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ANALGESIC AND ANTI INFLAMMATORY EFFICACY ON SIDDHA DRUG RASA CHENDOORAM

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Abstract: Rasa Chendooram (RC) is one of the herbo mineral preparations, traditionally used in Siddha medicine, which has been indicated for Vadha diseases. The use of metals and minerals particularly mercury in medicine is ancient practice in India, which is unique to Siddha system. The aim of this present study is to validate Analgesic and Anti inflammatory efficacy of RC at the doses of 50 mg/kg and 100 mg/kg of body weight in experimental animals. Analgesic activity was evaluated by Chemical induction method and Anti inflammatory activity was evaluated by Carrageenan induced paw edema in rats. Diclofenac sodium 50 mg/kg of body weight was employed as standard drug for both studies. Animals were randomized into 4 group (n=6).Control group receives vehicle only. RC treated with low and high dose which produced significant inhibition of edema and pain. This study confirms RC possesses significant Analgesic and Anti inflammatory efficacy.

Keywords: Rasa Chendooram, Siddha, vadha, Carrageenan, Diclofenac

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INTRODUCTION

Now a day the disease of locomotor system is a major problem among the people due to sedentary life style modification. The locomotor system includes the bones, joints, muscles and soft tissue structures such as tendons and ligaments. Pain and inflammation are an important defense against damage to human body. Pain has been defined as unpleasant sensory and emotional experience associated with actual or potential tissue damage [1]. Inflammation process involving the migration of WBC and release of complex mediator substances such as histamine, prostaglandin, cytokines etc. During this immune response the typical signs of inflammation such as pain, redness, swelling, heat and limited functions of the affected area may develop[2].

During inflammation treatment, the primary aim is to free from pain, swelling and improve the functions of the affected area. Drugs which are used currently for pain management and inflammatory conditions are either narcotic analgesics or NSAIDS and steroids. All the above drugs possess adverse and toxic effects such as constipation, peptic ulcer, respiratory and renal impairment. [3] Many safe, effective and challenging anti inflammatory and analgesic drugs are available in Siddha system of medicine.[4]

Rasa chendooram is a herbo mineral drug indication for vadha disease quoted in Prana Rakshamirtha Sindhu[5]. RC ingredients are Rasam, Ghandhagam and Karunthulasi. Rasam (Mercury) - Purifies blood, strengthen nerve plexuses and prevent senility and increase life span[6]. Karunthulasi (Ocimum sanctum) has potent antioxidant and anti inflammatory property [7]. The issues related to lack of scientific evidence about the efficacy and safety of herbo mineral remedies remains unresolved[8]. Preclinical toxicity studies are mandatory in determining a safety dose for human trial [9]. The present study is to validate Analgesic and Anti inflammatory efficacy of RC by Chemical induction method and Carrageenan induced paw edema respectively in rats.

MATERIAL AND METHODS

Source of Drugs

Rasam (Mercury) and Gandhagam (Sulphur) were procured from Sanjeevi pharmaceuticals Pvt.Ltd.,Chennai, traditional raw drugs dealer. Karunthulasi (Ocimum sanctum) leaves were collected from ABS Garden, Karipatti. Salem District. Materials were authenticated by Research Officer, (Pharmacognosy Department), SCRI, Chennai.

Preparation of Rasa chendooram

Purified Rasam and Gandhagam (each 35gm) were grind with karunthulasi juice in kalvam (stone mortar) then dried this material keep into bottle (Kasi Kuppi). After this procedure, Rasa chendooram prepared by Vaaluga enthiram, treat under the flame of deepakkini (mild flame-24 hour), kamalakkini (moderate flame24 hour) and kadakkini(high flame-24 hour) respectively. It is administered to animal with Amukkara chooranam (1:10 ratio)

Chemicals and Reagents and Animals

All chemicals and reagents were obtained from sigma chemicals Ltd, USA. All other reagents used in the study were of analytical grade were obtained from Qualigen fine chemicals Pvt. Ltd.

