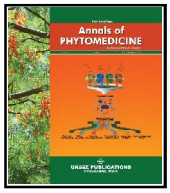
Annals of Phytomedicine 11(2): 284-289, 2022

DOI: http://dx.doi.org/10.54085/ap.2022.11.2.32

Annals of Phytomedicine: An International Journal

http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Siddha Formulation : Open Access

An antidiarrheal activity on Chukkupodi: A Siddha formulation

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Article Info

Article history

Received 5 October 2022

Revised 24 November 2022

Accepted 25 November 2022

Published Online 30 December-2022

Keywords

Siddha formulation

Chukkupodi

Antidiarrheal activity

Pediatric dysentery

Shigella dysenteriae

Abstract

Siddha system of medicine is an antediluvian system, dating back to pre-vedic period and strongly tantric and orientation, it got assorted up with the sect of nine million Siddhars. As per siddha literature, diseases were classified into 4448 types, seethakazhichal is one among them. All symptoms of seethakazhichal harmonize with the bacillary dysentery which is caused by a gram-negative bacteria, *Shigella* genus. This work has made to explore the efficient and indigenous herbal plant, *Zingiber officinale* (dry ginger-chukku) which is reported to contain antidiarrheal activity. Animals were divided into four groups; control, chukkupodi (CP) 200 mg/kg/PO, 400 mg/kg/PO (mixed with curd) and loperamide (3 mg/kg/PO) treated groups. The antidiarrheal activity was determined by charcoal meal test, castor oil induced hypermotility and castor oil induced enterpooling methods. The antidiarrheal activity of CP was confirmed by significant dose dependant reduction in peristalsis index, fecal weight and fecal moisture content compared to control. From this evident, CP used as antidiarrheal drug and also maintains the normal physiology of intestinal tissue and helps in retrieving the health of the patients.

1. Introduction

Siddha is an antediluvian system, dating back to pre-vedic period and strongly tantric and orientation, it got assorted up with the sect of nine million siddhars. Siddhars, who's defied the death, preached a philosophy of transmitting the sicken physical body possessed of impure matter (asuddhamaya) to the refined body of naturally pure matter, thereby exposé the body immutable and open from disability and limitations (Sethumathi *et al.*, 2021**)**.

As per Siddha system of medicine, *kazhicalnoi* (dysentry) was classified into many types, one among them is seethakazhichal. All symptoms of seethakazhichal harmonize with the bacillary dysentery which is caused by gram-negative bacteria, *Shigella dysenteriae*. Seethakazhichal (bacillary dysentery) is more common among children and adults with manifestations like loose, scanty stools with blood and mucus, abdominal cramp, sometimes nausea and hyperthermia. It is described in Siddha textbooks that, this disease may be acute and can lead to chronic conditions also.

Though, both adults and children are affected, it is important to prioritize the upcoming younger generation. Hence, our present work concentrates in protecting and treating children affected with bacillary dysentery and this attempt has made to explore the significant and indigenous herbal plant, *Z.officinale* (dry ginger-chukku), which is reported to contain antidiarrheal activity.

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2. Materials and Methods

2.1 Identification, confirmation and collection of raw drugs and herbomineral

The dry rhizome of *Z. officinale* (dry ginger-chukka) was identified and authenticated by Department of Medicinal Botany and Department of Gunapadam of Nandha Siddha Medical College and Hospital, Erode, Tamil Nadu.

2.2 Purification

2.2.1 Toxicity removal

250 g of dry ginger was taken and skin was removed, then it was covered by the mixture of 250 g of limestone and 100 ml of water, after that it was dried in sunlight for 3 h approximately. Finally, the dried ginger was purified by cleaning with water. An intake of skin covered ginger is harmful to our health (Thiagarajan, 2004), it affects the hepatic cells (hepatotoxin). Hence, before intake of the dry ginger, the purification process is mandatory.

2.3 Organoleptic characters

Shape: Irregular

Taste: Spicy and hot

Odour: Pungent and aromatic

Preparation of Chukkupodi formulation

The purified dry ginger of 200 g was powdered well. The powder was mixed with 70 ml of lemon juice. Then, make a small round shaped pieces like Ilandhai Kottai (Zizyphus seed) have been prepared from the mixer. The pieces were under gone into the"Pudam" process. After the Pudam, the pieces were powdered well and preserved in an air tight container (Venkatarajan, 2016).

Pudam: Pudam is one of the firing procedure using cow dung cakes. It is a process (Figure 1) of preparing medicine by burning something inside two pots hermetically closed after placing one upside down over the other.

