An open clinical study to evaluate the clinical efficacy of Siddha sasthric formulation

"*Pañcatīpākkiṉi cūraṇam*"

for the treatment of "*Āma kaḻiccal*"

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled "**An open clinical study to evaluate the Clinical efficacy of Siddha sasthric formulation *Pañcatīpākkiṉi cūraṇam* for the treatment of "*Āma kaḻiccal*"** is a bonafide work done by **Dr.Ar.Karthika, Government Siddha Medical College, Palayamkottai** in partial fulfilment of the university rules and regulation for the award of **M.D (Siddha), Branch-IV Kuzhanthai Maruthuvam Department** under my guidance and supervision during the academic year **2017-2019**

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **An open clinical study to evaluate the Clinical efficacy of Siddha sasthric formulation "*Pañcatīpākkiṉi cūraṇam*" for the treatment of "*Āma kaḻiccal*"** is a bonafide and genuine research work carried out by me under the guidance of **Prof.Dr.D.K.Soundararajan, M.D(S)., Head of the Department**, Post Graduate Department of **Kuzhanthai Maruthuvam,** Government Siddha Medical College, Palayamkottai has not formed the basis for the award of any Degree, Diploma, Fellowship or other similartitle.

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CONTENTS

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Note: All the ethnic Tamil words transliterated in to English letters based on transliteration ISO15919 scheme.

1 Introduction

Introduction:

Present health care in India is a highly complex framework that is composed by different medical systems of varying provenance and vintage and is heavily influenced by the colonial history and politics. Multiple medical systems such as biomedicine, Siddha, Ayurveda, Unani, Homeopathy and Yoga contribute to the health sector in India [1]. Among this, Siddha and Ayurveda were indigenous medical systems practiced in southern and northern part of Indian subcontinent respectively and Yoga is a part of both the traditions. Though Unani came from West-Asia about eight hundred years ago and biomedicine, homeopathy and naturopathy entered from Europe before two hundred years ago, over a period of time, they contested with the indigenous systems and got acculturated in the Indian culture [2]. During the twentieth century, due to the colonial and post-colonial effects, biomedicine completely dominated the other medical systems and became the main stream of medicine in India. This critical change in health sector was cleverly implemented in the colonial India by introduction of various medical policies based on Macaulay's minute on education. At present, medical systems other than biomedicine (including the indigenous medical systems that were the main stream of medicine for centuries) were considered as complementary /alternative medical systems and is grouped under AYUSH (Ayurveda, Yoga, Unani, Siddha and Homeopathy) [3]. Moreover, they have undergone a drastic change in many aspects. Though the indigenous medical systems were previously taught only on *kuru-cīṭaṉ* basis, during twentieth century, they were institutionalized similar to the western biomedicine in-order to be in compliance with the government policies [4]. This forceful adaptation of the policies of western biomedicine created a negative effect on the survival and growth of traditional Indian medicines.

Traditional Indian systems in general and Siddha in particular did not view the body as replaceable compared to enduring soul inside, rather it sort to preserve the material body which is the substratum for the soul. In the Siddha view, the body is

more than an organ system and disease cannot be accounted for organs alone[5]. It believes that the body is divided into different substrata and the healthiness of the substrata depends on the factors that nourish them. Gross body (*stūla uṭal*) is nourished by gross substances like food and water whereas subtle body (cūkkuma uṭal) is nourished by subtle substances like *pirāṉaṉ* thoughts and intellect [6]. These concepts are completely contrary to the biomedicine, which is laboratory centric and the diseases are gauged in terms of parameters that are measurable and can be demonstrated experimentally. The anatomical classification of body by western system does not go beyond the facts that can be observed in a cadaver. But the Indian traditional medicine system deals only with a living body because one can never study the flow of *pirāṉaṉ* or the thoughts in a dead body. Such a detailed knowledge can be obtained only after million years of usage and experience. The above discussions clearly highlight the epistemological and pedagogical difference between the contemporary biomedicine and Indian traditional medicine which contributes to the major challenge in the growth of Siddha.

Practically, it will be very difficult task for a Siddha physician to convince a patient by using a Siddha disease terminology, as most of the present Indian population is only aware of the disease terminologies of biomedicine and expect a Siddha physician to address the disease with the same. As Siddha classification of diseases are completely different from those of the biomedical classification, it is almost impossible to make one to one correlations or pick up equivalent terms. However, these intuitivemind-sets of the population have grown due to the inherent belief in the “superiority” of biomedicine and this has forced the Siddha practitioners to adopt both biomedical and Siddha disease terminologies in daily practice. Though this is not a healthy sign, Siddha practitioners have to accept and adopt few of the concepts followed by western biomedicine without losing the real essence of Siddha system in order to address the apprehensions among the public in consuming a Siddha drug. Hence in this work, an attempt was made to understand the effect of a traditional Siddha drug *Pañcatīpākkiṉi cūraṇam* (PDC), in treating the disease *Āma kaḻiccal*

(AK) based on Siddha system of disease classification by employing various voguish techniques of western biomedicine

1-A Aims and Objectives

Aim:

This study aims to clinically evaluate the effect of *Pañcatīpākkiṉi cūraṇam* (PDC) in children affected by *Āma kaḻiccal* (AK). In order to attain these following primary objectives were framed

Primary objectives:

- Preparation and characterization of PDC
- Establish the safety and efficacy of PDC in animal models.
- Understand the effect of PDC in management of AK in young children

In order to achieve these primary objectives, following secondary objectives were framed.

Secondary objectives:

- Identification, collection and authentication of raw materials of PDC
- Purification of raw materials and preparation of PDC
- Characterisation of PDC as per PLIM guidelines
- To evaluate the acute oral toxic effect of PDC in rat models as per OECD guidelines.
- To evaluate the 28-days repeated oral toxic effect of PDC in rat models as per OECD guidelines.
- To evaluate the effect of PDC in modifying the intestinal transit time in rat models.
- To evaluate the anti-diarrhoeal effect of PDC in rat models.
- Clinical evaluation of characters of AK through Siddha and biomedical parameters.
- Clinical evaluation of effect of PDC in management of AK through Siddha and biomedical parameters.

2 Review of literature

Review of Siddha literature:

'*Kaḻiccal'* refers to any undue looseness of the bowls, commonly caused due to eating of unsuitable food, vapid or tasteless cold rice, sudden changes in weather, chillness or from sudden fear, excitement etc[7]. Whereas *'athisaaram' and 'Kirāṇi'* refers to chronic (caused by aggravation of wind or all toads) and acute diarrhoea (marked by serous stools) respectively. Different types of classification of *kaḻiccal* are given in table. 2.1. Siddha maruthuvam, a siddha text followed by institution based Siddha scholars classifies kaḻiccal into 3 types: *PeruṅkaḻIccal, NiṇakkaḻIccal, Kaṭuppuk kaḻiccal*. *Peruṅ kaḻiccal and Niṇak kaḻiccal*. In turn are further subclassified based on *mukkuṟṟam* into four and twelve types respectively.

General classification of '*Kaḻiccal'* in Siddha:

Siddha texts describe diarrhoea by different terms such as *'kaḻiccal', 'athisaaram' and 'Kirāṇi'*.

Table 2.1: Classification of Kaḻiccal documented in various in Siddha texts

	1.*Peruṅkaḻiccal*	2.*Niṇakkaḻiccal*	3.*Kaṭuppuk Kaḻiccal* 4.*Ūḻi*
Potu Maruttuvam	1. *Vaḷi Peruṅkaḻiccal* 2. *Aḻal Peruṅkaḻiccal* 3. *Aiyam Peruṅkaḻiccal* 4. *Mukkuṟṟam Peruṅkaḻiccal* 5. *Cūrap Peruṅkaḻiccal* 6. *Tōṭap Peruṅkaḻiccal* 7. *Payam Peruṅkaḻiccal* 8. *Tukkam Peruṅkaḻiccal* 9. *Kurutik Peruṅkaḻiccal*	1. *Vaḷi Niṇakkaḻiccal* 2. *Aḻal Niṇakkaḻiccal* 3. *Aiyam Niṇakkaḻiccal* 4. *Mukkuṟṟam Niṇakkaḻiccal* 5. *Aḻaṟkāl Niṇakkaḻiccal* 6. *Kuṭaṟkāl Niṇakkaḻiccal* 7. *Kīḻ Vāyuk Niṇakkaḻiccal* 8. *Kuṉmak Niṇakkaḻiccal* 9. *Cūl Niṇakkaḻiccal* 10. *Oṭṭu Niṇakkaḻiccal* 11. *Ericcal Niṇakkaḻiccal*	1. *Vaḷi Ūḻi* 2. *Aḻal Ūḻi* 3. *Aiyam Ūḻi*
T.V. Sambasivam Pillai Medical Dictionary	1. *Cītak Kaḻiccal* 2. *Rattak Kaḻiccal* 3. *Calak Kaḻiccal* 4. *Caṅkarak Kaḻiccal*	5. *Cōpak Kaḻiccal* 6. *Veḷḷuṭaik Kaḻiccal* 7. *Vayiṟṟuk Kaḻiccal*	

Table 2.2:General classification of Kirāṇi documented in various Siddha texts (ref)

Yūkimuṉi Vaittiya Cintāmaṇi	*Aṉupava Vaittiya Tēva Rakaciyam*	*Yūkimuṉi Vaittiya Kāviyam*	*Carapēntirar Vaittiya Muṟaikaḷ*
1. ***Vātak Kirāṇi*** 2. ***Pitta Kirāṇi*** 3. ***Cilēttuma Kirāṇi*** 4. ***Tonta Kirāṇi*** 5. ***Uṣṇavāyu Kirāṇi*** 6. ***Arttarā Kirāṇi*** 7. ***Mūlavāyu Kirāṇi*** 8. ***Kuṉma Kirāṇi*** 9. ***Karppa Kirāṇi*** 10. ***Oṭṭu Kirāṇi*** 11. ***Caṅkirakak Kirāṇi***	1. *Uṣṇavāu Kirāṇi* 2. *Antaravāyu Kirāṇi* 3. *Mūlavāyu Kirāṇi* 4. *Kuṉma Kirāṇi* 5. *Karppa Kirāṇi* 6. *Oṭṭu Kirāṇi* 7. *Caṅkira Kirāṇi*	1. *Vātam* 2. *Pittam* 3. *Kapam* 4. *Pittakapam* 5. *Irattam* 6. *Vāyuviṉāl Uṇṭākum Kirāṇi*	1. *Vātak Kirāṇi* 2. *Pitta Kirāṇi* 3. *Cilēttuma Kirāṇi* 4. *Tiritōca Kirāṇi*

Different types of classification of *Kirāṇi*is given in table. 1.3. Though *Yūkimuṉi Vaittiya Cintāmaṇi, Yūkimuṉi Vaittiya Kāviyam* and *Carapēntirar Vaittiya Muṟaikaḷ*classifies*Kirāṇi*primarily based on themukkurram, Sub-classification of *Kirāṇi*in *Aṉupava Vaittiya Tēva Rakaciyam* is completely based on cause and symptoms. Altogether a significant variation could be noted among all the four texts analysed

Table 2.3: General classification of *Aticāram* documented in various Siddha texts (ref)

Yūkimuṉi Vaittiya Cintāmaṇi	*Aṉupava Vaittiya Tēva Rakaciyam*	*Ātmaraṭcāmirtam Eṉum Vaittiya Cāracaṅkirakam*	*Carapēntirar Vaittiya Muṟaikaḷ*
1. ***Vāta Aticāram*** 2. ***Pitta Aticāram*** 3. ***Cilēttuma Aticāram*** 4. ***Tiritōca Aticāram*** 5. ***Cura Aticāram*** 6. ***Caṉṉipāta Aticāram*** 7. ***Tōṣā Aticāram***	1. *Vāta Aticāram* 2. *Pitta Aticāram* 3. *Cilēttuma Aticāram* 4. *Tiritōca Aticāram* 5. *Payam Aticāram* 6. *Tukka Aticāram* 7. *Manta Aticāram* 8. *Ratta Aticāram*	1. *Vāta Aticāram* 2. *Pitta Aticāram* 3. *Cilēttuma Aticāram* 4. *Aticāra Tōṭam* 5. *Cura Aticāram*	1. *Vāta Aticāram* 2. *Pitta Aticāram* 3. *Cilēttuma Aticāram* 4. *Tiritōca Aticāram* 5. *Payam Aticāram* 6. *Tukkam Aticāram* 7. *Rattam Aticāram*

All the four known siddha texts that describe about *Aticāram (Yūkimuṉi Vaittiya Cintāmaṇi, Aṉupava Vaittiya Tēva Rakaciyam, Ātmaraṭcāmirtam Eṉum Vaittiya Cāracaṅkirakam and Carapēntirar Vaittiya Muṟaikaḷ*) are fundamentally based on the

difference in*mukkuṟṟam*. However, *Yūkimuṉi Vaittiya Cintāmaṇi, Aṉupava Vaittiya Tēva Rakaciyam, and Carapēntirar Vaittiya Muṟaikaḷ* also give importance to signs and symptoms to few extents.

Classification of Paediatric diarrhoea in Siddha:

Different school of thoughts espoused in various paediatric Siddha texts with respect to classification of diarrhoea in children is tabulated in table. 1.5.

Table 2.4: Classification of Kaḻiccal (diarrhoea) found in various paediatric siddha texts

Kuḻantai Maruttuvam & Pararācacēkara Vaittiya Kaiyēṭu	*Matalai Noy 2*		*Kōpāla Paṇikkar Ācāṉ Pāla Vākaṭam*	*Kumpa Muṉi Pāla Vākaṭam*	*Piḷḷai Piṇi Maruttuvam*
1. *Nīrppāṭu* **2. *Nīrpaṭuvaṉ*** **3. *Ceriyāppaṭuvaṉ*** **4. *Īraṟpaṭuvaṉ*** **5. *Rattapaṭuvaṉ*** **6. *Toṅkal Kaḻiccal*** **7. *Vayiṟṟukkaṭuppu*** **8. *Vayiṟṟuḷaivu*** **9. *Vayiṟṟukkotippu*** **10. *Mūlakkotippu*** **and** **1. *Āma*** **2. *Kaṇa*** **3. *Manta***	1. *Pāl* 2. *Varaḷ* 3. *Vānti* 4. *Irai* 5. *Kaṇai* 6. *Mānta* 7. *Veppu* 8. *Porumal* 9. *Aticāra* 10. *Cuḻimāntam* 11. *Āma* 12. *Viṭā* 13. *Paccilai* 14. *Iraimāntam* 15. *Tōṭa* 16. *Kaṭuppu* 17. *Ratta* 18. *Cala*	1. *Aticāra* 2. *Āma* 3. *Ratta* 4. *Kaṇai* 5. *Cala* 6. *Cura* 7. *Tōṭa* 8. *Paccilai* 9. *Pal Muḷaikkum Pōtu Kaḻiccal* 10. *Pāl*	1. *Pāl* 2. *Piraḷi* 3. *Mānta* 4. *Retta* 5. *Kaṇai* 6. *Āmai*	1. *Aticāra* 2. *Āma* 3. *Niṇa*	
			T.V. Sambasivam Pillai Tamil dictionary	*Pāla Vākaṭam*	
			1. *Cītak* 2. *Rattak* 3. *Calak* 4. *Caṅkarak* 5. *Cōpak* 6. *Veḷḷuṭaik* 7. *Vayiṟṟuk*	1. *Āma* 2. *Kaṇa* 3. *Manta*	

