Experimental Evaluation of *Karappan Chooranam* in the Management of *Pitha Karappan*

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ABSTRACT

Karappan is one of the intrinsic skin disorders described in Siddha medicine and is extensively mentioned in the Siddha pediatric textbook *Balavakadam*. *Pitha Karappan (PK)* is considered a subtype of *Karappan* and its clinical manifestations are comparable to Atopic Dermatitis described in contemporary allopathic medicine. According to Siddha literature, *PK* can be effectively managed using traditional Siddha polyherbal formulations. The present study aimed to evaluate the antihistaminic activity of the Siddha formulation *KC*, mentioned in *Sarabenthira Vaidhya Muraigal - Karappan Viranaroga Sikichai* for the management of *PK.* The study protocol was approved by the Institutional Animal Ethics Committee of S. A. Raja's College of Pharmacy. The antihistaminic activity was evaluated through an in vivo animal experiment using Swiss albino mice. The bar test method was employed to assess clonidine-induced catalepsy and determine the indirect antihistaminic activity of the formulation. The animals were randomly divided into five groups: one control group of three animals and four experimental groups of four animals each. The experimental groups were pretreated with *KC* at doses of 100, 200, and 300 mg/kg, respectively, while the standard group received chlorpheniramine maleate (10 mg/kg). Clonidine (1 mg/kg) was administered 30 minutes after treatment. The control group exhibited maximum catalepsy (169 ± 0.21 seconds) at 90 minutes following clonidine administration. Pretreatment with *KC* at low, medium, and high doses, as well as chlorpheniramine maleate (10 mg/kg), showed a statistically significant reduction in clonidine-induced catalepsy ($p<0.001$). The findings of the study suggest that *KC* possesses significant antihistaminic activity and may be beneficial in the management of *PK* (Atopic Dermatitis).

Keywords: Atopic Dermatitis, Clonidine-induced catalepsy, in vivo animal study, *Karappan*, *Karappan Chooranam*

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Introduction

Siddha Medicine is considered one of the oldest traditional medical systems in the world. Among the various treatment modalities described in *Siddha Medicine*, paediatrics occupies a special place because paediatric treatment is more challenging than in adults. Adults are able to clearly express their symptoms and clinical condition, whereas children are often unable to verbalize their discomfort. Therefore, the underlying disease condition in children is primarily determined through careful observation of their crying patterns, behaviour and actions, along with physical examination findings. In *Siddha* paediatric literature, diseases are broadly classified into two categories: those caused by intrinsic factors and those caused by extrinsic factors. One of the intrinsic skin diseases is known as *Karappan*. According to *Siddha* texts, *Karappan* is characterized by skin rashes, papules, vesicles, pustules, itching, fissures, oozing, ulceration, swelling, and hyperpigmented lesions. The *Siddha* textbook *Balavagadam* further describes *PK* as a condition characterized by headache (*Thalai Noi*), fever (*Suram*), itching (*Arippu*), erythema with burning sensation (*Udal Sivathaludan Erithal*), increased body heat (*Sudu*), vomiting (*Vaanthi*), burning micturition (*Neer Sivathal*), and constipation (*Malachikkal*). The clinical manifestations of *PK* described in *Siddha* literature are probably comparable to those of Atopic Dermatitis described in contemporary medical literature. Approximately 50% of affected children develop symptoms during the first year of life, while an additional 30% are diagnosed between 1 and 5 years of age.

Objectives of the study

The present study was undertaken to evaluate the antihistaminic activity of *KC* through an in vivo animal experiment using the bar test method for clonidine-induced catalepsy in Swiss albino mice, and to assess its dose-dependent antihistaminic effect at low (100 mg/kg), medium (200 mg/kg), and high (300 mg/kg) doses. Furthermore, the study aimed to compare the antihistaminic activity of *KC* with that of the standard drug chlorpheniramine maleate (10 mg/kg), to correlate the pharmacological findings with the traditional *Siddha* claims regarding the management of *PK*, and to provide scientific validation for the use of *KC* as a potential therapeutic agent in the management of *PK* (Atopic Dermatitis).

Materials and Methods

The present study was an experimental in vivo animal study conducted to evaluate the antihistaminic activity of *KC*, a traditional Siddha polyherbal formulation indicated for the management of *PK*. *KC* was prepared according to the formulation described in the classical Siddha text *Sarabenthira Vaithiya Muraigal*. The ingredients were authenticated, cleaned, shade-dried, powdered separately, sieved, and mixed uniformly. The prepared formulation was stored in an airtight container until use.

Preparation of the test drug

All the listed herbal ingredients (Table 1) were thoroughly dried and ground into a fine powder using a clean and dry mechanical grinder. The powder was then sieved to obtain a uniform particle size and mixed thoroughly to ensure homogeneity. The final formulation was stored in an airtight container in a cool, dry place.