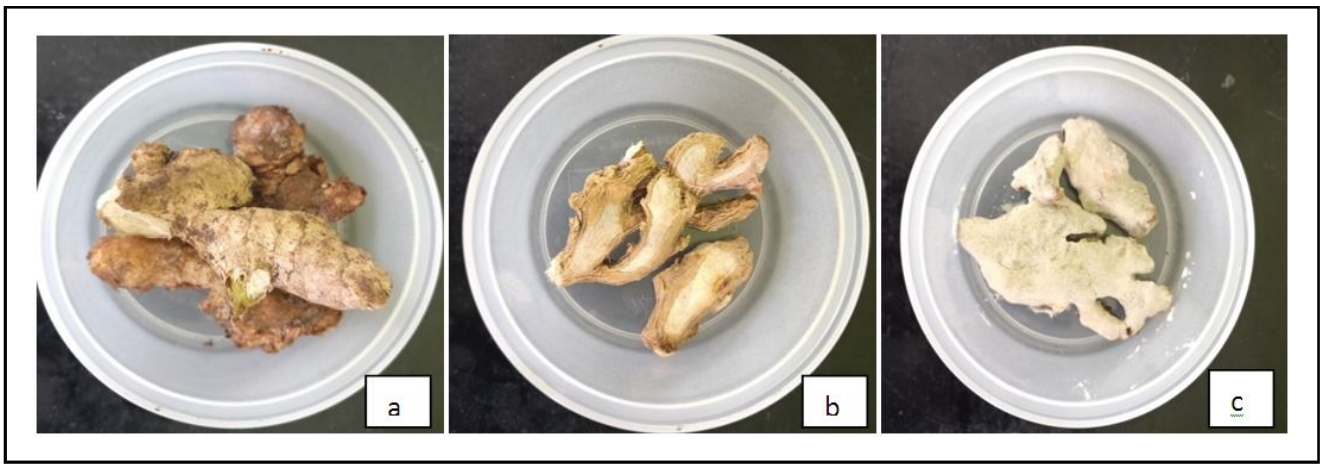

Figure 1: Fresh ginger, (a) Dried ginger, (b) and Dry ginger, (c) covered with limestone for purification.

Figure 2: Process of Pudam.

2.4 Profile of the drug

2.4.1 Dosage

100 mg to 200 mg (The dose of the medicine was adjusted according to the age and weight of the childrenand severity of the disease), 3 times a day, after food.

Adjuvant: Buffalo's curd

Indication:Seethakazhichal

2.4.2 Active ingredients in dry ginger

Volatile oil, camphene, phellandrene, cineol, citral, zingiberene, gingerol, and shogaol.

Action

Antidiarrheal, cooling, carminative, anodyne.

2.4.3 Active ingredients in lemon (added drug in chukkupodi)

Pectins, ascorbic acid, gamma-amino butyric acid, hesperedin, and naringenin,

Action: Astringent, refrigerant, appetizer, tonic, and anthelmintic.

2.4.4 Curd (adjuvant)

Curd is a product obtained after fermentation of processed or heated milk. Compared to milk, it gives a more nutritive values to humans, as lactic acid *bacillus* promotes the good bacteria in intestinal flora that are easily digestible than milk and also act as antidiarrheal agent. And so, curd is used as the adjuvant in this medicine (Raziuddin, 2014).

Composition (curd)

Water -85 to 88%

Fat -5 to 8%

Protein -3.2 to 3.4%

Lactose -4.6 to 5.2 %

Ash -0.7 to 0.72 %

Lactic acid -0.5 to 0.11%

2.5 Pharmacological analysis

2.5.1 Antidiarrheal activity

Selection of animals

For the experiment, wistar albino rats weighing around 150-300 g were selected. Disease free healthy rats were selected for this experiment. The rats were collected from the animal house of Nandha College of Pharmacy and Research Institute, Erode, Tamil Nadu, India.

Chemicals and drug

Castor oil and loperamide procured from Sigma Aldrich Chemical Pvt. Ltd. The drug chukupodi was prepared from Gunapadam, Department of Nandha Siddha Medical College and Hospital, Erode, Tamil Nadu, India.

Experimental animals

The wistar rats (150-300 g) were maintained in clean, sterile environment. Animals were housed at a temperature of 25 ± 3°C and humidity of 30-60%. Standard light and dark cycle procedure was maintained. The animals were provided with standard rodents' diet and free access to water. All the experimental procedures and protocols used in this study were reviewed by the Institutional animal ethics committee (688/2/CPCSEA), following the rules of the IAEC. As per the guidelines of the Committee for Purpose of Control and Supervision of Experiments on Animals (CPCSEA), animal care was given. After the experiment, animals were incinerated in accordance with the guidance of IAEC.