Contrary to the general Siddha literatures, which describe diarrhoea based on three terms: *kaḻiccal, Kirāṇi and athisaaram*, pediatric Siddha literatures use only kaḻiccal to address diarrhoea.However, *Kōpāla Paṇikkar Ācāṉ Pāla Vākaṭam and Piḷḷai Piṇi Maruttuvam* has*Aticāram kaḻiccal* as sub-classification of kaḻiccal. Though *matalai noy*, name eighteen types of *kaḻiccal*, detail descriptions werefound only for thirteen among them. *Pāl kaḻiccal, Ratta kaḻiccal andAticāra kaḻiccal* weredescribed only in *Matalai Noy, Kumpamuṉi Pāla Vākaṭam and Kōpāla Paṇikkar Ācāṉ Pāla Vākaṭam.* One possible reason for this could be the influence of geographical location.As all these three books belongs to ancient *thiruvithangoor samasthaanam*(southernmost part of present day Tamil Nadu and Kerala), it can be plausibly concluded that these

three forms of *kaḻiccal* were predominant only in *thrivithangoor* region. Another reason could be the difference in linguistic nature of these texts (mixed use of both Malayalam and Tamil words) from rest of the availableSiddha texts. As all the classifications were not described in detail, the chances of same disease being referred by different names due to linguistic variations could not be completely ruled out. *Pāl kaḻiccal* has been described as milky flour like diarrhoeain *kōpāla paṉikkar ācāṉ pāla vākaṭam* and as a diarrhoeal disease characterised by abdominal bloating, green coloured and curdy stools, fatigue, excessive sleep, vomiting, giddiness, fever, drooping of eyelids, pale and cool limbs in *kumpamuṉi pāla vākaṭam*. No descriptions of *Pāl kaḻiccal* could be noted in *Matalai Noy*. *Kumpamuṉi pāla vākaṭam* describes *ratta kaḻiccal* as uncontrolled vomiting following breastfeeding, fatigue, abdominal pain, diarrhoea with mucus, pus or blood, aphthous ulcer, head ache, fever, excessive `thirst, dryness of tongue, tremor, joint pain, anal pain followed by rectal prolapse, loss of weight and cyanosis. Whereas, *matalai noy and kōpāla paṉikkar ācāṉ pāla vākaṭam* characterize *ratta and kaḻiccal*as bloody diarrhoea, abdominal pain, coated tongue, anal pain and bloating as major symptoms. *Kuḻantai Maruttuvam and Pararācacēkara Vaittiya Kaiyēṭu* describe *paduvan* and *kothippu* as a sub-classification of *kaḻiccal* which represents cholera (*Ūḻi*) and thodam respectively. Apart from this,*toṅkal kaḻiccal*is described only in Kuḻantai Maruttuvam and *Pararācacēkara Vaittiya Kaiyēṭu* as a pediatric disease characterised by greeny diarrhoea due to ingestion of hair or foreign particles. Diarrhoea during teething is described as a separate classification only in *Kōpāla Paṉikkar Ācāṉ Pāla Vākaṭam.*Among the various diarrhoeal classifications mentioned above, *āma kaḻiccal, kaṇakaḻiccal, manta kaḻiccal* were common amongmost of the authors. This indicates that three these types are more prevalent in majority of population during different seasons and geographical location.

Āma kaḻiccal- Overview:

The term *āma kaḻiccal* (AK) literally means diarrhoea with mucus. Though many Siddha texts consider this as a disease of all age groups, most of the paediatric Siddha texts consider this as a paediatric disease that requires immediate medical attention.

Description about AK has been documented in various Siddha classics (shown in table 4.1). *Pararācacēkaram*, a paediatric Siddha classic of Sri Lankan origin statesAK as a diarrhoeaaccompanied by mucus or blood or both with abdominal pain. These were similar to the descriptions in *Kōpāla paṉikkar ācāṉpālavākaṭam*, which dictates AKin children as a disease characterised by fever with chilled limbs, bloating and diarrhoea with blood stained stool and vomiting. Analogously, *Piḷḷaippiṇi maruttuvam*, ascertainAKas a paediatric disease associated with headache, nausea, vomiting, abdominal pain, sore anus, abdominal flare (*vayiṟu puraṭṭal*) in initial stages followed by diarrhoea and mucoid stools in later stages. It further states that after 2 to 3 times of diarrhoea, abdominal pain and sore anus gets aggravated, resulting in stools with fresh blood and mucus and defecation will be highly painful with 50-60 times per day. Quite contrary to this, *Pālavākaṭam[8]*, the textbook followed by institutional based Siddha scholars, does not include diarrhoea as major symptom and says that *AK* in infants is characterised by regurgitation of breast milk, fatigue, anaemia (*irattam cuṇṭum*), pyrexia, low pitched voice and tirednessin both limbs. *Kōṣāyi aṉupōka vaittiya piramma irakaciyam*and *Matalai nōy[9]* vouches this as both the texts describe AK as a disease in infants characterised by regurgitation of breast milk, flatulence, blood discharge, fever, low pitched voice and chillness of both limbs.Gripping pain below umbilicus, respiratory distress, mucoid stools and loss of appetite were the characters of AK described in *Taṉvantiri vaittiyam.* Rivetingly, Tamil medical dictionary by T. V. Sambasivampillai, cite AKas Tamil description of catarrhal enteritis and is characterised by loss of appetite, fever, painful urination, nausea, vomiting, pain in the rectum and abdomen, stools mingled with mucus or blood or blood or both, dry tongue, pale and anxious face straining during defecation and scanty and high coloured urine. This also states that this is caused due to specific inflammation and

ஊட்டும் பாலை எதிரெடுக்கும் உள்ளே வயிறு தானிரையும்
சூட்டால் ரெத்தமது காணும் சூளும் சுரமும் காய்ச்சலுண்டாம்
நாட்டும் கைகால் குளிர்ந்திருக்கும் நவின்றார் ஆம கழிச்சலது
மீட்டும் மருந்தால் இது தீரும் மேன்மை பாரும் பண்டிதரே

மதலை நோய் தொகுதி - 2, 2008

உண்டபா லெதிரெடுக்கும் உடல்பல முழக்கங் காட்டும்
கண்டுமே ரத்த்தஞ் சாலச் சுரமிகுந் திருக்கு மேனி
கண்டுசேர் மொழியுந் தாழ்ந்து காலொடு கையும் நீத்து
விண்டிடி லாம் மென்று வெளம்பினார் முனிவர் தானே

- பாலவாகடம், 1993

ulceration of the mucus living of the large intestine resulting in phlegmatic evacuations in which the stool is mixed with mucus.

Table 2.5: Descriptions about documented in different Siddha classics

Siddha text	Description about *āma kaḻiccal*
Pararācacēkaram	Diarrhoea with either mucus or blood or both with abdominal pain
Kumpamuṉi pālavākaṭam	Loss of weight, respiratory distress with flatulence, vomiting and diarrhoea, dry tongue, sunken and pale eyes, green coloured stools, blood and mucus stained stools, nasal dripping, chillness of both limbs, fatigue and tremors
Taṉvantiri vaittiyam	Gripping pain below umbilicus, respiratory distress, mucoid stools and loss of appetite
Kōpāla paṉikkar ācāṉ pālavākaṭam	Bloating and diarrhoea, blood stained stool with vomiting and fever with chilled limbs
Matalai nōy	Regurgitation of breast milk, flatulence, blood discharge, fever and chillness of both limbs
Kōṣāyi aṉupōka vaittiya piramma irakaciyam	Regurgitation of breast milk, flatulence, blood discharge, fever, chillness of both limbs and low pitched voice
Pālavākaṭam	Regurgitation of breast milk, fatigue, fever, tiredness in both limbs, low pitched voice and anaemia
Piḷḷaippiṇi maruttuvam	Headache, nausea, vomiting, abdominal pain, sore anus, abdominal flare (*vayiṟu puraṭṭal*) in initial stages followed by diarrhoea and mucoid stools with fresh blood in later stages.
T. V. Sampasivampillai Medical dictionary	Loss of appetite, fever, painful urination, nausea and vomiting, pain in the rectum and abdomen, stools mingled with mucus or blood or both, dry tongue, pale and anxious face, straining during defecation, scanty and high coloured urine.

It is said to be indirectly due to chill weather and moist air residence in damp places, drinking impure water, heavy food, which excites wind etc. This is corroborated by *Kōpāla paṉikkar ācāṉ pālavākaṭam* which states that AK is primarily due to inflammation of digestive organs, large intestine and small intestine. When analysing all these literatures, it could be easily noted that diarrhoea with blood or mucus or both was the most common symptom mentioned in the five out of the eight siddha texts that describe about AK. Regurgitation of milk, flatulence and fever with chillness in both the limbs was also mentioned as major symptom of AK in significant number of Siddha texts. Other symptoms include fatigue, anaemia, low pitched voice, dry tongue, sunken and pale eyes, nausea and vomiting, scanty and high coloured urine, gripping pain below umbilicus, loss of appetite, nasal dripping and respiratory

distress. However, *Taṉvantiri vaittiyam, kōṣāyi aṉupōka vaittiya piramma irakaciyam* and *Pālavākaṭam* did not include diarrhoea with blood and mucus as characteristic symptom of AK. This can be due to the fact that sometimes, probably depending on age, sex, geographical location, seasonal variation and individual genotype the symptomatic manifestation of disease may vary. Moreover, it is also understandable that AKmay show loss of appetite, flatulence, nasal dripping, respiratory distress, fever, nausea and vomiting in initial stages followed by diarrhoea, mucoid stools, and blood containing stools in later stages. Dry tongue, sunken eyes, fatigue, low voice, and chillness of legs could possibly be due to the dehydration caused by diarrhoea. As bloody mucopurulent diarrhoea accompanied by dehydration is common among various types of enteritis in children. Various factors such as infection, drugs, psychological, environmental, autoimmune disorders etc were considered to be the major culprits in most of the enteritis in children. Hence in the present study, all these criteria were taken in to consideration while recruiting the subjects.

பாவையரே கேளினி ஆமைக் கழிச்சலின் பண்புதனையே பகருவேன்
பாருமுடல் மெலியுமே யீளையோடு பொருமலும் வாந்தியோடதி சாரமும்
தாவி வயறிரையுமே பாசிபோல் பாதியும் வழியயரும் நாவு வறளும்
தக்கயிரு நயனமும் பஞ்சென வெளுக்குமே கழிச்சலும் ரெத்த சளியும்
மேவிரு மூக்கினில் நீர் வடியுமே யினி கைகால் குளிரு மின்னும்
மெல்லவினி வெள்ளையாய் மயணையது போலவே சளி வீழும் மூலமழலும்
ஆவியுட லயருமே தாவியே நடுங்குமே உச்சி கண்ணிவை குழியுமே
அறிய குறுமுனியிதை உரையிதுபடி கவி உலகோரறியவோதினேன்
- கும்பமுனி பாலவாகடம், *2008*

Review of modern literature:

Diarrhoea – Overview:

Despite the rapid advancement of various therapeutic techniques in the past three decades, diarrhoea remains as the second leading cause of death among children under five years of age worldwide[10]. It is estimated that diarrhoea accounted for 9.9% of the 6.9 million deaths among children under 5 in 2011[10]. India recorded the largest number of under-5 deaths in 2015, at 1·3 million, followed by Nigeria and Pakistan [10]. Though most of the diarrhoea in children is associated with infections, other causes such as malnutrition, indigestion, drugs, psychological disturbances and few physiological processes such as teething also contributes to diarrhoea.

Normal fluid and electrolyte movement are inextricably linked to diarrhoea. Approximately 6 to 8 litres of fluid enter the small intestine per day. Among this, only

1.5 litres are contributed from the diet; the remainder of the overall fluid load is made up of gastric, salivary, pancreatic, and biliary secretions. Approximately 5.5 to 6 litres of fluid are absorbed in small intestine and only 1.5 to 2 litres of fluid enters large intestine. But colon has the capacity to absorb 4.5 to 5 litres per day. So, almost all the fluid (1.5 to 2 litres) entering colon will be reabsorbed and less than 100 to 200 ml of fluid is excreted via stools per day. This clearly shows that the colon is a more efficient absorptive organ than the small intestine. If there is a decrease in small intestinal fluid absorption, regardless of cause, diarrhoea will not develop until the absorptive capacity of the colon is exceeded. On the other hand, relatively small decreases in colonic absorption can lead to substantial increases in stool water excretion, and diarrhoea will result. Although most discussions of diarrhoea are concerned with water excretion, it is important to bear in mind that all gastrointestinal water flow is a result of solute movement. Water absorption is secondary to solute absorption, and water secretion follows solute secretion. Therefore, information on the body's ability to absorb and secrete sodium and chloride is crucial to the understanding of cellular events in acute diarrhoea.

General mechanism of Diarrhoea:

Several mechanisms may account for these alterations in fluid movement; these include

1. Increased luminal osmolality
2. Decreased fluid absorption
3. Increased intestinal secretion
4. Altered intestinal motility

Primary lactase deficiency will always resultin increased luminal osmolality. Decrease or absence of lactase, a brush-border enzyme of the small intestine, results in indigestion of dietary lactose, leading to the formation of a variety of short-chain fatty acids, carbon dioxide, and hydrogen. The resulting increase in luminal osmolality causes altered fluid movement and diarrhoea.

Diminished absorption of fluid and electrolytes is often secondary to mucosal damage in either the small or the large intestine. Any damage to jejunal villi resulting in

histologic abnormalities and mucosal inflammation of jejunumsubstantially decrease the mucosal absorptive function leading to diarrhoea.

Active electrolyte secretion is the third mechanism causing alterations in fluid and electrolyte movement. Agents that stimulate secretion, known as secretagogues, may be present in the small and large intestine. They are heterogeneous and frequently responsible for several diarrhea1 disorders. Intestinal secretagogues can be classified into three groups:

1. Bacterial enterotoxins
2. Hormones (either circulating or present as paracrine mediators)
3. Detergents (including bile acids, fatty acids, and commercial laxatives)

All of the secretagogues stimulate active chloride secretion, thus affecting sodium and chloride movement. For example, in toxigenic diarrhoea caused by in Escherichia coli, heat labile (or LT) enterotoxin stimulates active chloride secretion resulting in excess fluid secretion. The enterotoxins, however, do not usually cause structural damage to the small intestine nor alter absorptive function.

Hormones that increase intestinal secretion include vasoactive intestinal peptide, serotonin, and calcitonin. Prostaglandin El, which stimulates adenylate cyclase and increases mucosal cyclic adenosine monophosphate levels, has also been implicated as the mediator of diarrhoea in psychological disorders. Diarrhoea also has been noted as an adverse effect of prostaglandin administration. Although vasoactive intestinal peptide affects ion transport by increasing intracellular cyclic adenosine monophosphate levels, other secretagogues (e.g., serotonin) alter ion transport by acting as a calcium ionophore.

The mechanism by which fluid and electrolyte movement is affected by alterations in intestinal motility is not clearly understood. The precise relations between changes in motor function, changes in intraluminal pressure, changes between intraluminal pressure, and intestinal transit time need to be clarified.

Infection and diarrhoea:

Diarrhoea due to infection accounts for more than 90% of paediatric diarrhoea and is caused by various Enteropathogens such as bacteria, virus, protozoan and other pathogens[11]. Among the various viruses associated with diarrheal disorders,

rotavirus is the leading cause of death with 38.3% of the total deaths due to infection, followed by *Calcivirus* (13.8%), *Adenovirus* (4.3%) and *Astrovirus* (3%). Among the bacteria, enteropathogenic *Escherichia coli* top the list with 15.3%, followed by enterotoxigenic *Escherichia coli* (6.9), *Shigella spp* (4.7), *Campylobacter spp* (4.3%), *Salmonella spp* (3.5), and *Vibrio cholerae* (1.8%). Other species such are *Giardia lamblia* (3.1%), *Cryptosporidium spp* (2.7) and *Entamoeba hystolitica* (0.3) also contributes to the paediatric diarrhoea. [11] various factors such as seasonal change, poor nutrition, low economic status, improper hygiene, inadequate breast feeding enhance the chances of infection. Studies have shown that as many as one-half to two-thirds of children with severe acute malnutrition present with diarrhoea. Under nutrition precipitates deaths due to diarrhoea, and similarly, diarrhoea often leads to severe acute malnutrition in young children [12]. Enteropathogens that cause diarrhoeas affect the physiology of the gut in different ways. By modifying the equilibrium of water and electrolytes, they induce different types of diarrhoea. Thus, osmotic diarrhoeas result from an excess of non-absorbable and osmotically active solutes in the lumen and secretory diarrhoea results when the secretory activity of the mucosa exceeds its absorption capacity [13].