Table 1*:* Ingredients of *KC*

Sidhdha Name	Botanical Name	Quantity (g)
Sukku	*Zingiber officinale Roscoe*	35
Milaku	*Piper nigrum L.*	35
Thippili	*Piper longum L.*	35
Karungeerakam	*Nigella sativa L.*	35
Suthitha-kukkil	*Vateria indica L.*	175
Vellaruku	*Enicostemma axillare (Lam.) A. Raynal*	105

Healthy Swiss albino mice of either sex weighing 25–30 g were used for the study. The animals were obtained from an approved animal house and maintained under standard laboratory conditions (temperature 24 ± 1°C, relative humidity 55–65%, and a 12-hour light/dark cycle). Animals were provided with standard pellet diet and water and libitum.

Dose fixation and treatment schedule

The therapeutic dose of *KC* as specified in the *Siddha* classical text is 500 mg, administered thrice daily for adults. The animal equivalent dose was calculated using allometric dose translation, based on an average adult body weight of 60 kg, according to the method described by Paget and Barnes (1964).

The human equivalent dose was calculated as follows:

$$\text{Human equivalent dose} = \frac{\text{Adult dose (mg/day)}}{\text{Average body weight of human (kg)}}$$

$$= \frac{500}{60}$$

$$= 8.33 \text{ mg/kg}$$

The animal equivalent dose for mice was then derived by applying the species-specific conversion factor (12.33):

Animal equivalent dose = 8.33 × 12.33 = 102.71 ≈ 100 mg/kg (low dose)
Mid dose = 100 × 2 = 200 mg/kg
High dose = 100 × 3 = 300 mg/kg

Experimental Grouping

The animals were randomly divided into five groups:

Table 2: Treatment schedule for antihistaminic activity study

Group	Treatment	Dose/Route
Group I	Normal Control	Vehicle only / Oral
Group II	Chlorpheniramine maleate (Standard)	10 mg/kg /i.p.
Group III	*KC* (Low dose)	100 mg/kg / i.p.

Group IV	*KC* (Mid dose)	200 mg/kg / i.p.
Group V	*KC* (High dose)	300 mg/kg /i.p.

The antihistaminic activity of *KC* was evaluated using the clonidine-induced catalepsy model in mice. Catalepsy was assessed by the bar test method.

The animals were pretreated with the test drug or standard drug. Thirty minutes later, clonidine hydrochloride (1 mg/kg, subcutaneously) was administered to induce catalepsy. The duration of catalepsy was measured by placing the forepaws of each mouse on a horizontal bar elevated above the surface. The time during which the animal maintained the imposed posture was recorded in seconds.

Observations were made at 30, 60, 90, 120, 150, and 180 minutes following clonidine administration.

Human equivalent dose = Adult dose (mg/day)/ Average weight of Human (60 kg)
(Paget & Barnes, 1964).

Statistical analysis

The effect of KC on clonidine-induced catalepsy in Swiss albino mice was evaluated using the bar test method, and the results are presented in Table 2. Statistical analysis was performed using one-way ANOVA followed by Dunnett's post hoc test, with $p < 0.001$ considered statistically significant.

Results

Table 3: Effect of *KC* on Clonidine-Induced Catalepsy in Swiss Albino Mice (Mean ± SEM, seconds)

Group	Time Increasing (min)					
	30	60	90	120	150	180
Control	27.02±0.02	45.05±0.01	169.50±0.01	145.01±0.01	98.20±0.07	69.05±0.05

Low dose (100mg/kg)	24.01±0.03	40.05±0.06	45.04±0.01	42.10±0.01	40.05±0.04	39.04±1.01
Mid dose (200	26.04±0.01	42.02±0.03	43.01±0.13	44.03±0.10	41.05±0.10	38.05±0.03
High Dose (300	27.04±0.04	39.02±0.01	34.01±0.10	32.01±0.02	29.01±0.02	28.07±0.05
CPM 10	28.40±0.05	31.05±0.07	33.04±0.21	31.07±0.01	29.03±0.02	26.32±0.47

Values are expressed as Mean ± SEM (n = 3 for control; n = 4 for all other groups).

**p < 0.001 vs. control group (one-way ANOVA followed by Dunnett's post hoc test).*

CPM = Chlorpheniramine maleate; KC = Karappan Chooranam.

In the control group, catalepsy progressively increased following clonidine administration (1 mg/kg, s.c.), reaching a maximum duration of 169.50 ± 0.01 seconds at 90 minutes, after which it gradually declined to 69.05 ± 0.05 seconds at 180 minutes. This confirmed the catalepsy-inducing effect of clonidine in untreated animals.

