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PHARMACOLOGICAL ANALYSIS OF A SIDDHA FORMULATION KARUNCHEERAGA CHURANAM

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ABSTRACT

The holistic approach in treating dermatological problems like Eczema and allergic disorders in Siddha has earned higher confidence in common people. KARUNCHEERAGA CHURANAM (KCC), a siddha medicine is one such formulation indicated for eczema and allergic disorder. The evidence based research among these formulations will focus them in scientific arena. The aim of the study is to explore the anti-inflammatory, analgesic and anti-histamine action of the test drug KCC. Acute anti-inflammatory study was done by hind paw method in albino rats. It was tested in 2 different doses. The chronic anti-inflammatory activity was studied in albino rats by Cotton pellets implantation (granuloma) method. The analgesic study was done by the tail-flick method in albino rats. The anti-histamine effect of the test drug was done in the isolated ileum of the guinea pig. The test drug is prepared by mixing 5gm of the test drug KCC with 50ml water. The chemical analysis of the drug revealed that it has the analyzable amount of calcium and ferrous iron. Pharmacologically test drug KCC has significant anti-histamine action. It has moderate analgesic action and moderate anti-inflammatory action in both acute and chronic studies. The test drug KCC has significant efficacy of anti-allergic property and it can be used in eczema and urticaria rashes.

Keywords: Anti-histamine action, *Karuncheeraga churanam*, Pharmacological analysis, *Siddha* medicine.

INTRODUCTION

India has very long, safe and continuous usage of many herbal drugs in the officially recognized alternative systems of health viz. Ayurveda, Yoga, Unani, Siddha, and Naturopathy. These systems have rightfully existed side-by-side with Allopathy and are not in 'the domain of obscurity', as stated by Venkat Subramanian.[1] More than 70% of India's 1.1 billion populations still use these non-allopathic systems of medicine.[2] World statistics shows, increases in the prevalence of allergies, asthma, and eczema were more commonly seen among children between the ages of 6 and 7 than among children aged 13 and 14. In 2004 the World Allergy Organization's Specialty and Training Council conducted a survey of World Allergy Organization (WAO) member societies to obtain information about the status of the specialty of allergy worldwide. Responses were received from 33 countries, representing a population of 1.39 billion people, of whom it was estimated that 22% may suffer from some form of allergic disease. Allergy was reported by 23 respondents to be a certified or accredited specialty in their country, and the number of certified allergists per head of population ranged from 1:25 million to 1:16,000. Allergists were ranked as the fifth most likely clinicians to see cases of allergic asthma, third most likely to see allergic rhinitis, and fourth most likely to see eczema or sinusitis. The survey results highlight a pressing need for the development of allergy services worldwide[3].

Siddha medicine

Siddha system is an integral part of socio-cultural milieu of Tamil Nadu. The history of Siddha medicine is as old as the history of the Tamil culture and civilization[4]. Scientific documentation of traditional system of medicine is increasing and need for preparing it for Siddha formulation has become the need of the hour[5]. Scientifically validated and technologically standardized botanical products may be explored on a fast track using innovative approaches like reverse pharmacology and systems biology, which are based on traditional medicine knowledge[6]. In siddha system of medicine eczema is described as Karappan; it was treated and mended by many herbal combinations given in the ancient Siddha Literatures.

OBJECTIVE

The rationale of the study is to prove the anti-allergic property of the test drug Karuncheeraga Chooranam (KCC), which is indicated for Eczema like conditions in Siddha literature. To generate scientific evidence of its role in curing skin ailments was evaluated to meet the need of significant drug regimen for allergic conditions.

MATERIALS AND METHODS

Drug Review

The test drug KCC contains Indigofera aspalathoides (*Sivanar vembu*), Clerodendron inerme (*Sankan kuppi*), and Coldenia procumbens linn. (*Seruppadai*),Enicostemma axillare (*Vellarugu*),Smilax china (*Parangi pattai*),Acalypha fruticosa (*Chinni*),Jatropa curcas (*Kattaamanakku*),Capparis sepiaria linn. (*Chenkatthari pattai)*,Cassia senna (*Nila avaarai*),Azima tetracantha linn. (*Sankam pattai*) each 12.5 grams(30 *varagan edai*)Nigella sativa linn. (*Karuncheeragam*), Trachyspermum ammi *(Omum)* each 35 grams (*one palam*). The raw drugs were collected from authorized country shop. The drugs were cleaned and shadow dried .Then they were crushed, powdered and mixed well. Human dosage is one gram *(verukadi*), thrice in a day, with hot water. The given Indications are all types of eczema, vigorous itch, and chronic skin lesions.[7]