Swiss albino rats of either sex weighing 220-250grams were obtained from Animal house department, King Institute, Guindy, Chennai. Rats were housed in individually in poly propylene cages and fed with standard rodent pellet obtained and water ad libitum.The animals were subjected to a 12:12 hrs light:dark cycle under standard laboratory conditions at a temperature of 24-28ºC with a relative humidity of 60%-70%. The experimental protocol was approved by the Institutional Animal Ethical Committee (IAEC/XXXIX/07/CLBMCP/2013 dated 29.6.2013) of C.L Baid Metha Collelge of Pharmacy, ThuraiPakkam, Chennai,Tamil nadu.

Acute oral toxicity

Three female nulliparous and non-pregnant rats were used for acute oral toxicity study according to Organization for Economic Cooperation Development (OECD) guideline 423 [10]. RC was administered orally 2000 mg/kg body weight of different groups of rats and absorbed for toxicological study. The animals were observed individually after dosing the first 30 mins, periodically during the first 24h, with special attention given during the first 4h, and daily thereafter, for 14 days. Observations included changes in skin, fur, eyes, mucous membrane (nasal), autonomic (salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation), and central nervous system (drowsiness, gait, tremors, and convulsions) changes respectively. Mortality, if any, was determined over a period of 2 weeks.

Sub acute oral toxicity

In this study, the animals were divided into three groups of each 6 animals (3 males and 3 females) and treated with low (50 mg/kg of body weight) and high dose(100 mg/kg of body weight) levels to be administered for 28 days . Group 1 received 0.025% CMC in water and served as control, Groups 2 and 3 received 50mg/kg and 100 mg/kg RC (suspended in 0.025% CMC solution) body weight orally, respectively. The drug was administered daily for 28 days at

the same time and observed at least twice for morbidity and mortality. This sub-acute oral toxicity study was carried out according to OECD guideline 407[11,12].

Evaluation of Anti inflammatory activity by Carrageenan induced rat paw oedema

The acute anti inflammatory effect of RC was studied according to the method followed by Winter et al [13]. Acute inflammation was induced in all groups by injecting 0.1 ml of 1% w/v carrageenan into the sub plantar region of the right hind paw of rats. The rats were divided into four groups(n=6). Group I received Negative control - injecting 0.1 ml of 1% w/v carrageenan into the sub plantar region of the hind paw of rats. Group II received carrageenan + Low dose of test drug (50 mg/kg of body weight).Group III received carrageenan + High dose of test drug (100 mg/kg of body weight).Group IV received carrageenan + Standard Diclofenac sodium (50 mg/kg) per oral

Drug treatment &Paw volume measurement

Test drug was administered one hour prior to the carrageenan injection and paw volume was measure before and after injection of carrageenan at a fixed interval of 0,30,60,120 and 180 mins. Standard Diclofenac sodium (50 mg/kg) p.o were used as standard drug and administered as CMC suspension by oral route.

The change in hind paw volume was measured using plethysmometer and expressed as mean paw volume of the rats. The change in paw volume was measured as the difference between the final and initial paw volume. The percentage of edema inhibition was calculated with the following formula.

$$PI=100\times (Vc-Vt) / Vc$$

PI- The percentage of edema inhibition, Vc-volume of the edema in control, Vt- volume of the edema in animals treated with test drug.

Evaluation of Analgesic activity by Chemical induction method

Induction carried out by 1 % 0.03 ml of formalin injected in to the plantar region of right hind paw of each rats [14]. The licking response of formalin injected hind paw was counted in two phase. First phase 0 to 10 mins immediately after the injection of the formalin and the second phase was 15 to 30 min after injection. Reduction in the number of paw licking or biting is an indication of analgesic property. Test drug was administered one hour prior to the formalin injection Standard Diclofenac sodium (50 mg/kg) p.o were used as standard drug and administered as CMC suspension by oral route.