2.5.2 Acute toxicity studies

The study was done in two segments, wistar albino rats of approximate weight of 150 to 300 g were divided into 4 groups of three animals in the pattern of 3 males and 3 females each (n=6). Animals received 3 g and 6 g/kg of the chukkupodi with curd. Assessment was done over a period of two weeks, mortality and the response of the animals noted too as per OECD guidelines 423 (Taur and Patil, 2011). Behavioral changes like excitability, seizures, and fatigue were supervised at least once a day for two weeks. LD_{50} was calculated using the formula:

$$LD_{50} = C \times D$$

where,

C = the highest dose at which no death occurred.

D = the leastdoseat which death occurred.

2.5.3 Charcoal meal test gastrointestinal motility

The wistar rats weighing 150-300 g were fasted for 12 h with rat diet. Animals were divided in four groups, each group containing six animals. At first, charcoal was administered orally to these animals.

Group I: Normal control (normal saline solution and 1ml/kg charcoal meal), orally.

Group II: Standard (loperamide 3 mg/kg and 1ml/kg charcoal meal), orally.

Group III: CP with curd (200 mg/kg and 1ml/kg charcoal meal), orally.

Group IV: CP with curd (400 mg/kg and 1 ml/kg charcoal meal), orally.

One hour after treatment, each rat was given 1ml/kg of 5% charcoal suspension. After 30 min, the animals were sacrificed by cervical dislocation and were dissected. The entire length of the intestine (from the pylorus to the caecum) was removed and placed length wise on a white paper. The distance travelled by the charcoal meal and the total length of the intestine was measured. The peristaltic index was calculated. (Akindele and Adevemi, 2006).

2.5.4 Castor oil induced diarrheal activity

The induction of diarrhea with castor oil was achieved through the action of ricinoleic acid which was formed by hydrolysis of oil with exhibited certain changes in the transport of water and electrolyte and it resulted in hyper secretory responses (Lalitha *et al*., 2021).Wistar rats weighing 150-300 g were allowed to starvation for 12 h with rodents' diet. The rats were housed individually in cages and divided into 4 groups of six animals.

Group I: Normal control (normal saline solution), orally.

Group II: Standard (loperamide 3 mg/kg), orally.

Group III: CP with curd (200 mg/kg), orally.

Group IV: CP with curd (400 mg/kg), orally

After 2 h later, each rat was orally administered with 0.2 ml/rat of castor oil. The animals were then caged singly in cages lined with white blotting paper. After 3 h, total number of both dry and wet feces excreted by rats, was measured and it was compared with the control group.

2.5.5 Castor oil enterpooling

Wistar rats weighing 150-300 g were starved for 12 h with rat diet. They were lodged individually in cages and separated into 4 groups of six animals.

Group I: Normal control (normal saline solution), orally.

Group II: Standard (loperamide 3 mg/kg), orally.

Group III: CP with curd (200 mg/kg), orally.

Group IV: CP with curd (400 mg/kg), orally. After 2 h later, castor oil 0.2 ml/ rat was administered orally.

Then, after 1 h following administration of castor oil, all the rats were sacrificed by overdose of diethylether. The whole length of the intestine from pylorus to caecum was dissected out, its content was collected in measuring cylinder and volume measured (Chitme *et al.*, 2004).

3. Results

3.1 Acute toxicity study

Chukkupodi was administered orally and showed to be safe at a dose of 2000 mg/kg PO and produced no signs of toxicity. However, at 5 g/kg of CP caused slow movement of animal but did not cause any negative behavioral changes such as respiratory distress, hyperactivity, coma or seizures. No mortality was observed up to two weeks, Hence, the median LD_{50} of the chukkupodi was then >2000 mg/kg body weight. So, doses 200 and 400 mg/kg were selected for the experiment.

3.2 Effect of CP with curd on charcoal meal induced hyperperistalsis

The antidiarrheal activity of the Siddha formulation Chukkupodi was assessed by charcoal meal hyperperistalsis test. When comparing, animals given with charcoal, animals provided CP with curd (200 and 400 mg/kg), showed a significant (p<0.01) antidiarrheal activity. From two doses given, 400 mg showed the maximum antidiarrheal activity (56.82 ± 0.72) (Figure 2) than that of the standard charcoal (45.64 ± 0.76).