Diarrhoea and indigestion:

Indigestion could be directly related with the daily food habits and indirectly related with nature, type and quantity of food consumed. As early as 10th century, Avicenna stated cow's milk as cause of diarrhoea in infants and advised milk free diets [14]. High dietary fat was considered to be the major culprit in paediatric diarrhoea due to indigestion and the chances of diarrhoea are more in subjects with defective bile production. Children known to have gall stones or undergone cholecystectomy will have frequent diarrhoea due to defective bile secretion. Even in normal subjects repeated consumption of high fat diet will lead to diarrhoea after certain period of time [15]

Diarrhoea and drugs:

As intestinal mucosa is the first absorption site of orally administered drugs, incidence of drug-induced diarrhoea is relatively high. Diarrhoea contributes for about 7 per

cent of all drug adverse effects[13] and up to 4 per cent of people suffering from diarrhoea are induced as a side effects of prescribedmedications [16]. Antibiotic-associated diarrhoea are responsible for 25 per cent of drug-induced diarrhoea[17]. The mechanism of drug-induced diarrhoea is often multifactorial and sometimes remains unclear. More than 700 drugs have been implicated in causing diarrhoea; those most frequently involved are antimicrobials, laxatives, magnesium- containing antacids, lactose- or sorbitol-containing products, nonsteroidal anti- inflammatory drugs, prostaglandins, colchicine, antineoplastics, antiarrhythmic drugs and cholinergic agents[13]. New drugs are likely to induce diarrhoea because of their pharmacodynamics properties, for example, lipase inhibitors and cholinesterase inhibitors. Several pathophysiological mechanisms[16, 17]are involved in drug-induced diarrhoea: osmotic diarrhoea, secretory diarrhoea, shortened transit time, exudative diarrhoea and protein-losing enteropathy, and malabsorption or maldigestion of fat and carbohydrates. Often 2 or more mechanisms are present simultaneously. Major pathological mechanisms of drug induced diarrhoea are described in figure. 2.1.

The disease spectrum of antibiotic-associated diarrhoea ranges from benign diarrhoea to potentially life-threatening pseudo-membranous colitis (reported in 10% of patients receiving clindamycin). Most frequently, however, diarrhoea is benign, appearing during the first days of treatment, whatever the class of antibacterial, and resolving spontaneously after discontinuation of treatment[18].Paediatric data regarding the prevalence of drug induced diarrhoea is scarce with very few studies all over the world and no Indian studies[19].However, globally, the rate of antibiotic-associated diarrhoea in children seems to be around 11% in the youngest children[20]. Antibiotics cause diarrhoea by several mechanisms. First, suppression of anaerobic bacteria by drugs such as aminopenicillins, cephalosporins, and clindamycin results in reduced metabolism of carbohydrates leading to osmotic diarrhoea [17].

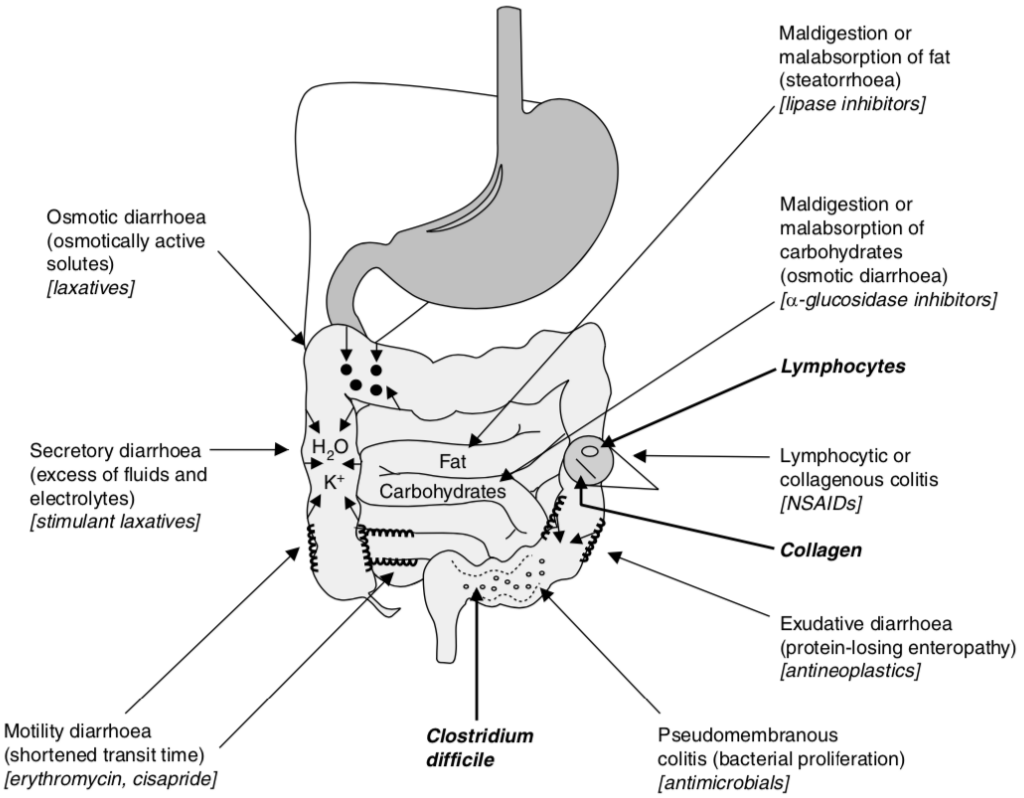

Figure 2 1:Major pathophysiological mechanisms of drug-induced diarrhoea [16]

Second, antibiotics may change the gut flora resulting in overgrowth of potentially pathogenic organisms such as Clostridium difficile, Salmonella, Clostridium perfringens type A, Staphylococcus aureus, and Candida albicans. Finally, antibiotics with prokinetic activity, such as erythromycin and clavulanate, promote diarrhoea[21]. Antibiotic-associated diarrhoea has a spectrum of severity including uncomplicated diarrhoea, colitis and pseudo- membranous colitis. Epidemiologic studies are limited to the clinical description of non-C. Difficile-associated cases, but C. difficile AAD has also been well described. In the general healthcare-associated population, most of the cases of C.difficile AAD are uncomplicated diarrhoea (10–30 out of 100 patients), while colitis is less frequent (5–10 out of 100 patients) and pseudo- membranous colitis is infrequent (0.1–1 out of 100 patients)[18].

Dentition and diarrhoea:

Despite being a natural process of child development, the impacts of primary tooth eruption in diarrhoea of children has been debated for many centuries, and traditional beliefs on the issue have still not been entirely supplanted by scientific findings[22]. Hippocrates mentions that if dentition is associated with diarrhoea, the chances of the child getting convulsions are very limited, whereas if the child gets constipation during teething, the chance of getting convulsions is more. Work by few well know ancient physicians such a Aristotle, Homer, Celsus, and others vouch the association between diarrhoea and tooth eruption.

Table 2.6: Drugs used in management of diarrhoea during dentition in Siddha

1. ***Iraṭṭai Pēymiraṭṭi*** **(Leaf Juice)**
2. ***Thiratchai*** **(Fruit Juice)**
3. ***Tāḷicapattiri*** **(Leaf Juice- 5-10 Drops)**
4. **Juice of *vāḻaippū, puḷiyārai* and *tuḷaci* extracted by steam cooking**

Avicenna recommends a milk free diet consisting of goat's cheese in cold water, egg yolk, and bread or wheat flour boiled in water in infants with intractable diarrhoea during teething [14] Atharva-veda recommends a prayer and special diet for prevention of complications of teething in children. Few Siddha literatures also recommend specific medications for management of diarrhoea during teething in children (shown in table 2.6). Though it's been believed that teething is associated with diarrhoea in earlier stages, it's been strongly criticised by many physicians as early as 17th century. However, in 1839, 5016 deaths in England and Wales were attributed to teething [23]. Most medical professionals now agree that teething does not cause life-threatening illness, but they disagree about which symptoms may be associated with tooth eruption.

Anxiety, fear and diarrhoea:

Anxiety and fear may cause diarrhoea, while depressed patients are four to five times more likely to report constipation [13].Diarrhoea predominant irritable bowel syndrome is a diarrhoeal disease precipitated by anxiety, fear, depression or anger and is viewed as resulting from the interactions of a number of factors, such as abnormal gastrointestinal motility, visceral hypersensitivity, and psychosocial factors [24]. A growing attention on the interaction between the central and enteric nervous systems has led to the suggestion that the disease could be related to a hyper reactivity of the

brain-gut axis, which is a model describing bidirectional pathways linking emotional and cognitive areas in the central nervous system with visceral afferent sensation and intestinal function.Diarrhoea predominant irritable bowel syndrome subjects showed increased number of enter endocrine cells and postprandial plasmatic serotonin levels and were always associated with high rates of psychiatric comorbidity and history of sexual abuse [25]. Serotonin is widely distributed throughout the gut within both the enteric nerves and enterochromaffin (EC) cells. EC cells are located in the gut mucosa with maximal numbers in the duodenum and rectum where they act as signal transducers, responding to pressure and luminal substances both bacterial and dietary. Activation leads to serotonin release which acts on a range of receptors on mucosal afferent and myenteric interneurons to initiate secretomotor reflexes. These cause nausea and vomiting as well as intestinal secretion, propulsion and if pronounced, diarrhoea [26].

Conventional Management of diarrhoea:

Therapeutic feeding strategies

Management of Diarrhoea in children primarily include diet restrictions followed by symptomatic management. Current WHO guidelines on the management and treatment of diarrhoea in children strongly recommend continued feeding alongside administration of oral rehydration solutions, plus zinc therapy [27]. Continued feeding is now widely accepted as a key component of appropriate treatment for childhood diarrhoea, but with the exception of consensus on continued breastfeeding, there remains some debate regarding the optimal diet or dietary ingredients for hastening recovery and maintaining nutritional status in children with diarrhoea. Lactose malabsorption is a common complication of diarrhoea, especially among malnourished children.So, limiting milk intake among young children can promote further nutritional deficiency if substitute sources of protein and energy are not consumed sufficiently. Hence, any commercial lactose-free formulations or soy-based preparations may be effective alternative to milk.

For Infective diarrhoea:

Antibiotics are recommended only in patients who are severely affected by bacterial infection and show signs of systemic involvement, including high fever and prostration. Antibiotics like oxytetracycline, amoxicillin, tetracycline, ampicillin, chloramphenicol, doxycycline, metranidazole are given to treat diarrhoea. It is not uncommon for Salmonella to become resistant to commonly used antimicrobial agents such as amoxicillin. Campylobacter is sensitive to erythromycin and tetracycline, while ciprofloxacin is effective against both organisms [13]. Nitazoxanide has been shown to be effective against infection with G. lamblia and Cryptosporidium parvum in children with diarrhoea [12]. But they have their own merits and demerits. Antibiotics upset the normal intestinal flora. Nowadays, treatment with antibiotics is not successful because of the development of multi drug resistant strains. Many anti-diarrhoeal preparations have proved to be either ineffective or too powerful, resulting in serious complications or even death in some cases [28]

For Drug induced diarrhoea:

Initially dose and duration of the drug should be adjusted based on the requirement to check for reduction in diarrhoea. However, if diarrhoea persists even after modification of dose and duration, immediate drug withdrawal is recommended and adequate hydration is ensured. If diarrhoea persists even after withdrawal, it is important to exclude pseudomembranous colitis by performing a sigmoidoscopy and sending a stool for cytotoxin assay. Using antidiarrhoeal agents are not recommended as they delay the return of bacterial flora to normal [16].

For diarrhoea due to fear and anxiety:

Mainstay of treatment in diarrhoea due to fear and anxietyincludes oral corticosteroids such as prednisolone or intravenous hydrocortisone for severe disease and 5-aminosalicylates. Immunosuppressant drugs will be given as second-line agents for resistant disease while nutritional therapy may also be incorporated based on treatment response[29].

Despite of the presence of various class of therapies, present day diarrhoeal management in general and paediatric diarrhoeal management in particular remains incomplete. In most of the cases, antibiotic therapy was ineffective because of the delay in proper diagnosis and development of disease resistant strains.Moreover, most of the diarrhoea of viral origin is very difficult to manage due to lack of specific anti-viral drugs and only fluid management is followed in such cases. Oral corticosteroids and immune suppressants cannot be administered in diarrhoea precipitated by fear and anxiety due to the toxicity associated with them. Hence, there is a definite need for alternative therapies in addressing the lacunas present in the current day management of paediatric diarrhoea.

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3 Preparation and standardization

Preparation and standardization - Overview:

The test drug *Pañcatīpākkiṉi cūraṇam* (PDC) was prepared by following traditional parameters and presence of major ingredients in this are determined using basic qualitative analysis. The PLIM standards were also measured in order to establish a standard for quality assessment of the drug.

Background:

The term PDC literally means a drug with five flames. This could possibly due to the fact that this drug formulation is composed of five ingredients*: māṅkoṭṭai paruppu* (kernel of Mangifera indica*), kaṟivēppilai* (leaves of Murraya koenigii), *cuṇṭaivaraṟṟal* (dried fruits of Solanum torvum), *ventayam* (Seeds of Trigonella foenum graecum) and *omam* (seeds of Carum copticum)[30] . There are few other formulations with the same name. For instance, in *citta vaittiya tiraṭṭu*, a formulation has been given under the same name PDC (from now it will be referred as PDC1) but with different ingredients: *cukku,miḷaku,tippili,ēlam*, *cīrakam*[31]. However, the therapeutic indications for both the formulations are different. PDC is indicated for treatment of *cītakkaḻiccal*, *peruṅkaḻiccal, vayiṟu iraiccaluṭaṉ kūṭiyakaḻiccal* and *vayiṟṟukkaṭuppu*, whereas, PDC1 is indicated for Indigestion,*mayakkam, porumal, atticuram, cilēttumanōy, uṣṇa nōy,cūlai, veṭṭai, mūla vāyvu.* Moreover, there are few drugs which have the ingredients of PDC as major content along with other herbs.*cuṇṭai vaṟṟal cūraṇam*[31] is one among them, which includes *nellivaṟṟal* and *mātuḷampaḻattōl*along with*cuṇṭai vaṟṟal*,*kaṟivēppilai* , *māṅkoṭṭai paruppu*, *omam* and*ventayam*. However, its indications are very similar to the indications of PDC such as *porumal, māntam, iraiccal, kaḻiccal, mūlam, aticāram, kirakaṇi*. Another formulation in *yūkimuṉivar vaittiya cintāmaṇi*[32] indicates a *curam* prepared from

*omam,cuṇṭai varṟal, kaṟivēppilai, uppu, peruṅkāyam,cukku,miḷaku,tippili,*for treatment of *kunma kirāṇi*(a disease characterised by head ache, excessive sleep, rheum, intense thirst, giddiness, excessive sweat, burning sensation, abdominal distension with bloating). Furthermore, a herbo-metallic formulation indicated for *karuppa kirāṇi*[32] (a disease in pregnant women characterized by diarrhoea, stomach ache, weakness of upper and lower limbs, yellow eyes, excessive thirst and vomiting. These symptoms will prevail till the foetus gets aborted) in *yūkimuṉivar vaittiya cintāmaṇi* is found to have *omam,cuṇṭai varṟal,māṅkoṭṭai paruppu, tirikaṭuku, intuppu, kirāmpu, cātikkāy,cātipattiri,apiṉi, kāntam, liṅkam,naṟcīrakam, ēlam, lavaṅkakapaṭṭai, karuñcīrakam, ativiṭayam*as main ingredients. Though all these formulations were indicated for different symptoms and diseases, most of the diseases indicated are more or less related to gastro-intestinal tract and hyper peristalsis. Hence it can be concluded that the ingredients of PDC is specific for management for hyper peristalsis.

