medicine (chapter 2-14) written by Dr. M. Shanmugavelu & Dr. G. D. Naidu. Published by: G. D. Naidu Charities, 84, President hall, Coimbatore, 18118.
7. Akaogi, J., T. Nozaki, M. Satoh and H. Yamada, Role of PGE2 and EP receptors in the pathogenesis of rheumatoid arthritis and as a novel therapeutic strategy. Endocr. Metab. Immune Disord. Drug Targets, 2006; 6: 383-394.
8. B. Moulisha, B. Kaushik, K.K. Tarun, S. Bhattacharya, K.G. Ashoke, K.H. Pallab Evaluation of analgesic and anti-inflammatory activities of *Terminalia arjuna* leaf J. Phytol., 2011; 3(1): 33-38.