Pretreatment with KC at the low dose (100 mg/kg) resulted in a marked reduction in catalepsy duration compared to the control group, with values ranging from 24.01 ± 0.03 seconds at 30 minutes to 39.04 ± 1.01 seconds at 180 minutes. The mid dose group (200 mg/kg) demonstrated a similar pattern of inhibition, with catalepsy values ranging from 26.04 ± 0.01 seconds at 30 minutes to 38.05 ± 0.03 seconds at 180 minutes. The high dose group (300 mg/kg) exhibited the greatest reduction in catalepsy among the KC-treated groups, with values declining from 27.04 ± 0.04 seconds at 30 minutes to 28.07 ± 0.05 seconds at 180 minutes, indicating a dose-dependent antihistaminic effect.

The standard drug CPM (10 mg/kg) produced consistent suppression of clonidine-induced catalepsy throughout the observation period, with values ranging from 28.40 ± 0.05 seconds at 30 minutes to 26.32 ± 0.47 seconds at 180 minutes, which was comparable to the effect observed with KC at the high dose.

Discussion

The present study was undertaken to evaluate the antihistaminic

activity of *KC*, a traditional Siddha polyherbal formulation indicated for the management of *PK*. The antihistaminic potential of the formulation was assessed using the clonidine-induced catalepsy model in Swiss albino mice, which is a well-established experimental model for evaluating histamine-mediated responses.

The results demonstrated that *KC* significantly inhibited clonidine-induced catalepsy in a dose-dependent manner. The control group exhibited maximum catalepsy at 90 minutes following clonidine administration, whereas animals pretreated with *KC* showed a marked reduction in cataleptic duration. Among the tested doses, the high dose (300 mg/kg) produced the greatest inhibition and showed activity comparable to the standard antihistamine drug chlorpheniramine maleate. These findings indicate that *KC* possesses significant anti-histaminic activity.

The observed reduction in catalepsy may be attributed to the pharmacological properties of the ingredients present in *KC*. Clonidine-induced catalepsy is mediated through the release of histamine from mast cells and subsequent activation of histamine H1 receptors. Therefore, agents capable of inhibiting histamine release, stabilizing mast cells, or blocking histamine receptors can reduce cataleptic responses. The ingredients of *KC*, such as *Nigella sativa*, *Piper longum*, *Piper nigrum*, and *Zingiber officinale*, have been reported to possess anti-inflammatory, antiallergic, antioxidant, and immunomodulatory activities. These pharmacological actions may contribute to the inhibition of histamine-mediated responses observed in the present study.

The findings of the present study are consistent with previous experimental studies. Lakdawala et al. (1980) and Jadhav et al. (1983) reported that clonidine-induced catalepsy is mediated through histamine H1 receptors and can be effectively inhibited by antihistaminic agents. Dhanalakshmi et al. (2004) further demonstrated that plant extracts possessing antihistaminic and mast cell-stabilizing properties significantly reduce clonidine-induced catalepsy in experimental animals. Similar observations have also been reported for several herbal formulations and medicinal plant extracts with antiallergic activity, where suppression of histamine release resulted in decreased cataleptic responses.

The dose-dependent inhibition observed in the present study suggests that *KC* may exert its effects through modulation of histamine-mediated pathways. Since histamine plays a crucial role in the pathogenesis of allergic disorders, including Atopic Dermatitis, the demonstrated antihistaminic activity provides scientific support for the traditional Siddha use of *KC* in the management of *PK*.

Overall, the results of this study provide experimental evidence that *KC* possesses significant antihistaminic activity and may serve as a promising Siddha therapeutic agent for the management of allergic and inflammatory skin disorders. However, further pharmacological investigations and well-designed clinical studies are necessary to elucidate its exact mechanism of action and establish its clinical efficacy.

Conclusion

The present study demonstrated that *KC* possesses significant antihistaminic activity against clonidine-induced catalepsy in Swiss albino mice. The formulation showed dose-dependent inhibition of catalepsy, comparable to the standard drug chlorpheniramine maleate, indicating its potential role in suppressing histamine-mediated responses. Since clonidine-induced catalepsy is mediated through histamine H1 receptors, the observed activity suggests that *KC* may exert its therapeutic effect through antihistaminic and possible mast cell-stabilizing mechanisms.

These findings scientifically support the traditional Siddha claim regarding the efficacy of *KC* in the management of *PK*, which clinically resembles Atopic Dermatitis. Therefore, the study highlights the potential of this Siddha polyherbal formulation as a promising therapeutic agent for allergic and inflammatory skin disorders.

These results provide scientific evidence supporting its traditional use in *PK* (Atopic Dermatitis). However, further studies with larger sample sizes and clinical trials are necessary.

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