Materials and methods:

General protocol for preparation of any *Siddha* formulation involves the following steps:

1. Collection of raw material
2. Authentication of raw material
2. Purification
3. Preparation
4. Authentication of final drug

Even in this study the same protocol was espoused for the preparation of PDC.

Collection of Raw materials:

Māṅkoṭṭai paruppu and *kaṟivēppilai* were collected from R. Puthupalayam, Rasipuram, Namakkal district, Tamilnadu – 637402 during the month of November,

2018. *cuṇṭaivarar̲r̲al, ventayam and omam* were purchased from raw drug stores in Palayamkottai, Tirunelveli, Tamilnadu – 627002.

Authentication of Raw material:

One of the major issues while researching the traditional medicine is the authentication of the raw materials. Even among the practitioners of traditional medicine, it is well accepted that authenticating the raw material in general and herbs in particular is not a straightforward task. Hence all the ingredients of PDC were initially identified by experienced traditional practitioner and authenticated by taxonomist in Government Siddha Medical College, Palayamkottai.

Purification:

As there is no specific purification methods for any of the ingredients of PDC in Siddha literature, all the ingredients of the PDC were shade dried and any adulteration in purchased drugs were removed manually.

Characterization of PDC:

TGA (Thermo-gravimetry analysis) was performed by placing 2-5 mg of sample in an alumina cup and heated at the rate of 10°C/min up to 1000°C in a nitrogen atmosphere with a flow rate of 100 ml/min using an SDT Q600 (TA Instruments, USA).

Qualitative analysis:

Presences of various chemicals in PDC are determined using following methods.

1. **Test for calcium** - 2ml of the above prepared extract is taken in a clean test tube. To this add 2ml of 4% ammonium oxalate solution.
2. **Test for sulphate** - 2ml of the extract is added to 5% barium chloride solution
3. **Test for chloride** - The extract is treated with silver nitrate solution.
4. **Test for carbonate** - The substance is treated with concentrated HC.
5. **Test for starch** - The extract is added with weak iodine solution
6. **Test for ferric iron** - The extract is acidified with glacial acetic acid and potassium ferro cyanide.
7. **Test for ferrous iron** - The extract is treated with concentrated nitric acid and ammonium thiocyanate solution.

8. **Test for phosphate** - The extract is treated with ammonium molybdate and concentrated nitric acid
9. **Test for albumin** - The extract is treated with esbach's reagent
10. **Test for tannic acid** - This extract is treated with ferric chloride.
11. **Test for unsaturation** - Potassium permanganate solution is added to the extract.
12. **Test for the reducing sugar** - 5ml of benedict's qualitative solution is taken in a test tube and allowed to boil for 2 minutes and add 8-10 drops of the extract and again boil it for 2 minutes
13. **Test for amino acid** - One or two drops of the extract is placed on a filter paper and dried well. After drying 1% ninydrin is sprayed over the same and dried it well.
14. **Test for zinc** - The extract is treated with potassium ferro cyanide.

PLIM parameters:

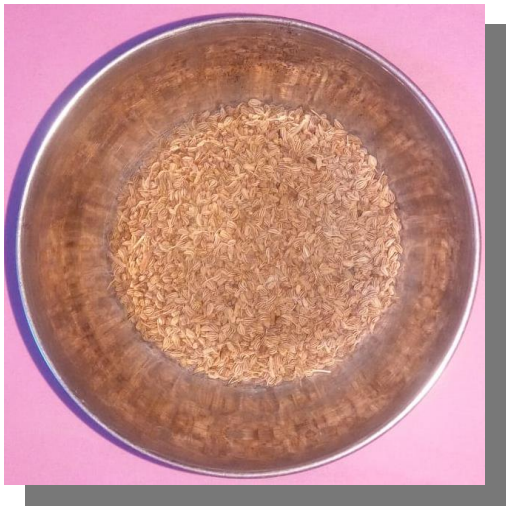
Various analytical specifications were performed as per the Pharmacopoeial laboratory of Indian Medicine guidelines[33] and the reference followed for analysis is tabulated below.

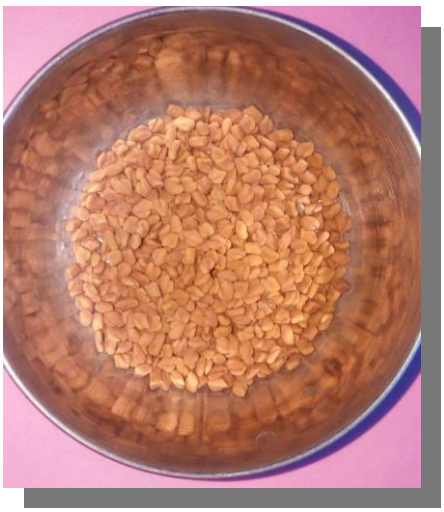
\Table 3.1: Methods followed for PLIM parameters analysis

S No	Parameters	Reference of test methods
1	Appearance	IP Vol-I, 1996, p7
2	Total solids	IP Vol-I, 2014, p277
3	Total Ash	IP Vol-I, 2014, p98
4	Acid insoluble ash	IP Vol-I, 2014, p98
5	Loss on Drying at 105°C	IP Vol-I, 2014, p162
6	Carbohydrates	Biochemical Methods, Sadasivam.S,2005,p8-9

Results:

The results of preparation and characterisation are given below





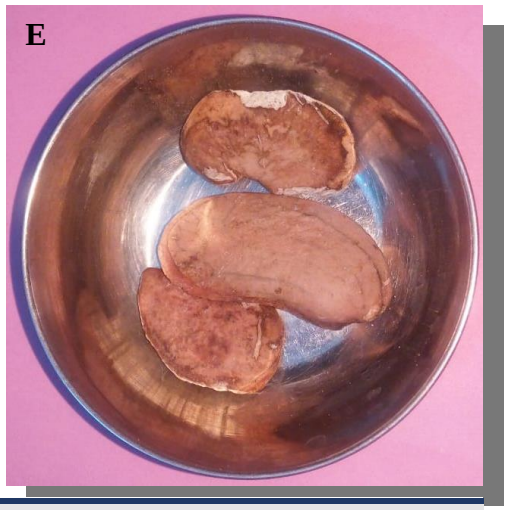


Figure 3.1: Representative images of raw materials used in preparation of PDC A)*kaṟivēppilaiventayam* B) *omam* C) *ventayam* D) *cuṇṭai vaṟṟal* E) *māṅkoṭṭai paruppu*

Preparation:

All the 5 ingredients are taken in equal quantity and powdered together in a pulveriser. Initial and final weights of the materials are noted to calculate the wastage during the preparation process. Then the pulverised material is sieved to remove the large fibre particles. The weight of all the intermediate is tabulated in table 2.1.

Table 3.2: Preparation of PDC (mass measurements)

Weight of Raw material	20g + 20g + 20g + 20g + 20g = 100g
Weight of the pulverised sample	92g
Wastage	100-92 = 8
Weight after sieving	80g
Weight of thippi	12g

Characterisation:

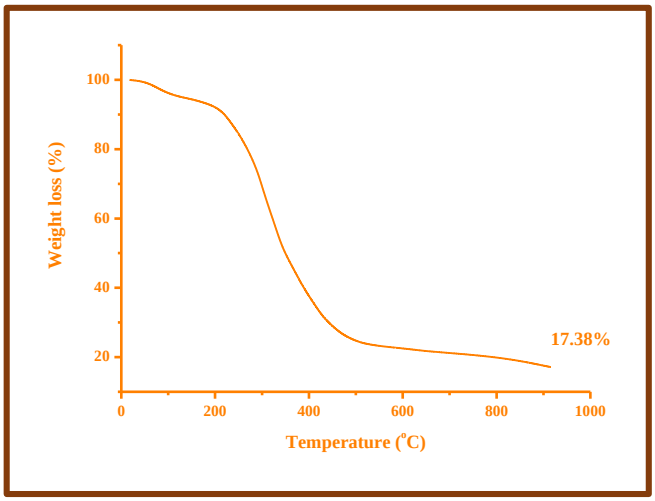


Figure 3.2: Thermo gravimetric analysis of PDC

TGA analysis of PDC is shown in figure 2.1. This shows that most of the substances in PDC are organic and maximum degradation happen around 400 ^{o}C.

Primary chemical analysis of PDC showed the presence of calcium, sulphate, chloride, starch, ferrous form of iron and amino acid. Few substances such as carbonate, ferric form of iron, phosphate, albumin, tannic acid, zinc and reducing sugar are absent in PDC.

Table 3.3:Results of PLIM parameters in PDC

S No	Parameters	Results
1	Appearance	Brown coloured powder
2	Total solids	11.01%w/w
3	Total Ash	5.167%w/w
4	Acid insoluble ash	0.4241%w/w
5	Loss on Drying at 105°C	3.582%w/w
6	Carbohydrates	19.86%w/w

Discussion and Conclusion:

PDC was successfully prepared by strictly following the traditional procedures. As, the degradation percentage of PDC after heating up to 1000^0C, it's very clear that few inorganic substances such as calcium, sodium, silica, iron etc., may be present in the prepared PDC. This was vouched by the qualitative analysis performed in PDC. The PLIM standard analysis parameters were established and this can be used for establishing standards in future and determination of shelf life. Although this work has showed some insight about the nature of PDC, there are still open questions that need to be addressed in the future. Primarily the synergistic activity ofall the five plants together need to be established. Besides, the rationale behind the exact choice of the plant for their action needs clearer understanding.

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4 Pre-Clinical experiments on PDC

Pre-Clinical experiments on PDC - Overview:

Preparation and characterization of *Pañcatīpākkiṉi cūraṇam* (PDC) was discussed in the previous chapter. This chapter involves the pre-clinical assessment of the activity and safety of PDC *in-vitro* and *in-vivo*. Initially, the anti-microbial activity of PDC in various bacterial strains was performed and its minimum inhibitory concentration was established. Then the safety of PDC was evaluated using standard animal models with respect to OECD guidelines. After that, the anti-diarrhoeal activity of the PDC is determined using castor oil induced diarrhoeal model and charcoal meal transit time test in wistar rats.

Background:

Though the use of animals for drug research is not appreciated by all medical systems, it was widely believed to be the most reliable method to demonstrate the quality of the candidate drug[34]. Almost all the Western Bio-medicine (WBM) drugs do have the detail documentation of their pharmacological and toxicological nature tested in animal species. Though Siddha medical system does have some traditional quality control methods/tests to ensure the quality of the prepared traditional drug, they do not have any detailed classical texts dealing with animal experiments. This is considered to be one of the major hurdles in global acceptance of Siddha drugs by the scientific and medical community. So, in the past few years various Siddha researchers have involved themselves in experimentation of Siddha drugs in animal species[35-37]. However, most of these experiments have not produced convincing results as these experimental procedures were primarily designed for WBM drugs that completely differ from Siddha drugs in many aspects. Siddha medical system has a

personalized, multi-factorial and holistic approach. Each Siddha formulation in general and PDC in particular is a composition of many molecules with multiple targets as opposed to single molecule and single target strategy of WBM. Moreover, all the Siddha formulations are administered with suitable vehicles like honey, ghee and butter that will influence the therapeutic/toxic effect through the various molecules present in them[8]. These concepts of usage of same drug with vehicles for different disorders do not exist in WBM system. Furthermore, most of the Siddha formulations were administered with strict dietary restrictions depending on the nature of the disease and drug ingredients. So, all these factors will have a synergistic effect in the pharmacological/toxicological nature of Siddha formulation.Apart from these basic differences, most of the Siddha formulations will have a history of its clinical use for centauries in humans and the purpose of the pre-clinical study is to strengthen/document the already know safety/activity of the drug by demonstrating in animals. But in WBM, the candidate drug will be mostly a new chemical entity and the major objective of the pre-clinical study will be to evaluate any toxic effects in animals. Hence the experimental protocols of WBM should be manipulated in such a way that it addresses all these extra requirements of Siddha drugs. Considering all these limitations, the present study was designed to understand the following.

1. Anti-microbial activity
2. Safety
    a. Acute toxicity study
    b. Sub-acute toxicity study
3. Efficacy
    a. Anti-diarrhoeal activity
    b. Anti-hyper-peristaltic activity

Materials and Methods:

Anti-microbial activity:

Mullen-Hinton agar was used to for the estimation of minimum inhibitory concentration of PDC against various bacterial strains. The components of medium are given below

Components of medium:

1. Beef extract – 300g/L
2. Agar – 17g/L
3. Starch – 1.5g/L
4. Caesin hydropyxalate – 17.5 g/L
5. Distilled water – 1000mL
6. pH – 7.6

Briefly, after preparing the agar plates, the organism was streaked on the medium and the test drug was loaded using disc method with the concentration of 4mg/ml and amikacin was used as the control. The plates were inspected after incubation at 37^0C for overnight and zone of inhibition was observed.

Animal Experiments:

Adult Wistar rats (6-8 weeks) of both sexes, procured from the Central Animal Facility, Kalasalingam University, were used for this study. The animals were kept at 22±2 °C with a 12 h light/dark cycle, with free access to standard rat pellet diet (Hindustan Lever, India) and water *ad libitum*. The experimental protocols were performed after obtaining the necessary approval (CPCSEA approval number: AKCP/IAEC/95/2018-19) from the Institutional Animal Ethical Committee (IAEC) of Kalasalingam University.

Dose concentration:

As the human therapeutic dose of PDC is already established in the *Siddha* texts (250 mg/dose) for normal adult with 3 times a day, animal equivalent dose was calculated using allometric dose translations[38]. Considering the weight of a normal adult as 60kg, animal therapeutic equivalent was calculated as

$$Animale\ quivalentdose(rat) = Humandose \times \frac{HumanKm}{AnimalKm}$$

$$Animal\ equivalentdose(rat) = 12.5 \times \frac{37}{6} = 77.08\,mg/day$$

Acute Oral Toxicity Study:

This study was performed in compliance with OECD 425 (Up and Down method) guidelines[39]. Female rats were fed with 2000mg/kg of test substance and observed individually at least once during the first 30 minutes after dosing, periodically during the first 24 hours (with special attention given during the first 4 hours), and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely sacrificed for animal welfare reasons or are found dead. Body weight was measured once in a week and feed consumption was measured daily. Animals were sacrificed at day 14 and gross pathology, if any were noted and taken for further investigation.

28-days repeated oral toxicity:

This study was performed in compliance with OECD 407 (repeated dose 28-day oral toxicity) guidelines[40]. Animals were totally divided into 4 groups (Normal control, low dose, medium dose, high dose) with 6 animals (3male and 3female) in each group. Normal control animals were administered only with distilled water. Low (therapeutic dose), medium (10 x therapeutic dose) and high (100 x therapeutic dose) drug treated groups were administered with respective concentrations of PDC dispersed in cow's curd. The drug was administered for a period of 28 days orally using oral gavage tube. All the animals were sacrificed after 28 days and required biological samples were collected for further analysis. Body weight changes were noted once in a week and feed consumption was noted daily.Animal equivalent therapeutic dose was fixed as low dose. Medium and high dose were fixed as 10 times and 100 times that of the low dose respectively.

Hematology and Biochemical analysis:

About 1mL of blood samples were collectedfrom all the animals on 29th day from retro-orbital plexus before sacrifice.

Hematology analysis was performed in whole blood using Haematology analyser.

The serum was separated by allowing the remaining blood sample to coagulate at room temperature followed by centrifugation at 605rcf for 10 minutes. Biochemical analysis was performed in this serum using A 15 auto analyzer.

Histopathology analysis:

After sacrifice, the specific organs were isolated, washed with cold saline, weighed and finally fixed in 10% buffered formalin solution for histopathological studies. The fixed tissues were embedded in paraffin and the sections were cut in 3-5µm slices and were stained using haematoxylin and eosin. The stained tissues were observed under light microscope. The scoring was given to the pathological features seen in the slide as 0 for normal, 1 for minimal, 2 for mild, 3 for moderate, and 4 for marked and 5 for severe.