Physical properties

The assays for analyzing the physical properties were done as per the methods of Indian Pharmacopeia.

a. Loss on drying

Five grams of the test drug KCC was heated in a hot oven at 40° c to constant weight. The percentage of loss of weight was calculated.

b. Determination of ash Value

2-3 grams of tarred pl test drug KCC was taken in atinum or silica dish and incinerate at a temperature not exceeding 450° c until free from carbon. It was cooled and weighed. The percentage of ash was calculated with reference to the air dried drug.

c. Acid insoluble ash

The ash was mixed with 25 ml of 1:1 dilute HCL and boiled for five minutes, and then insoluble matters were collected in Gooch-crucible on an ash less filter paper, and washed with hot water. Then it was ignited, cooled in a desiccator and weighed. The percentage of acid insoluble ash with reference to the air dried drug was calculated.

d. Water soluble ash

25ml of water was added into the Gooch crucible containing the total ash, and boiled for 5 minutes. The insoluble matter was collected in a sintered glass crucible or an ash less filter paper. Then

it was washed with hot water and ignited in a crucible for 15 minutes at a temperature not exceeding 450° C. The weight of the insoluble matter was subtracted from the weight of the ash; the difference of weight represented the water soluble ash. The percentage of water soluble ash was calculated with reference to the air dried drug.

e. Alkalinity of Water soluble ash

Five grams of the test drug KCC was converted to ash then boiled with water and filtered. Filtrate was titrated against 0.1 N of HCL using phenolphthalein as an indicator.

Alkalinity of water soluble ash = X x of acid/0.1xW

X = Titer value

W = Weight of the material taken.

Alkalinity is given as ml of 0.1 N of HCL equated to 1 gm.

f. pH

Five grams of the test drug KCC is weighed and placed in clear 100ml beaker. Then 50ml of distilled water was added to it and dissolved well. After 30 minutes of time interval, the test solution was applied into pH meter at standard buffer solution of 4.0, 7.0 and 9.2.

Bio-chemical Qualitative Analysis

5 grams of the test drug KCC was weighed and taken in a 250 ml clean beaker. 50ml distilled water was added and dissolved well. It was boiled for 10 minutes and was cooled and filtered in a 100ml volumetric flask and was made up to 100ml with distilled water. This fluid was taken for analysis. The methods of the bio chemical assays are given in Table No: 1

Table 1: shows the bio-chemical Qualitative Analysis of the test drug KCC.

S. No	Experiment	Observation
01.	Test for Calcium	
	2ml of the above prepared extract was taken in a clean test tube. To this 2ml of 4% of ammonium oxalate solution was added.	A white precipitate was formed
02.	Test for Sulphate	
	2ml of the extract was added to 5% barium chloride solution.	No white precipitate was formed
03.	Test for Chloride	
	The extract was treated with silver nitrate solution.	No white precipitate was formed
04.	Test for Carbonate	
	The substance was treated with conc. Hcl.	No brisk effervescence was formed
05.	Test for starch	
	The extract was added with weak iodine solution.	No blue colour was developed
06.	Test for Ferric iron	
	The extract was treated with glacial acetic acid and potassium Ferro-cyanide.	No blue colour was developed
07.	Test for ferrous iron	
	The extract was treated with concentrated nitric acid and ammonium thio-cyanate.	Blood red colour was formed
08.	Test for phosphate	
	The extract was treated with Ammonium molybdate and concentrated Nitric acid.	No yellow precipitate was formed
09.	Test for Albumin	
	The extract was treated with Esbach's reagent	No yellow precipitate was formed
10.	Test for tannic acid	
	The extract was treated with ferric chloride.	No blue black precipitate was formed
11.	Test for Unsaturated Compound	
	Potassium permanganate solution was added to the extract.	No discoloration