RESULTS AND OBSERVATION

Toxicity studies

No signs of major or significant intoxication were observed in animals from lower to higher dose groups during the dosing period of 28 days

Carrageenan induced rat paw oedema

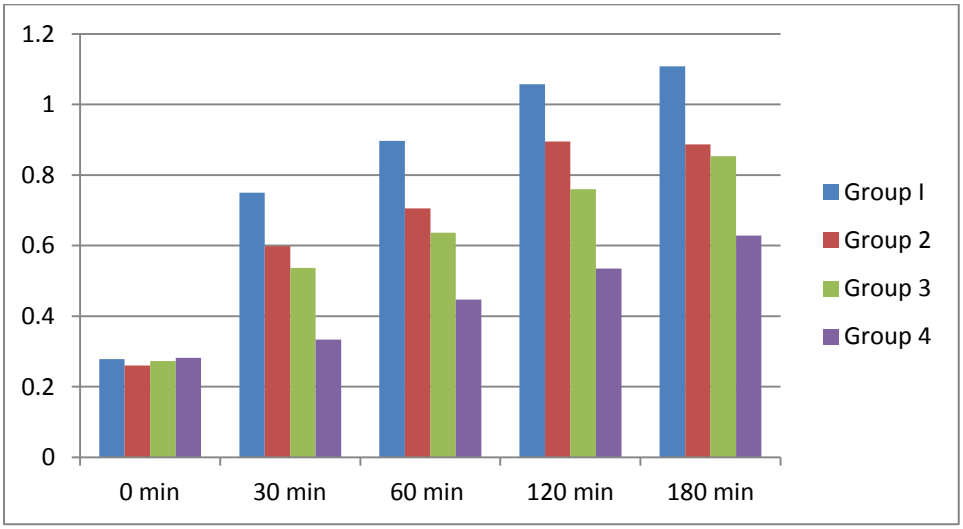
The result of effect of RC on Carrageenan induced rat paw oedema is given table 1.Change in paw volume was measured by plethysmometer as the difference between the final and initial paw volume. Percentage of edema inhibition of RC (50 mg&100mg) and standard drug were statistically calculated and compared with control.The results were showed significant(P<0.01) . Percentage of edema inhibition in 3 hours show 19.97% and 22.28% for RC 50 mg/kg and 100mg/kg respectively. Standard drug Diclofenac sodium 50 mg/kg has 43.29% of inhibition.

Table 1: Carrageenan induced rat paw oedema

Paw Volume (ml)Was Measured On Days /Mean Displacement Value (ml)					
Carrageenan	**0min**	**30min**	**60min**	**120 min**	**180 min**
Mean	0.2783	0.75	0.8967	1.057	1.108
Std.Deviation(SD)	0.01602	0.03464	0.03204	0.00816	0.01835
Std.Error of mean(SEM)	0.00654	0.01414	0.01308	0.00333	0.007491
Low Dose of test drug					
Mean	0.26	0.5983**	0.705**	0.895**	0.8867** (19.97%)
Std.Deviation(SD)	0.01673	0.03817	0.01871	0.04722	0.06121
Std.Error of mean(SEM)	0.006831	0.01558	0.007638	0.01928	0.02499
High dose of test drug					
Mean	0.2733	0.5367**	0.6367**	0.76**	0.8533**(22.28%)
Std.Deviation(SD)	0.01366	0.01633	0.02733	0.03225	0.02422
Std.Error of mean(SEM)	0.005578	0.006667	0.01116	0.01317	0.009888
Diclofenac sodium (50mg/kg)					
Mean	0.2817	0.3333**	0.4467**	0.535**	0.6283**(43.29%)
Std.Deviation(SD)	0.007528	0.02805	0.03266	0.02811	0.02041
Std.Error of mean(SEM)	0.003073	0.01145	0.01333	0.01147	0.00833

Values are expressed as mean ± S.E.M (Dunnett's test).*P<0.05,**P<0.01,***P<0.001 *vs* control; N=6

Figure I: Carrageenan induced rat paw oedema(Mean Value)