Castor Oil-Induced Diarrhea in rats:

This test was done based on the method used by Sunday A. Ejehet al[41]. 24 rats were divided in to 4 groups: Disease control, Standard Control, Low dose and High dose, with 6 animals in each group and placed in separate cages. The drug administration was performed as per the descriptions in table 4.1. After the over-night fasting, the first group received distilled water (10ml/kg) and the second group received loperamide (3mg/kg), serving as negative control (NC) and positive controls (PC), respectively. Groups 3&4 received therapeutic dose and two times the therapeutic dose of PDC, respectively. After one hour, all the animalsreceived 0.5ml/animal of castor oil orally. The severity of diarrhea was assessed for 4 hours. The mean total number of feces (dry and wet diarrheal droppings) was determined and compared with the negative control group.

Table 4.1:Study plan for Castor Oil-Induced diarrhoea in rats

Groups	No. of animals	Treatment protocol
Disease control	5	Distilled water (10mL/kg)
Standard control	5	Loperamide (3mg/kg)
Low dose	5	77.08mg/kg of PDC
High dose	5	154.16mg/kg of test drug

The percentage inhibition of total defecation and the percentage inhibition of diarrheawere calculated using:

$$\%\ \text{of inhibition of defecation} = \frac{\text{Total number of feaces in N. C} - \text{total number of feces in treated group}}{\text{Total number of feces in N. C}} \times 100$$

$$\%\ \text{inhibition of diarrhoea} = \frac{\text{Total number of diarrhoeal feaces in N. C} - \text{total number of diarrhoeal feces in treated group}}{\text{Total number of diarrhoeal feces in N. C}} \times 100$$

Note: The feces which are not in proper pellet form due to more amount of water in it are considered as diarrhoeal feces.

Anti-hyper peristaltic activity:

This test was done by determining the influence of PDC in Intestinal transit timebased on the method described by [42] in rats. In brief, 25 rats were divided into five groups: Disease control, Standard Control, Low dose, Medium dose and High dose with 5 animals in each group and placed in separate cages. The drug administration was performed as per the descriptions in table. 4.2. One hour after treatment with respective doses of drugs, diarrhoea will be induced by oral administration of 2 ml castor oil in each animal. Then, all the animals will be ingested with 1 ml/kg (p.o) of standard charcoal meal (10 % suspension in 5% tragacanth powder). All of the animals in each treatment group were sacrificed 20 min after administration of the charcoal meal and their small intestine were immediately isolated.

Table 4.2: Study plan for anti-peristaltic activity in rats

Groups	No. of animals	Treatment protocol
Disease control	5	2 ml of castor oil, 1 hour after study initiation
Standard control	5	Loperamide at the beginning of the study + 2 ml of castor oil, 1 hour after study initiation
Low dose	5	Low dose of test drug at the beginning of the study + 2 ml of castor oil, 1 hour after study initiation
Medium dose	5	Medium dose of test drug at the beginning of the study + 2 ml of castor oil, 1 hour after study initiation
High dose	5	High dose of test drug at the beginning of the study + 2 ml of castor oil, 1 hour after study initiation

The travelled distance of the charcoal plug from pylorus to caecum as the peristaltic index (PI) was determined and expressed as a percentage of the total length of the small intestine.

Statistical analysis:

All the results are expressed as mean ± SD (n= 8-10). One way ANOVA, followed by Dunnett's post hoc test was performed to show the significance of the test results. $p<0.05$ was considered to be statistically significant

Results:

Anti-microbial activity:

The results of anti-microbial activity of PDC is shown in table 4.3

Table 4.3: Anti-microbial effect of PDC

Organism	Sensitivity	Zone of drug	Zone of control
Klebsiella pneumoniae	Resistant	-	16mm (Amikacin)
Streptococcus pneumoniae	Sensitive	16mm	18mm (Amikacin)
Pseudomonas aeruginosa	Resistant	-	18mm (Erythromycin)
Staphylococcus aureus	Resistant	-	18mm (Erythromycin)

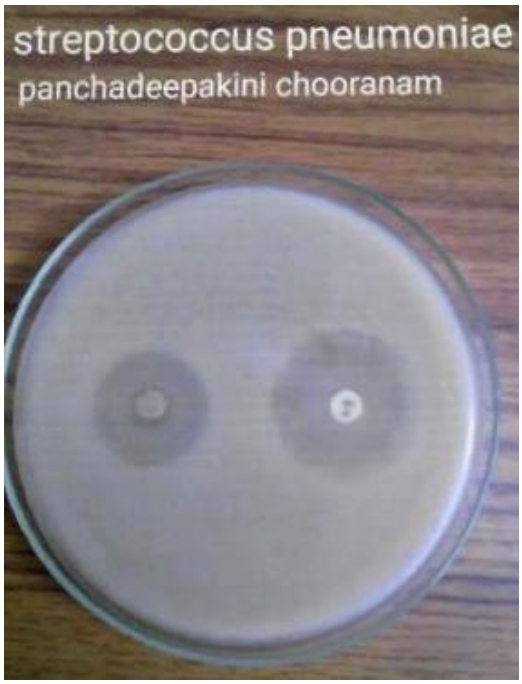

Figure 4.1: Representative image of anti-microbial activity study

Acute toxicity study:

No significant change in feed and water consumption was noted in any of the groups. A gradual increase in body weight was observed from day 1 to 14 in all the animals. No mortality was observed throughout the study. Gross observation of the soft tissues after sacrifice did not show any significant pathological changes after 14 days[36]

28-days repeated oral toxicity:

Cage side observations:

No significant change in feed and water consumption was noted in any of the groups. A gradual increase in body weight was observed from day 1 to 28 in all the groups. No mortality was observed throughout the study in animals of any group.

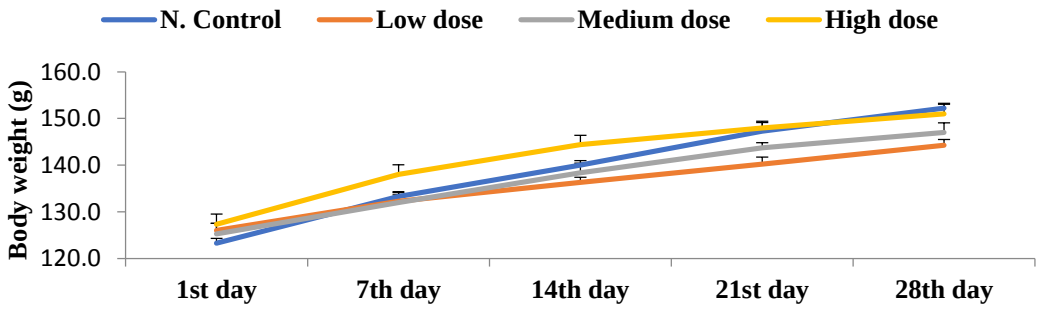

Figure 4.2: Body weight changes in animals of PDC treated groups compared with normal control

Gross Pathology:

Gross observation of the soft tissues did not show any significant pathological changes at the time of sacrifice.

Biochemical parameters:

The biochemical and haematological parameters of all the test animals were measured at the end of experiment and the results are depicted below.

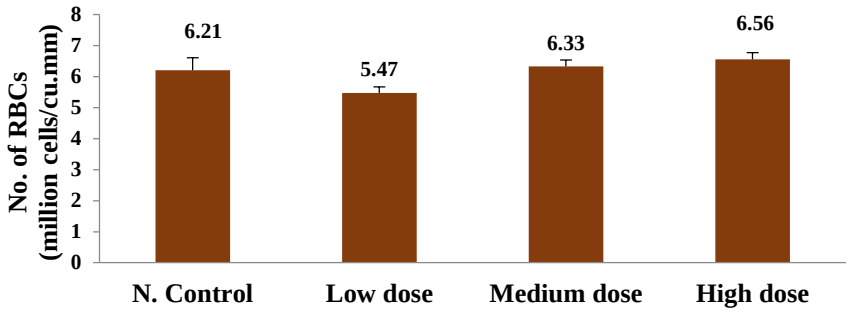

Figure 4.3: Changes in RBC levels of PDC treated animals compared with normal control

There is no significant difference between the level of RBCs in low dose, medium dose and high dose PDC treated groups compared with normal control.

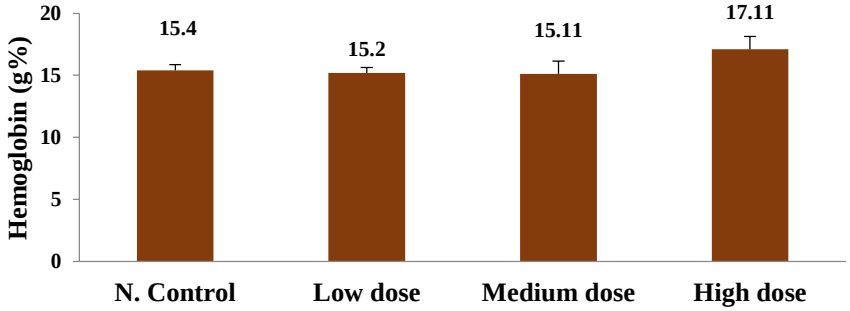

Figure 4.4: Changes in haemoglobin levels of PDC treated animals compared with normal control

There is no significant difference between the level of haemoglobin in low dose, medium dose and high dose PDC treated groups compared with normal control.

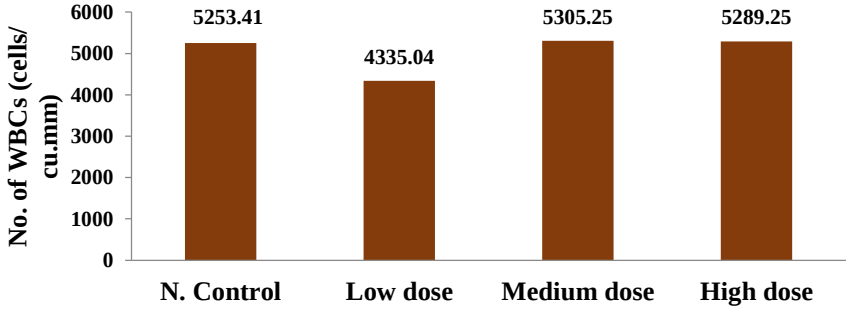

Figure 4.5: Changes in WBC levels of PDC treated animals compared with normal control

There is no significant difference between the level of WBCs in low dose, medium dose and high dose PDC treated groups compared with normal control.

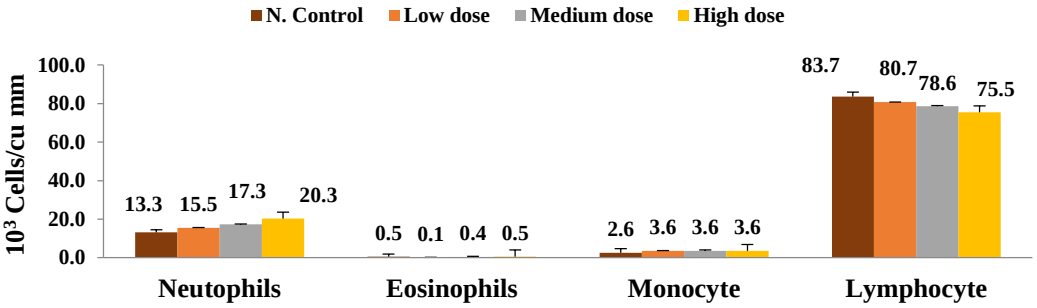

Figure 4.6: Effect of PDC in levels of neutrophils, eosinophils, monocyte and lymphocyte

There is no significant difference between the level of neutrophils, eosinophils, monocyte and lymphocytes in low dose, medium dose and high dose PDC treated groups compared with normal control.

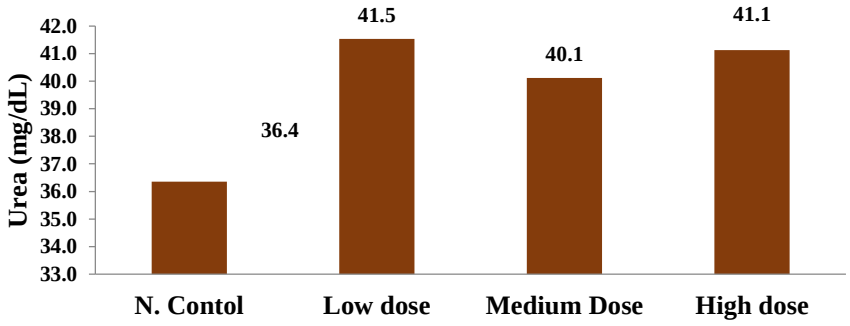

Figure 4.7: Changes in serum urea levels of PDC treated animals compared with normal control

There is no significant difference between the level of serum urea in low dose, medium dose and high dose PDC treated groups compared with normal control.

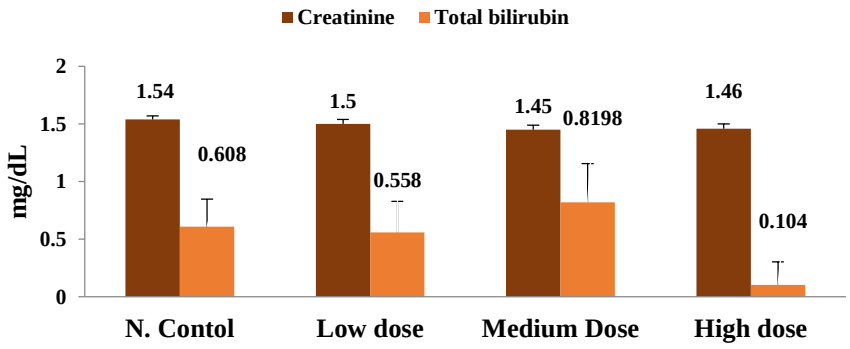

Figure 4.8: Changes in creatinine and total bilirubin levels of PDC treated animals compared with normal control

There is no significant difference between the level of serum creatinine in low dose, medium dose and high dose PDC treated groups compared with normal control.

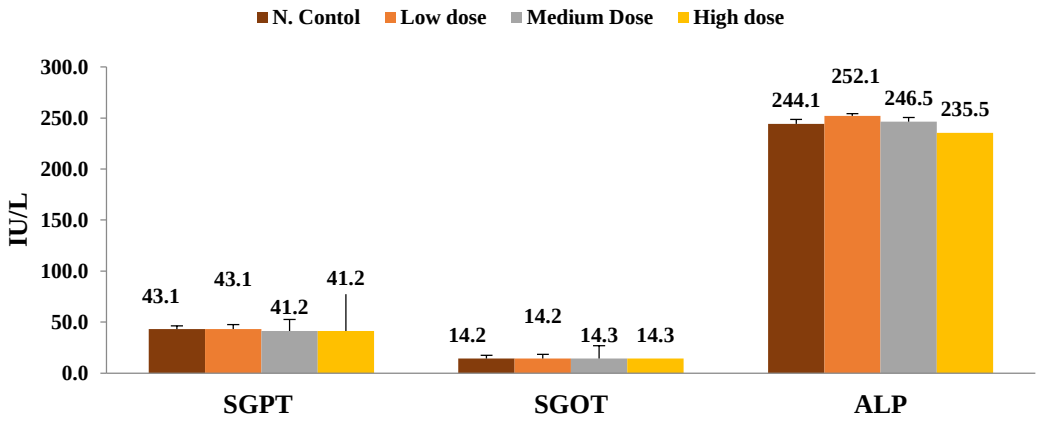

Figure 4.9: Changes in SGOT, SGPT and ALP levels of PDC treated animals compared with normal control

\There is no significant difference between the level of SGOT, SGPT and ALP in low dose, medium dose and high dose PDC treated groups compared with normal control.

Anti-diarrhoeal activity:

There is a significant difference in standard control compared with disease control in time of onset of diarrhoea (shown in Figure 4.10). However, time of onset of diarrhoea in low dose and high dose group compared with disease control in not very significant.