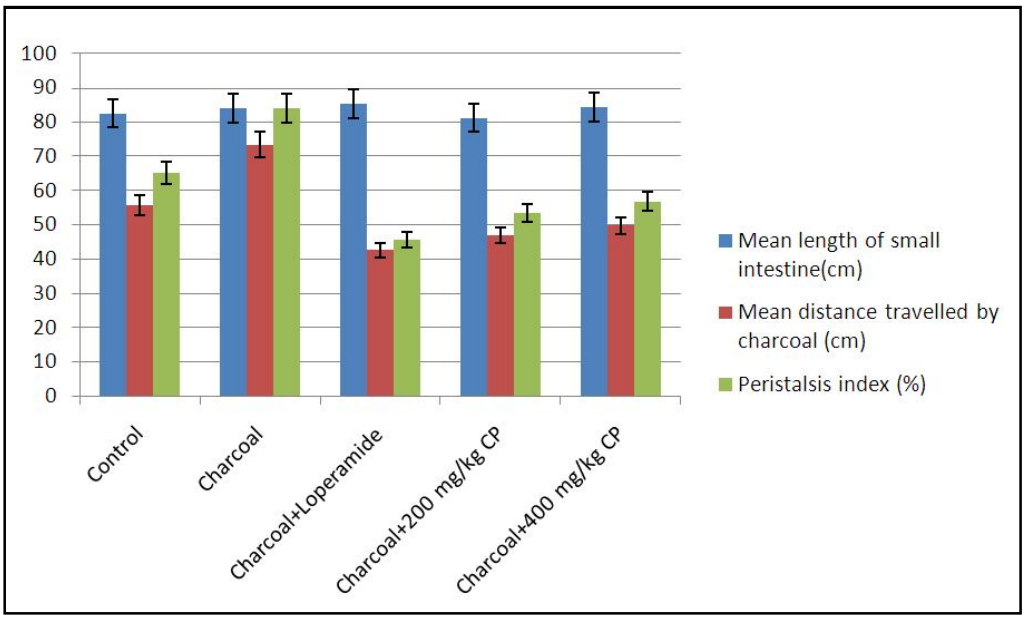

Figure 2: Effect of CP with curd on charcoal meal induced hyperperistalsis.

3.3 Effect of CP with curd on antidiarrheal effect on castor oil induced diarrhea in wistar rats

Parameter observation and analysis of results showed significant antidiarrheal effect. When compared to normal animals, some changes like increase water, feed intake and weight of fecal matter was observed in the rats treated with castor oil. The drug CP with curd shows decreases in water, feed intake, weight of fecal matter comparing the rat treated with castor oil. The maximum antidiarrheal effect with of the drug CP with curd 400 mg/kg (4.68 ± 0.04), and 200 mg/kg (5.11 ± 0.06) (Table 1) was nearer to the loperamide treated animals.

Table 1: Effect of CP with curd on antidiarrheal effect on castor oil induced diarrhea in wistar rats

Group	Water intake (ml)	Feed intake (g)	Weight of fecal matters in 3h (g)
Control	16.2 ± 0.2	15.11 ± 0.2	3.92 ± 0.04
Castor oil	20.2 ± 0.4[a]	16.38 ± 0.6[a]	5.98 ± 0.88[a]
Castor oil + Loperamide	17.8 ± 0.7[c]	14.87 ± 0.8[c]	4.21 ± 0.02[c]
Castor oil + CP 200 mg/kg	19.8 ± 0.6[c]	15.69 ± 0.5[b]	5.11 ± 0.06[b]
Castor oil + CP 400 mg/kg	19.0 ± 0.6[c]	15.48 ± 0.8[c]	4.68 ± 0.04[c]

Values mean ± SEM, n=6, [a]$p<0.01$ vs control, [b]$p<0.05$, [c]$p<0.01$ when compared to charcoal treated group.