Pharmacological studies

I. Acute anti-inflammatory study

Acute anti-inflammatory Study was done by Hind paw method in Albino rats.1gm of the test drug KCC was suspended in 10ml of water. From this solution 5 ml test drug was administered orally.1ml contain 100 mg of the test drug KCC. Six healthy albino rats, of 100-150gms of weight were divided into 3 groups, each consisting of 2 rats. First group was kept as control by giving distilled water of 1ml/100gm of body weight. The second group was given Ibu brufen at doses of 20 mg /100gm of body weight. The third group was given the test drug at a dose of 100 mg/100gm body weight. Before administration of test drug, the hind paw volumes of all rats were measured. This was done by dipping the hind paw (up to tibio-tarsal junction) into a mercury Plethysmograph. While dipping the hind paw, by pulling the syringe position, the level of mercury in the small tube was made to coincide with red- marking and reading was noted from the Plethysmograph. Soon after the measurement, the drugs were administered orally. One hour later a sub cutaneous injection of 0.1 ml of 1% w/v carrageenan in water was administered into the plantar surface of both hind paw of each rat. One and half an hour after injection the hind paw volume was measured once again. The difference between the initial and final volume would show the amount of inflammation taking the volume in the control group as100% of inflammation. Anti-inflammatory effect of the test group was calculated.

II. Chronic anti-inflammatory study

Chronic anti-inflammatory study was done by cotton pellets implantation (granuloma) method in albino rats. Cotton pellets each weighing 10 mg was prepared and sterilized in an auto clave for about one hour less than 15 lbs atmosphere pressure. Six albino rats weighing between 100-200 grams were selected; it was divided into 3 groups. Each rat was anaesthetized with ether and cotton pellets were implanted subcutaneously in the groin, two in each side. From the day of implantation, one group of animals received the test drug KCC at a dose of 100gm of body weight. Another group of animals were received distilled water. Last group was given ibu brufen at the dose of 20 mg/100gm body weight. On the eighth day the rats were sacrificed and the pellets were removed and weighed. Then they were put in an incubator at 60° c-80°c and then weighed. The concordant weight was noted for all groups.

III. Analgesic study

The analgesic effect was evaluated by the tail-flick method in albino rats.1 gram of the test drug KCC was dissolved in 10ml of distilled water. A dose 1ml was given to each rat. This 1ml contains 100mg of test drug. Analgesiometer or Dolorimeter, using heated nichrome wire, was used as the source of stimulus. Three groups of healthy albino rats with each group having 2 rats on both sexes were selected. Each rat was put inside a rat holder with the tail projecting out fully. The tip of the tail was kept over the nichrome wire of the analgesiometer without touching it. Now the current of 5 mA was passed through the analgesiometer to heat the nichrome wire by

switching it on, at the same time starting a stop watch. The time taken for the rat to flick the tail was noted. This is the reaction time. The reaction time was noted for each rat and the average was calculated. First group was given 2ml of distilled water and kept as control. Second group was administered with Paracetamol at a dose of 20mg/100gm of body weight orally. The test drug KCC was administered to the third group at dose of 200 mg/100mg of body weight. After a lapse of 1 hour , the reaction time of each rat was noted in each at an interval of 2 minutes (when a rat fails to flick the tail, it should not be continued beyond 8 seconds to avoid injury) and the average is calculated.

IV. Anti-Histamine study

5gms of the test drug KCC was added with 50ml of water and made into decoction of 10ml.It was used for anti-histamine studies against the 1 in 1, 00,000 strength solution of histamine. A Guinea pig weighing about 450 grams was starved for 48 hours and only water was allowed. It was killed by stunning with a sharp blow on the head and cutting its throat to bleed it, to death. The abdomen was quickly opened and the viscera inspected and loops of intestine identified using the patch as a land mark. Then the ileum was removed and placed in a shallow-dish containing warm "Tyrode solution" mixed with atropines with the help of 25 ml pipette the lumen of the ileum was gently rinsed out with saline. It was cut into segments of required length, generally 4cm, in a fully relaxed state and the sutures were made with needle and tied at either ends. The segment was suspended in an isolated organ bath. It was aerated by an oxygen tube and immersed in Tyrode solution at 37^0c. The test drug solution was given to study the inhibitory effect of histamine induced contractions.

RESULTS

A. Physical properties

The results of physical properties are given in Table no: 2.

B.Bio-chemical Qualitative Analysis

Bio-chemically the test drug KCC had the presence of calcium and ferrous iron.

I. Acute anti-inflammatory study

Tabulations of the results were recorded and given in Table no: 3. the test drug KCC has moderate anti-inflammatory action.