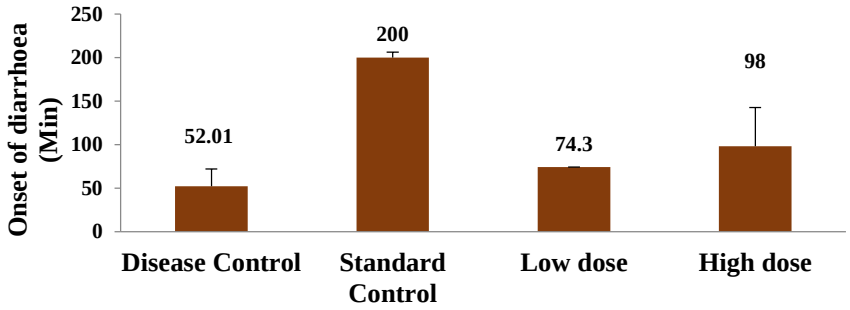

Figure 4.10: Effect of PDC in onset of diarrhoea in animals treated with castor oil

There is a significant decrease in standard control compared with disease control in weight of stools (shown in Figure 4.11). However, no significant difference is found between stool weight of low dose and disease control. High dose shows almost 3 times increase in stool weight compared with disease control.

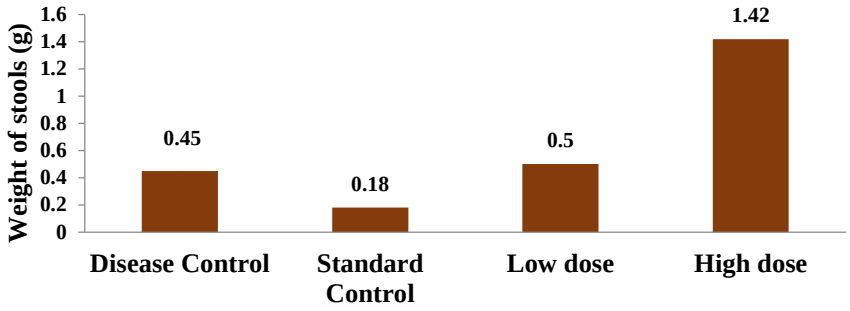

Figure 4. 11: Effect of PDC in weight of stools in animals treated with castor oil

There is a significant decrease in total number of feces in standard control and high dose group compared with disease control (shown in Figure 4.12). However, total number of feces in low dose group compared with disease control in not very significant.

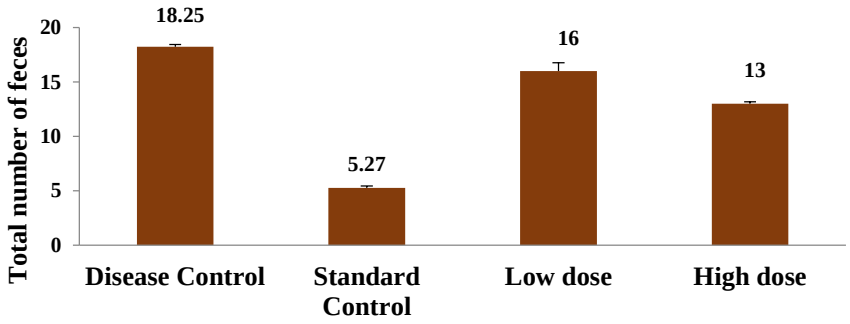

Figure 4. 12: Effect of PDC in total number of fecal output in animals treated with castor oil

There is a significant decrease in total number of diarrhoeal feces in standard control, low dose and high dose group compared with disease control (shown in Figure 4. 13).

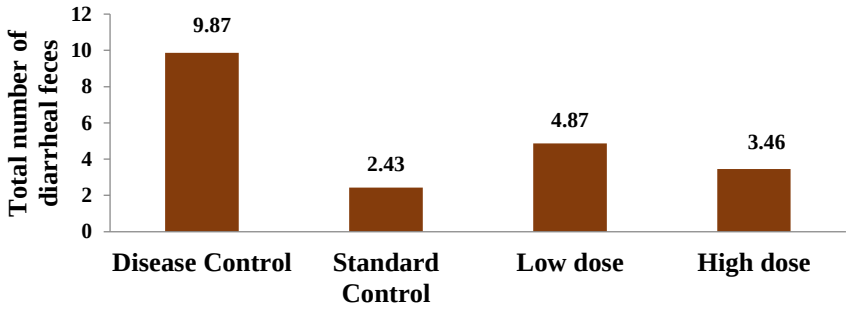

Figure 4.13: Effect of PDC in total number of fecal output with diarrhoea in animals treated with castor oil

The percentage of inhibition of diarrhoea was significantly higher in standard control, low dose and high dose treated groups (shown in figure 4.14).

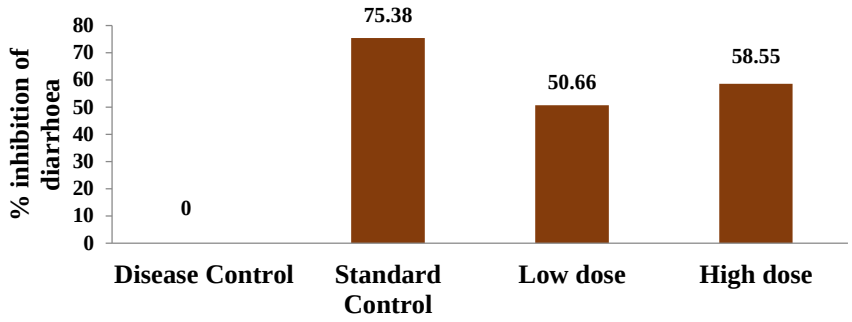

Figure 4.14: Effect of PDC in percentage inhibition of diarrhoea in animals treated with castor oil

The percentage of inhibition of defecation was significantly higher in standard control. However, low dose and high dose treated groups show a moderate inhibition in a dose dependent manner (shown in figure 4.15).

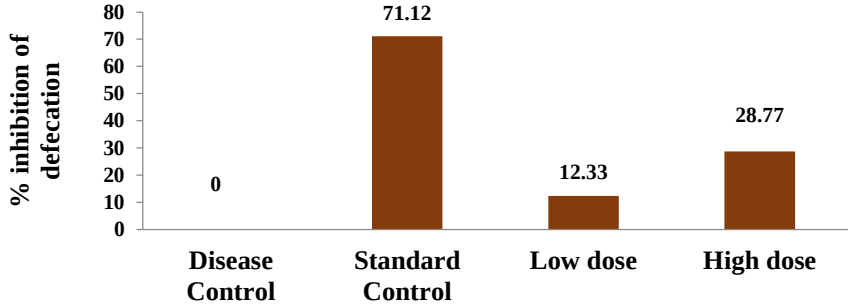

Figure 4.15:Effect of PDC in percentage inhibition of diarrhoea in animals treated with castor oil

Intestinal transit time estimation in Rats:

Figure 4.16:Representative image of intestine isolated from rat after administration of charcoal meal

There is a significant difference between the distance travelled by charcoal meal in high dose group and standard control group (shown in figure 4.16 and Figure 4.17). However, no statistically significant difference was found in low dose and medium dose compared with disease control group.

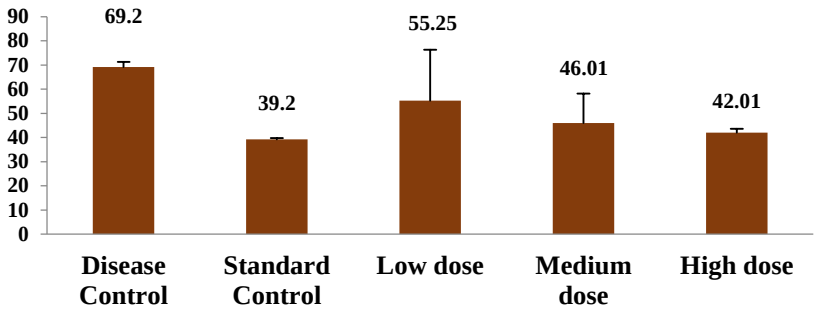

Figure 4.17: Effect of PDC in regulating the peristaltic movements

Discussion:

The primary objective of this study was to establish the safety profile of PDC on short term and long term oral administration. The single dose administration of 100 times the therapeutic dose of PDC did not show any significant change in cage side observations. Moreover, no mortality was observed in the animals for a period of 14 days after oral administration. This clearly indicates that PDCis very safe at oral administration and do not produce any toxic symptom even at very high doses.

After 28 days of drug administration, the absence of any notable cage side abnormalities, absence in body weight changes and absence of animal mortality indicates that oral administration of 100 times the therapeutic dose of PDC do not produce any lethal toxic effects.

However, in order to understand non-lethal toxic effects, systemic analysis of the biochemical and haematological parameters are performed. Among the 7 haematological parameters measured, no significant changes could be noted inany of the treated groups. Moreover,asno alterations in any liver functions parameters such as bilirubin, AST, ALT, ALP and triglycerides are noted, it is concluded that PDC did not have any toxic effect in liver.

In the intervention of diarrhoea, antimotility and antisecretory agents remain as the main agents used to decrease such patho-physiologic changes. Castor oil has been widely used for induction of diarrhoea in antidiarrheal activity studies because it releases ricinoleic acid, a metabolite that causes diarrhoea, upon metabolism in the gut [41]. Ricinoleic acid initiates diarrhoea via mechanisms such as irritation of GI mucosa, leading to the release of prostaglandin which stimulates gastrointestinal motility and electrolyte secretion, reducing electrolyte absorption from the intestine and colon; these are similar to the pathophysiologic processes resulting in diarrhoea. Therefore, the antidiarrheal activity of the plant might be due to the activities that oppose the actions of castor oil for induction of diarrhoea or pathophysiologic processes leading to diarrhoea. The PDC has been shown to decrease the intestinal fluid accumulation. This suggests that the PDC may decrease water and electrolyte secretion to the intestinal lumen while promoting their absorption, which in turn could decrease intestinal overload and distension, leading to a decrease in intestinal motility (giving a longer time for absorption) and water contents of the faecal drops and hence overall reduction in the total number of defecation instances and diarrheal drops in treated groups. This is consistent with the mechanism of action of loperamide for its antidiarrheal effect as presented in the literatures. In addition, PDC may have an anticholinergic activity and cause reduction in intestinal motility and secretion, which is in agreement with the action of atropine on the intestine.

Conclusion:

The World Health Organization suggests that traditional medicines have the potential to heal various diseases that western biomedicine is unable to cure. However, many formulations, which forms the core part of some Asian traditional medicines such as *Siddha* medicine, Ayurveda medicine and Chinese traditional medicine do not get global recognition due to repeated reports of toxicity associated with them [38]. In this work, PDC, an herbal drug of Siddha origin was tested for its toxicity in wistar rats. Animals were administered with 3 different doses (therapeutic dose, 10 X therapeutic doses and 100X therapeutic dose) of PDC and various haematological, biochemical and histopathology parameters were performed to understand the effect

of PDC. Apart from this the therapeutic effect of PDC was evaluated by its effect in reducing the diarrhoea and regulating the peristaltic movements. From all these analysis following conclusions were drawn

1. No lethal effects were noted in oral administration of PDC from therapeutic dose to 100 times the therapeutic dose.
2. No symptoms of toxicity were noted in oral administration of PDCfromtherapeutic dose to 100 times the therapeutic dose.
3. Anti-diarrhoeal property of PDC was found to be more efficient at high doses.

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5 Clinical features and management of *āma kaḻiccal* with PDC

Clinical features and management of āma kaḻiccal with PDC:

The effect of *pañcatīpākkiṉi cūraṇam* (PDC) therapy on treatment of *Āma KaḻIccal (*AK) was studied clinically in 40 subjects of both sex aged between 1-12 years. Various causative factors such as infection, indigestion, fear, anxiety and teething were taken in to consideration. In addition, other influencing factors such as age, sex, geographical location, seasonal variation were also taken into account before analysis. This study showed PDC therapy was significantly effective in AK caused due to infection, indigestion and fear but not in teething.

Background:

A detailed study about AK is very few in contemporary literature. List of drugs previously studied for management of AK is shown in table 5.1. Briefly, *Patturayan* et al reported that *Poṭutalai Camūlam* was effective in 80% of the subjects affected by AK in 2005. A year later, Kamalanathan et al., reported the effect of *Ventaya Cūraṇam* in subjects affected by AK. *Cītapēti Cūraṇam* is found to be clinically effective in 60% of the AK affected subjected treated by Naadimuthu et al.*Cukku Poṭi* and *Mātuḷampiñcu Cūraṇam* was reported to be significantly effective in management of bacillary and amoebic dysentery. Beatrice et al reported the effect of *Oma chooranam* in management of bacillary dysentery, spasmodic abdominal pain and rectal tenesmus and claimed that it help in maintenance of electrolytes and normal intestinal flora. However, in all these works, AK is considered analogous to bacillary dysentery and reported to be significantly effective against it though most of these reports were hand-wavy without any corroborating evidences. Quite antithetical to this, most of the Siddha texts describe AK

as specific inflammation and ulceration of the mucus living of the large intestine due to any reason resulting in phlegmatic evacuations in which the stool is mixed with mucus [7]. As these symptoms are seen in many type of enteritis other than bacillary dysentery, it is very clear that bacillary dysentery is not the best homolog for AK. Moreover, according to TVS Tamil medical dictionary, AK is the Tamil term for catarrhal enteritis. From the above discussions it can be indisputably concluded that AK represents enteritis of all origin and bacillary dysentery just is one among them. This implies that a detailed study on diseases precipitating with enteritis is essential to understand the nature of AK described in Siddha texts. In order to address this, AK was selected as the research topic and present study was designed carefully to have a complete contemporary understanding of AK. As more than eight Siddha formulations were previously known to be tested clinically for treatment of AK (at least for bacillary dysentery), a detailed literature search was performed across various Siddha classics to collect information about various class of medications for general *kaḻiccal* initially followed by specific search for medications for AK.

Treatment strategies for management of kaḻiccal in Siddha:

Various classes of medications prescribed for kaḻiccal in Siddha literature is shown in table. 5.1. *Cūraṇam, Lēkiyam, Cāṟu, Kaṟkam, Māttirai, Kuṭinīr* and Ney were the most commonly used medications for the management of kaḻiccal. Though most of the drugs prescribed are of purely herbal origin, there was notable number of drugs of animal and metal origin too. Few mercury based medicines such as *Liṅka Meḻuku, Liṅkatuvar Centūram, Caṇṭa mārutam* were also prescribed for uncontrolled diarrhoea. This could be due to the well-known anti-microbial property of mercury based drugs. Drugs such as *Aṉṉapēti Centūram,* which is iron based is also commonly used due to its well-established anti-peristaltic effect. However, when it comes to paediatric cases most of the medications are of herbal origin and very few drugs are of mineral origin *(Pāla Cañacīvi Māttirai)*. Apart from these lists of drugs shown in table 1.6 there are lot of medications that are listed in various Siddha drugs but were not in current use. PDC is one among them and no research has been performed till date to evaluate the effect of its activity against AK.