Analgesic activity by Chemical induction method

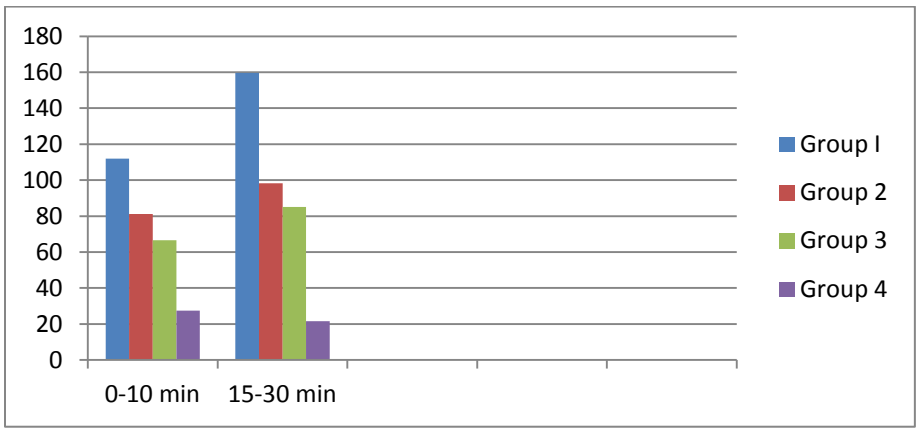
The result of effect of RC on pain induced by 1 % 0.03 ml of formalin injected in to the plantar region of paw of rats are given table 2. Reduction in the number of paw licking or biting is an indication of analgesic property.The mean values of RC (50 mg&100mg) and standard drug(50 mg/kg) compared with control at two phase (10 min,30 min after). The results were showed significant($P<0.01$).The percentage of reaction time increased with dose dependent response.

Table 2 Analgesic activity by Chemical induction method

No of Paw Licking		
Carrageenan	**0 to 10 min**	**15 to 30 min**
Mean	112	159.7
Std.Deviation (SD)	6.723	4.967
Std.Error of mean(SEM)	2.745	2.028
Low Dose of test drug		
Mean	81.17**	98.33**
Std.Deviation (SD)	4.875	4.719
Std.Error of mean(SEM)	1.99	1.926
High dose of test drug		
Mean	66.5**	85.17**
Std.Deviation (SD)	4.875	4.916
Std.Error of mean(SEM)	2.335	2.007
Diclfenac sodium (50 g/kg)		
Mean	27.5**	31.5**
Std.Deviation(SD)	5.431	3.619
Std.Error of mean(SEM)	2.217	1.478

Values are expressed as mean ± S.E.M (Dunnett's test).*P<0.05,**P<0.01,***P<0.001 *vs* control; N=6

Figure II: Analgesic activity by Chemical (Formalin) induction method (Mean Value)



Statistical Analysis

All of the data were expressed as mean ± SEM. Statistical significance between more than two groups were using one way ANOVA followed by Dunnet test. Calculations were done using GraphPad Instat -3 version software. The significance level was set at p value ≤ 0.05 for all tests.

DISCUSSION

Anti inflammatory activity

Inflammation is a complex process initiated by several factors ranging from bacterial infection and chemical injury to environmental pollution that result in cell injury or death [15]. NSAIDS generally inhibit the release of chemical mediators such as histamine, serotonin. Percentage of edema inhibition of RC (50 mg&100mg) and standard drug were statistically calculated and compared with control. Results obtained from this study show RC significantly reduce edema induced by Carrageenan. The mechanism of anti inflammatory effect of RC may be related with inhibition of prostaglandin synthesis and degranulation of mast cells.

Analgesic activity

The result of analgesic activity was evaluated by Chemical (Formalin)induction method and licking response of rats were counted in 2 phase(10 min&30 min).Values of low ,high dose of RC and Diclofenac (50 mg) treated animals compared with control group (P<0.01).RC was found to exert a significant inhibitory activity in two dose level more effect at dose level 100 mg/kg.

CONCLUSION

On the basis of study results showed RC has significant analgesic and anti inflammatory properties. Hence, RC can be useful for treatment of inflammatory condition and better alternative for NSAID drugs in future.

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