II. Chronic anti-inflammatory study

The concordant weight was compared and given in Table no: 4. the test drug has moderate chronic anti-inflammatory action.

III. Analgesic study

The results of control group, Standard group and the drug treated group were tabulated in Table no: 5 and compared. The test drug has moderate analgesic action.

IV. Anti-Histamine study

The test drug KCC was given to study the inhibitory effect of histamine induced contractions. The test drug has a significant anti-histamine action. It is given in Fig: 1.

A. Physical properties

S. No	Parameter	Results
01.	Loss on drying @ 105^o c	6.72
02.	Ash value	12.89
03.	Water soluble	9.80
04.	Alkalinity as CaCo3 in water soluble ash	0.05
05.	Acid insoluble ash	5.25
06.	pH at 10% aqueous solution	5.68

Table 2: Shows the results of preliminary physico-chemical analysis.

I. Acute anti-inflammatory study

S. No	Group	Dose/100mg/BW	Mean difference	% of inflammation	% of inhibition
01.	Control water	1ml	0.85	100	-
02.	Standard-ibu-brufen	20mg/1ml	0.05	6.25	93.75
03.	Test drug –KCC	100mg/1ml	0.45	56.25	43.75

Table: 3 shows the results of acute anti-inflammatory Study of the test drug KCC.

II. Chronic anti-inflammatory study

S. No	Group	Dose/100mg/BW	Concordant wt in mg	% of inflammation	% of inhibition
01.	Control water	1ml	250	100	-
02.	Standard ibu-brufen	20mg/1ml	56	22.4	77.6
03.	Test drug –KCC	100mg/1ml	143	57	43

Table: 4 shows the results of chronic anti-inflammatory Study of the test drug KCC

III. Analgesic study

S. No	Group	Drugs	Dose/100mg of BW	Initial reading in seconds	After ½ an hour	After 1 hour	After $1_{1/2}$ hour
01.	Control	Water	1ml/kg	2.5sec.	2.5sec.	2.5sec.	3sec.
02.	Standard	Paracetamol	20mg/kg	2.5sec.	4sec.	5.5sec.	6.5sec.
03.	Test drug	KCC	100mg/ml	2.5sec	3.5sec.	4sec.	4.5sec.

Table: 5 shows the results of analgesic study of the test drug KCC.

IV. Anti-Histamine study

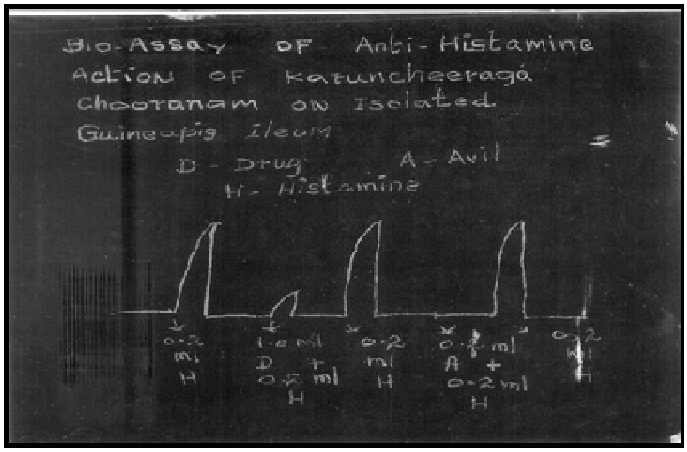

Fig. 1: shows the bio-Assay of Anti-Histamine Action of the test drug KCC

DISCUSSION

The test drug KCC indicated for the chronic skin ailments which can be substantiated by the above studies. The test drug had shown the moderate anti-inflammatory action (both acute & chronic) at 100 mg/1ml of body weight. It had the moderate analgesic action at the same dose level in laboratory animals. The test drug KCC had revealed significant anti-histamine action in the isolated ileum of the guinea pig.

CONCLUSION

The test drug Karuncheeraga Churanam can be used in the treatment of Eczema and other allergic skin diseases. Pre-clinically, it has worthy pharmacological effect on anti-allergic property. Therefore, these scientific investigations may be utilized to develop drugs from the siddha literary source for these diseases. Further research is deserved to find out the clinical efficacy of the test drug Karuncheeraga Churanam responsible for the observed biological activity.

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