Table 5. 1: Commonly used siddha drugs for management of adult and paediatric diarrhoea

General Medications		Paediatric medications	
Paṟpam	1. *Pavaḷa Paṟpam* 2. *Nattai Paṟpam* 3. *Muttu Paṟpam* 4. *Nāka Paṟpam* 5. *Palakaṟai Paṟpam* 6. *Cilācattu Paṟpam*	***Cūraṇam***	1. *Kapitāṣṭaka cūraṇam (avbr)* 2. *Tayircuṇṭi Cūraṇam[43]* 3. *Mātuḷṅkkōtuc Cūraṇam[43]* 4. *Kācukaṭṭi Cūraṇam[43]* 5. *Cuṇlai Vaṟṟal Cūraṇam [44]* 6. *Panjadeepakni Cūraṇam[30]*
Lēkiyam	1. *Iñci Lēkiyam* 2. *Cātikkāy Lēkiyam* 3. *Vilvāti Lēkiyam*	***Lēkiyam***	1. *Vaccira Kaṇṭi Lēkiyam [8]*
Centūram	1. *Aṉṉapēti Centūram* 2. *Liṅkatuvar Centūram* 3. *Caṇṭamārutam*	***Ney***	1. *Vaṭṭattiruppi Ney[30]* 2. *Uppili Ney[8]* 3. *Vēliparutti Ney[30]*
Maṇapāku	1. *Vilvāti Maṇapāku* 2. *Cemparutti Maṇapāku*	***Kaṟkam***	1. *Kuṉṟi Kaṟkam [45]* 2. *Kīḻānelli Vēr Kaṟkam[8]*
Māttirai	1. *Kapāṭa Māttirai* 2. *Vaccira Māttirai* 3. *Cātikāy Māttirai*	***Māttirai***	1. *Ativiṭaya Māttirai* 2. *Kapāṭa Māttirai* 3. *Tāmarai Vaḷaiya Ēlātk Kuḷikai* 4. *Vāḻaippottik Kuḷikai* 5. *Pāla Cañacīvi Māttirai*
Kuṭinīr	1. *Tippiliyāti Kuṭinīr* 2. *Maramañcaḷ Kuṭinīr* 3. *Ativiṭaya Kuṭinīr*	***Kuṭinīr***	1. *Aṉṉak Kuṭinīr* 2. *Mātuḷam Paḻattōl* 3. *Maramañcaḷ*
Meḻuku	1. Liṅka Meḻuku 2. Cātikkāy Meḻuku	***Others***	1. *Puḷiyārai Cāru[8]* 2. *Paṭikaliṅkkatuvar [43]* 3. *Āmaiyōṭṭu Paṟpam [43]*

Considering all these information, the present study was designed to evaluate the effect of PDC in treatment of subjects affected by AK. List of drugs previously studied for management of AK is shown in table 1.6. Briefly, Patturayan et al reported that *Poṭutalai Camūlam* was effective in 80% of the subjects affected by AK in 2005. A year later, Kamalanathan et al., reported the effect of *Ventaya Cūraṇam* in subjects affected by AK. *Cītapēti Cūraṇam* is found to be clinically effective in 60% of the AK affected subjected treated by Naadimuthu *et al*. *Cukku Poṭi and Mātuḷampiñcu Cūraṇam* was reported to be significantly effective in management of bacillary and amoebic dysentery.

Table 5. 2: List of drugs previously studied for management of aama kaḻiccal

Medicine	Guide and Investigators	Year
Poṭutalai Camūlam	Dr. R. Patturayan	March 2005
Ventaya Cūraṇam	Dr. Kamalanathan & Dr. R. Patturayan	March 2006
Cītapēti Cūraṇam	Dr. Naadimuthu & Dr. R. Patturayan	September 2007
Vilvāti Cūraṇam	Dr. Gowsalya & Dr. N. Chandra Mohan	September 2008
Mātuḻampiñcu Cūraṇam	Dr. K. Shyamala	March 2009
Cukku Poṭi	Dr. D. K. Soundararajan	April 2011
Ōmac Cūraṇam	Dr. A. Beatrice & Dr. K. Shyamala	April 2012
Cītapēti Cūraṇam	Dr. K. Salma Ryhana & Dr. D. K. Soundararajan	October 2015

Beatrice et al reported the effect of *Oma chooranam* in management of bacillary dysentery, spasmodic abdominal pain and rectal tenesmus and claimed that it help in maintenance of electrolytes and normal intestinal flora. However, in all these works, AK is considered analogous to bacillary dysentery and reported to be significantly effective against it though most of these reports were hand wavy without any corroborating evidences. Quite antithetical to this, most of the Siddha texts describe AK as specific inflammation and ulceration of the mucus living of the large intestine due to any reason resulting in phlegmatic evacuations in which the stool is mixed with mucus[7]. As these symptoms are seen in many type of enteritis other than bacillary dysentery, it is very clear that bacillary dysentery is not the best homolog for AK. Moreover, according to TVS Tamil medical dictionary, AK is the Tamil term for catarrhal enteritis. From the above discussions it can be indisputably concluded that AK represents enteritis of all origin and bacillary dysentery just is one among them. This implies that a detailed study on diseases precipitating with enteritis is essential to understand the nature of AK described in Siddha texts. In order to address this, AK was selected as the research topic and present study was designed carefully to have a complete contemporary understanding of AK.

Materials and methods:

The patients reporting to out-patient department of Kuzhanthai Maruthuvam will be screened for following parameters and will be included in the study.

- **Patient history** - History of recent food intake, recent travel, recent antibiotic intake, recent infection and any other relevant history will be taken into consideration.

- **Physical Examination** - All the subjects will be physically examined in the following order: Inspection, auscultation, percussion, palpation.
- **Investigation** – The patients will be subjected to various blood investigations such as TC, DC, ESR & haemoglobin. Apart from that the stool examination will be performed to evaluate the presence of ova, cyst, and occult blood.

The subject recruitments for the study will be performed based on the criteria given in table.5.3.

Table 5. 3: Criteria followed for sample recruitment

Inclusion Criteria	Exclusion Criteria	Withdrawal criteria
1. Children aged between 1-12 years of both sex 2. Children with diarrhoea and any of the following symptoms (stools with blood and mucus, pyrexia, low pitch voice, loss of appetite, nausea and vomiting)	1. Severe Dehydration 2. Acute life threatening diseases 3. Abdominal distension due to any other serious illness	1. Patient turned unwilling to continue the course 2. Occurrence of any serious illness 3. Occurrence of any adverse drug reactions

Drug Administration:

Mode of administration – three times a day after food orally with cow's curd (however, based on the requirement it will be administered up to six times a day).

Dose - 250 mg /40 kg

Assessment parameters:

The prognosis of the subject after treatment will be described based on four categories:

- **General Criteria** – age, sex, seasonal variation, geographical location and diet habits.
- **Cause** – history of indigestion, infection, antibiotic intake, teething and fear.
- **Siddha Parameters** - *Uṭal tātukkaḷ, Uyir tātukkaḷ, Eṇvakait tērvu*
- **Signs and symptoms** – hyper peristalsis, abdominal pain, abdominal tenderness, dehydration, sore anus, vomiting and urinary output.
- **Nature of stools** – frequency of diarrhea, presence of blood and mucus, smell, colour and flatulence.

General Criteria:

Seasonal variation – Siddha classics describe the seasonal variation into six stages that are tabulated in table 5.4 and prognostic difference will be expressed based on that

Geographical distribution - Siddha classics describe the geographical location into six that are tabulated in table 5.5 and prognostic difference will be expressed based on that.

Table 5.4: Seasonal variations described in Tamill classics

	Tamil month	Gregorian calendar
Kārkālam	*āvaṇi, puraṭṭāci*	August – October
Kūtirkālam	*aippaci, kārttikai*	October – December
Muṉpaṉi	*mārkaḻi, tai*	December – February
Piṉpaṉi	*māci,paṅkuṉi*	February – April
Iḷavēṉil	*cittirai,vaikāci*	April –June
Mutuvēṉil	*āṭi, āṇi*	June –August

Table 5.5: Geographical distribution of Tirunelveli district with respect to Tamil classification

Geographical location	Description	Geographical distribution in Tirunelveli district
Kuṟiñci	The mountain and hill areas	The Western Ghats
Mullai	The forest region	The Kalakkad and Mundanthurai forests
Marutam	The plains	The river beds at Cheranmahadevi, Tirunelveli, Gangaikondan, Vallanad and Srivaikuntam
Neytal	Sea and seashore	Koodankulam and uvari
Pālai	Sandy deserts	Thisaiyanvilai, saattankulam, Udangudi

Prognostic difference based on age, sex and diet habits will be assessed by using standard methods.

Cause:

Cause of the disease will be assessed based on

1. Intake of any antibiotics within 3 days of disease progression, fear and teething
2. **Indigestion** –will be determined based on last three days of food consumed and percussion.
3. **Infection** –will be determined based on the past history of diarrhea within 3 months, recent travel, and hygiene and stool investigation.

Siddha Parameters

This will be accessed based on three categories:

1. *Uyir tātukkaḷ*, - *Vātam, Pittam,* and *Kapam* will be analyzed based on the descriptions in table 5.3and 5.4 respectively

2. *Uṭal tātukkaḷ*,-*Cāram, Cennīr, Ūṇ, Koḻuppu, Eṉpu, Mūḷai* and *Cukkilam*will be analyzed based on the descriptions in table 5.8.

Table 5.6: Disparity of *Uyir tātukkaḷ* (*Vātam*) in subjects affected by AK

Uyir Tātukkaḷ (Vātam)	Functions	Relation with disease
Pirāṇaṉ	Digestion, inspiration and expiration	Indigestion
Apāṉaṉ	Evacuation of urine and feces. Proper functions of anal spincters, expulsion of menstrual flow and sperm, ingested food extracts to respected places	Loose stools, urinary retention
Viyāṉaṉ	Regulates voluntary and involuntary movements, helps in sensory perceptions, absorption and utilization of digested food	Loose stools, dyspnea
Utāṉaṉ	Storage and release of absorbed food materials, responsible for speech, self-confidence, attitude, memory and skin tone.	Vomiting, low pitched voice
Camāṉāṉ	Digestion, assimilation and prevents the aggravation of other vayus.	Indigestion
Nākaṉ	Opening and blinking of eyes, piloerection improves learning skills.	No relation
Kūrman	Ocular movements, visual perception, yawning, lacrimal secretion	
Kirukaraṉ	Salivary secretion, nasal secretion, hunger, concentration of mind in particular thing, cough, sneezing	Loss of appetite
Tēvatattaṉ	Responsible for ocular movements, laziness, anger, internal conflict, etc.	
Taṉañceyaṉ	Performs its functions only after death	

Table 5.7:Disparity of *Uyir tātukkaḷ* (*Pittam* and *Kapam*) in subjects affected by AK

Uyir Tātukkaḷ	Functions	Relation with disease
Aṉaṟpittam	helps in digestion	Indigestion
Irañcakappittam	Increase the quantity of blood and responsible for red colour, conversion of food extract into blood.	Anemia
Cātakappittam	Helps to achieve one's desires with the help of mind, intellect and determination	
Ālōcakam	Visual perception	
Pirācakam	Gives complexion and shining	
Avalampakam	Helps in respiration, cardiac functions and regulates other kabas	Disparity in other Kabas
Kilētakam	Make the food particles soft and assist in digestion	Indigestion
Pōtakam	Sense of taste	
Taṟpakam	Cooling and refreshing all organs	Burning sensation of eyes
Cantikam	Maintains joint mobility.	

Table 5.8:Disparity of *Udal tātukkaḷ* (*Pittam* and *Kapam*) in subjects affected by AK

Udal thathukkal	Disparity seen aamka kalichal
Cāram	Loss of appetite
Cennīr	Anemia
Ūṉ	No relation
Koḻuppu	No relation
Eṉpu	No relation
Mūḷai	No relation
Cukkilam	No relation

Table 5.9: *Eṇvakait tērvu* analysis in subjects affected by AK

	Parameters have to be considered	Disparity in AK
Sparicam	Heat or coldness of the body, pain and skin nature.	Hot(fever) Cold(dehydration)
Nā	colour of the tongue, local lesion (ulceration, redness), coating, deposition and dryness of the tongue.	Pallor (anemia)
niṟam	Color of skin, conjunctiva, teeth, nail bud	No relation
moḻi	speech and voice	No relation
viḻi	Colour of eye (redness, pallor), tears, rheum	Pallor (anemia)
Malam		Loose stools
Mūttiram	Colour, odour, froth, frequency and quantity of urine	Urinary retention

Signs and symptoms:

Prognostic difference with respect to sore anus, vomiting and urinary output will be assessed with the help of verbal communication with the subject.

Hyper peristalsis – the subject will be auscultated and increase in peristaltic sounds above 30 /minute will be considered as hyperperistalsis and prognosis will be assessed based on that.

Abdominal pain / tenderness – The abdomen will be palpated and the tenderness / pain in nine regions of abdomen will be noted for prognostic assessment.

Dehydration – The dehydration status of the patient will be assessed using the method described by *Emmanuel Ademola et al* and is given in table 5. 10.

Table 5.10: Dehydration scale described by Emmanuel Ademola *et al.*

	Score of 0	Score of 1	Score of 2
General appearance	Normal	Thirsty, restless or lethargic but irritable when touched	Drowsy, limp, cold, sweaty comatose
Eyes	Normal	Slightly sunken	Very sunken
Mucus membrane	Moist	Sticky	Dry
Tears	Tears	Decreased tears	Absent tears

A score of 0 indicates no dehydration, 1-4 indicates mild to moderate dehydration and 5-8 indicates severe dehydration

Nature of stools:

Frequency of diarrhoea, presence of blood and mucus, smell and colour will be considered for prognostic assessment.

Flatulence – Abdominal flatulence will be assessed by percussion of the abdomen and will be considered for prognosis.

Results:

The clinical outcome of the effect of PDC in management of *AK*is measured in terms of three categories. They include

1. General criterion
2. Signs and symptoms
3. Causative factors
4. Nature of stools

General criterion:

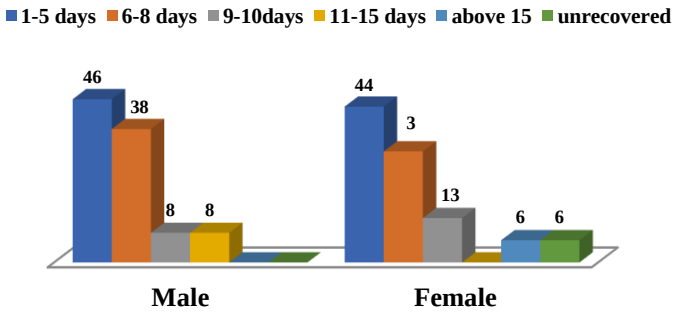

Figure 5. 1: Impact of sex in effect of PDC in subjects affected by āma kaḻiccal; n = Male(24), Female(16)

The impact due to variation in age, sex, dietary habits, seasonal variation and geographical location in efficacy of PDC in subjects affected by AK were analysed under general criterion. Approximately 75% of male and female recovered within 8 days (Figure. 5.1). 6% of female did not

recover during the course of treatment. No other significant changes were noted between male and female in recovery

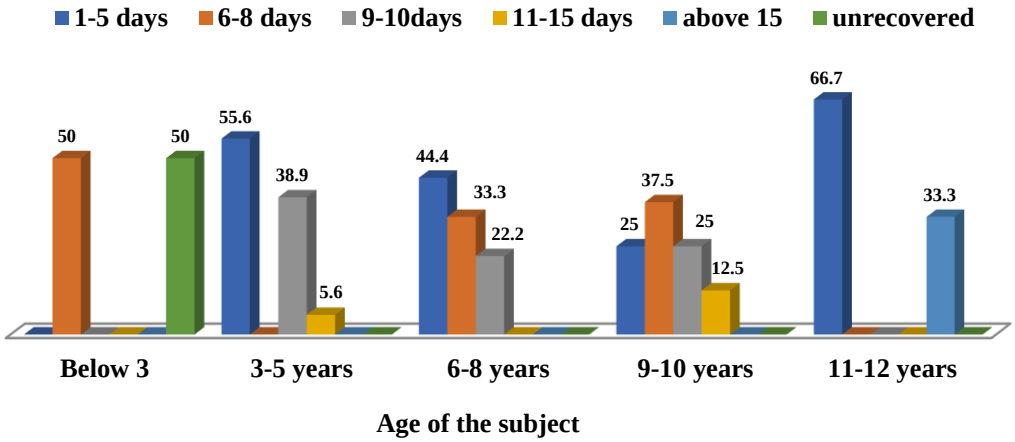

Figure 5.2:: Impact of age in effect of PDC among the subjects affected by *āma kaḻiccal*; n = Below 3 years (2), 3-5 years(18), 6-8 years(9), 9-10 years(8), 11-12 years(3)

Significant number of subjects aged between 3-12 years recovered with 5 days (Figure. 5.2). However, 33% of subjects aged between 11-12 years took more than 15 days to recover. Moreover, approximately 35% of 6-10 years children took 6-8 days for recovery. One child below 3 years did not recover during treatment.