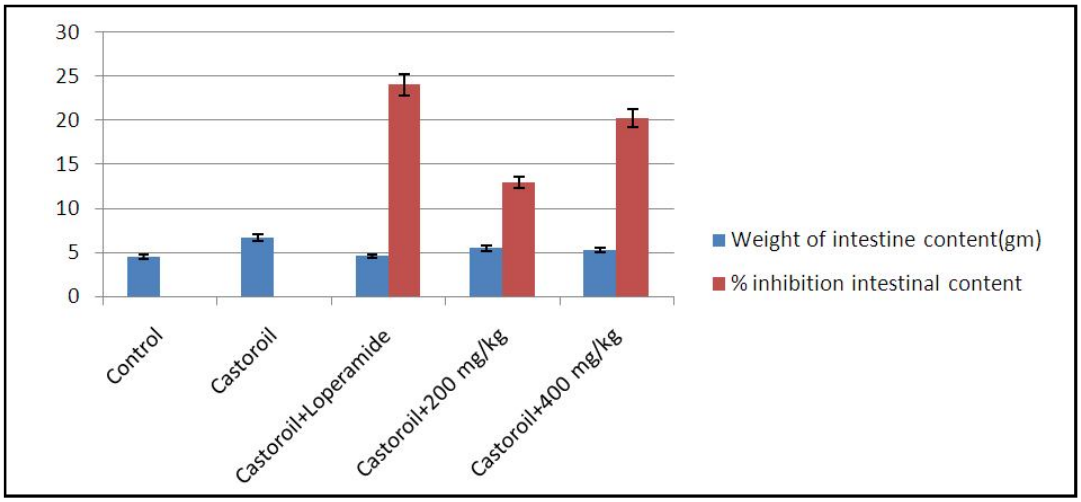

Figure 3: Effect of CP with curd on castor oil enterpooling in wistar rats.

3.4 Effect of CP with curd on castor oil enterpooling in wistar rats

The antidiarrheal activity of the CP with curd was estimated by castor oil enterpooling test. Comparing the normal rats, castor oil treated rats exhibited increased weight of intestinal contents. CP (200 and 400 mg/kg) with curd given to the rats revealed decreased intestinal contents (5.5 and 5.3) (Figure 3). The loperamide and castor oil drug administrated wistar rats' revealed significant (20.22%) inhibition rate of intestinal content. CP with curd exhibited antidiarrheal effect in dose dependant manner, the 400 mg/kg showed significant result and it was nearer to the loperamide examined wistar rats.

4. Discussion

Seethakazhichal (bacillary dysentery) in Siddha textbook Balavagadam described that, it is one type of dysentery more common in children. When seethakazhichal is compared with modern system of medicine, it is said that the causative responsible for bacillary dysentery is *Shigella* genus. This bacterium can survive the gastric acidity and also invades the colonic mucosa causing dysentery. Complications are most often seen in infection with *S. dysenteriae*. Our present study proclaim that chukkupodi contain certain biochemical substance like calcium, aminoacids, unsaturated compounds and ferrous iron (Vadivelan *et al.*, 2021). Based on previous study on phytochemicals of chukkupodi, the presence of ferrous ion in chukkupodi may help in haemoglobin synthesis in mild or acute anaemic patients, caused due to blood loss along with faces in seethakazhichal (Jain *et al.*, 1989; Zhou *et al.*, 2022).

Along with chukkupodi, lemon is one of the main ingredients in this process. Since lemon contains pectin which plays a chief role protecting the injured mucosa and also exhibit healing property (Ahangarpour *et al.*, 2011). Pectins are carbohydrate product extracted from the inner portion of citrus fruits. It acts by producing a mechanical coating in the gastrointestinal tract (Lalitha *et al.*, 2015). That contains vitamins such as vitamin B complex (thiamine, riboflavin, niacin) and protein like pectin (Kummer *et al.*, 2013). This protective layer helps to get rid of any irritations in the intestinal tract by which the spasmodic effect of the intestine can be reduced and pectin can create antispasmodic and antidiarrheal effects (Sri Bharathi *et al.*, 2021). Further, presence of various vitamins and amino acids may assist and accelerate the healing process of ulceration and inflammation in the wall of the gastrointestinal tract.

Pharmacological analysis of some articles proves that the study drug has antidiarrheal activity. Some articles evidence of selected drug shows antimicrobial, antipyretic, anti-inflammatory, antispasmodic effects and styptic activity. Hence, this drug was selected for the research work.

5. Conclusion

The study concludes antidiarrheal activity of chukupodi by using different animal models. From the outcome (antidiarrheal), it is evident that the chosen drug chukupodi has no adverse effect and this drug is herbal product, harmless to infant and children. Chukkupodi produced dose-dependent and significant (p<0.05-0.01) protection of wistar rats against castor oil and inhibited intestinal transit and delayed gastric emptying in rats when compared with standard drug loperamide. Hence, the results prove that it is adequate to use as pediatric drug to treat children with seethakazhichal. These substances not only help to get rid of pathogenic microorganisms in intestine and, also maintain the normal physiology of intestinal tissue and helps in retrieving the health of the patients. Future assessments are important to prove this drug efficacy and to work out exact principal of action involved in antidiarrheal activity of this Siddha formulation Chukkupodi.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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Citation **T. Sarojini, S. Vadivelan, K. Manjuparkavi, V. Lalitha, P. P. Sethumathi, K. Praniga, M. Menaka and T. Meena (2022). An antidiarrheal activity on Chukkupodi: A Siddha formulation. Ann. Phytomed., 11(2):284-289. http://dx.doi.org/10.54085/ap.2022.11.2.32.**