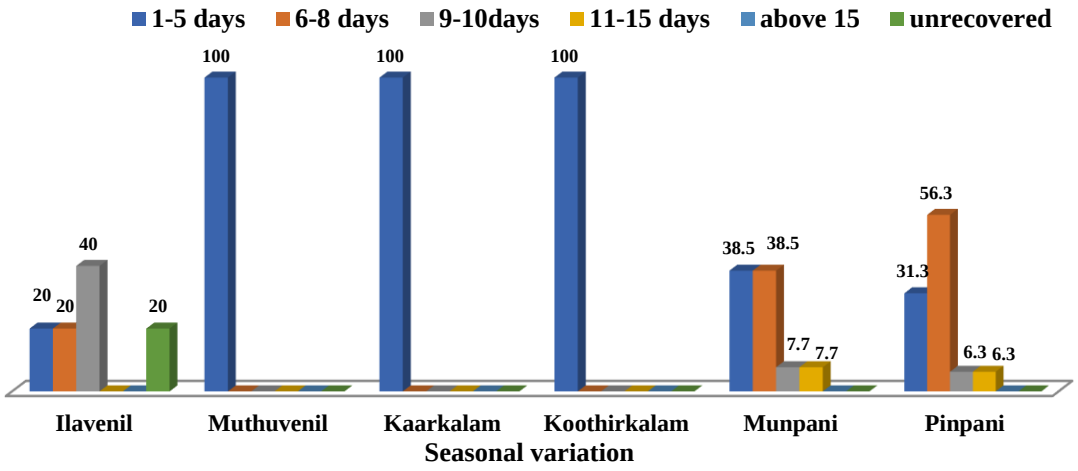

Figure 5.3: Impact of seasonal variation in effect of PDC in subjects affected by *āma kaḻiccal*; n = *Ilavenil* (5), *mutuvēṉil* (1), *Kārkālam* (3), *Kūtirkālam* (2), *muṉpaṉi* (13), *piṉpaṉi*(16)

All the Subjects affected during *mutuvēṉil, kārkālam* and *kūtirkālam* recovered within 5 days (shown in Figure.5.3). Majority of subjects affected during *muṉpaṉi* and *piṉpaṉi* recovered within 8 days. Significant number of subjects treated during *iḷavēṉil,* took more than 9 days to recover and 20% of subjects did not recover during the PDC therapy.

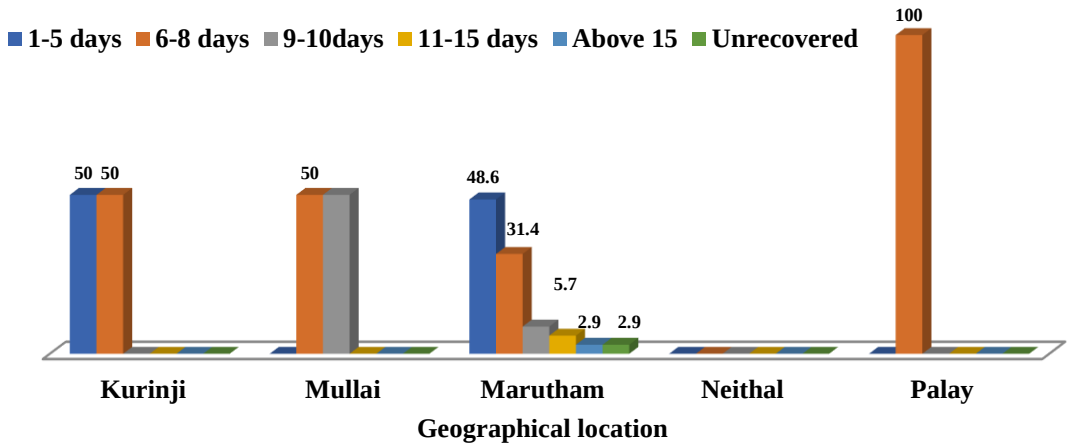

Figure 5.4: Impact of geographical location in effect of PDC in subjects affected by *āma kaḻiccal* n = *Kuṟiñci* (2), *Mullai* (2), *Marutam* (35), *Neytal* (0), *Pālai* (1)

1. Approximately 50% of subjects in *kuṟiñci, mullai, marutam, neytal, pālai and Marutham* recovered within 5 days (figure 5.4). This implies that recovery was fast in subjects living in *kuṟiñci* and *marutamtiṇai*. Significant number of recoveries was noted within 6-8 days in *kuṟiñci, mullai, marutam, pālai tiṇai*. Delayed recovery is noted in more numbers in *marutam* and *mullai.*

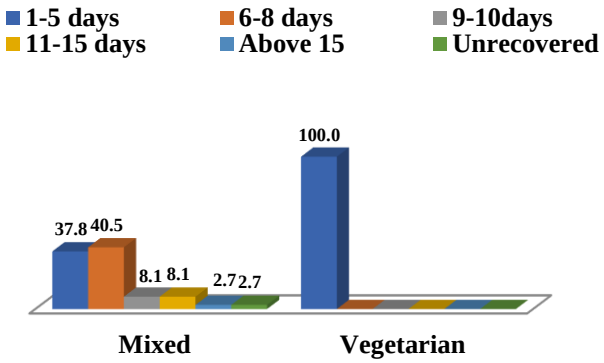

Figure 5.5: Impact of dietary habits in effect of PDC in subjects affected by *āma kaḻiccal* n = Mixed (37), Vegetarian (3)

Among 40 patients only 3 were vegetarian, however all the vegetarian subjects recovered within 5 days (Figure. 5.1). Whereas, only 37.8% subjects consuming mixed diet recovered in 1-5 days.Approximately 60% subjects took more than 6 days to recover. 2.7% subjects did not recover during the course of PDC therapy.

Siddha Assessment:

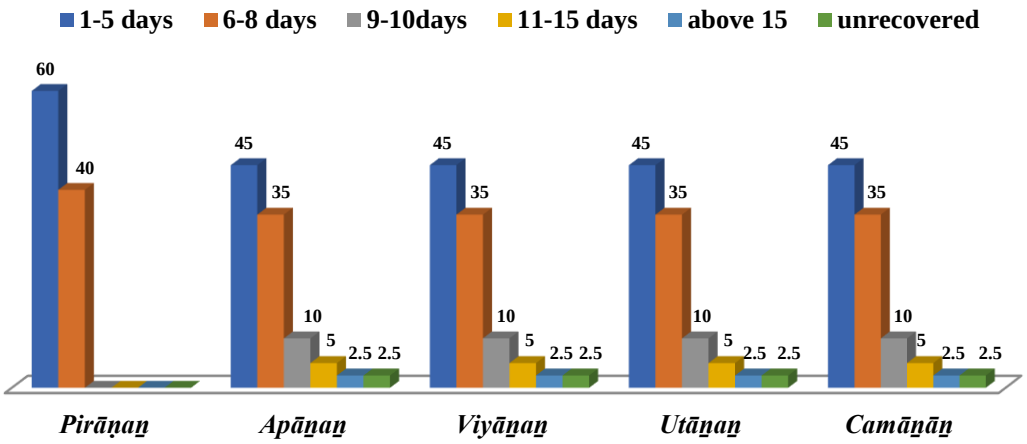

Figure 5.6: Effect PDC in normalising*Pirāṇaṉ*, *Apāṉaṉ*, *Viyāṉaṉ*, *Utāṉaṉ*and *Camāṉāṉ*among the subjects affected by *āma kaḻiccal* n=*Pirāṇaṉ*(10), *Apāṉaṉ*(40), *Viyāṉaṉ*(40), *Utāṉaṉ*(40)and *Camāṉāṉ*(40)

Among subjects affected by AK, disparity in seen in *Pirāṇaṉ*, *Apāṉaṉ, Viyāṉaṉ, Utāṉaṉ*and *Camāṉāṉ*. However, *Pirāṇaṉ*reverted back to normal in all the subjects within 8 days.Whereas, significantly *Apāṉaṉ, Viyāṉaṉ, Utāṉaṉ*, *Camāṉāṉ*and *Kirukaraṉ*were revertedback to normal within 8 days in 80% of subjects but took more than 15 days in few subjects.

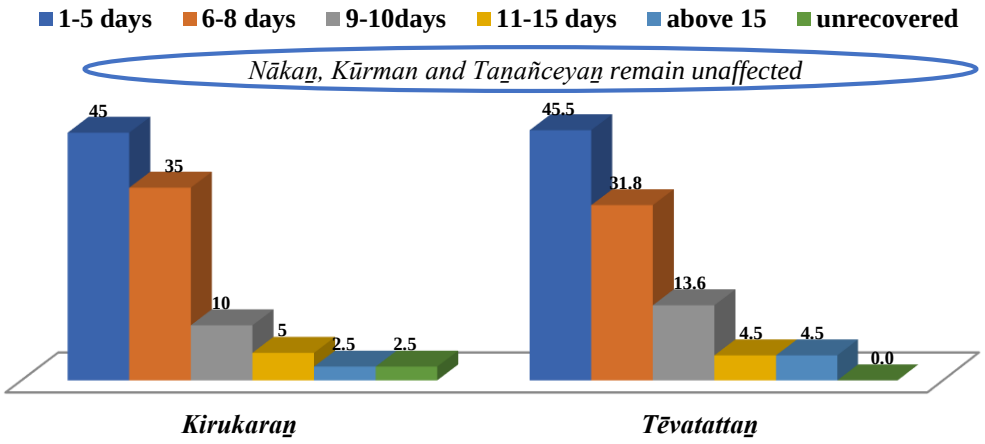

Figure 5.7: Effect PDC in normalising*Nākaṉ*, *Kūrman*, *Kirukaraṉ*, *Tēvatattaṉ*and*Taṉañceyaṉ* among the subjects affected by *āma kaḻiccal* n=*Nākaṉ*(0), *Kūrman*(0), *Kirukaraṉ*(40), *Tēvatattaṉ*(22)and*Taṉañceyaṉ*(0)

In ubapranadhi vayukkal, kirukaran is affected among 40 subjects.

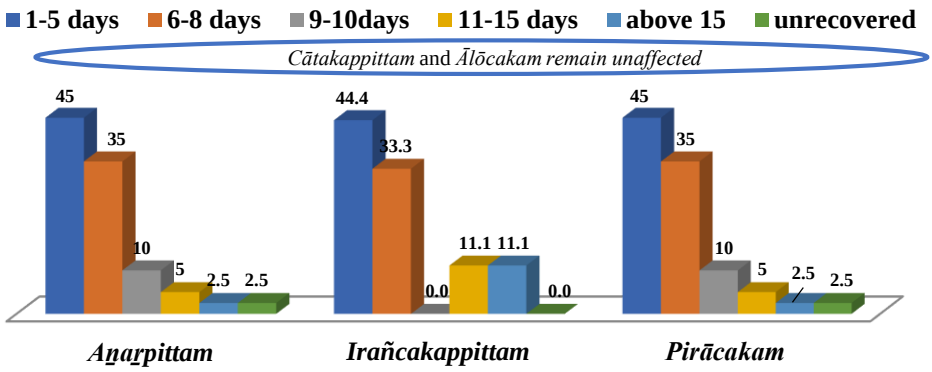

Figure 5.8:Effect PDC in normalising *Aṉaṟpittam*, *Irañcakappittam*, *Cātakappittam*, *Ālōcakam* and *Pirācakam* among the subjects affected by *āma kaḻiccal* n= *Aṉaṟpittam*(40), *Irañcakappittam*(9), *Cātakappittam*(0), *Ālōcakam*(0) and *Pirācakam*(40)

Disparity of *Aṉaṟpittam* and *Pirācakam* were noted in all the subjects and significant recovery is seen within 8 days. *Irañcakap pittam* disparity is seen in approximately 25% of the subjects and most of the subjects recovered within 8 days.

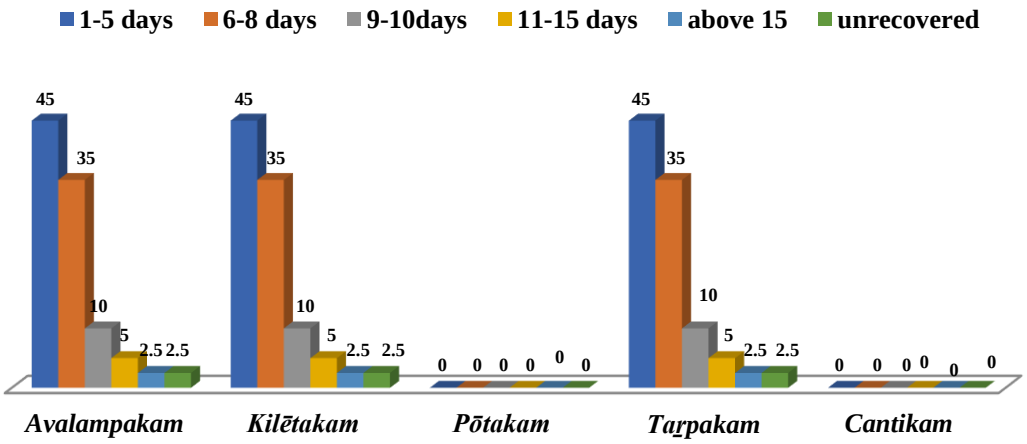

Figure 5.9: Effect PDC in normalising *Avalampakam*, *Kilētakam*, *Pōtakam*, *Taṟpakam* and *Cantikam* among the subjects affected by *āma kaḻiccal* n = *Avalampakam(40)*, *Kilētakam(40)*, *Pōtakam(0)*, *Taṟpakam(40)* and *Cantikam(0)*

Disparity of *Avalampakam, Kilētakam*and *Taṟpakam* werenoted in all the subjects and significant recovery is seen within 8 days.

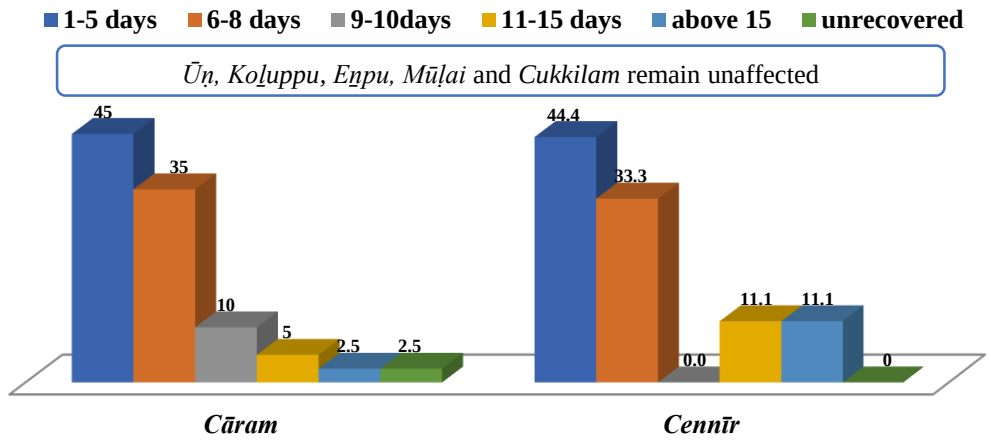

Figure 5.10: Effect of PDC in normalising *Cāram*, *Cennīr*, *Ūṇ*, *Koḻuppu*, *Eṉpu*, *Mūḷai* and *Cukkilam* among the subjects affected by *āma kaḻiccal* n = *Cāram* (40), *Cennīr*(9) , *Ūṇ*(0), *Koḻuppu*(0), *Eṉpu*(0), *Mūḷai*(0)and *Cukkilam*(0)

Cāram and *Cennīr* was affected in significant number of subjects and majority of the subjects recovered within 8 days.

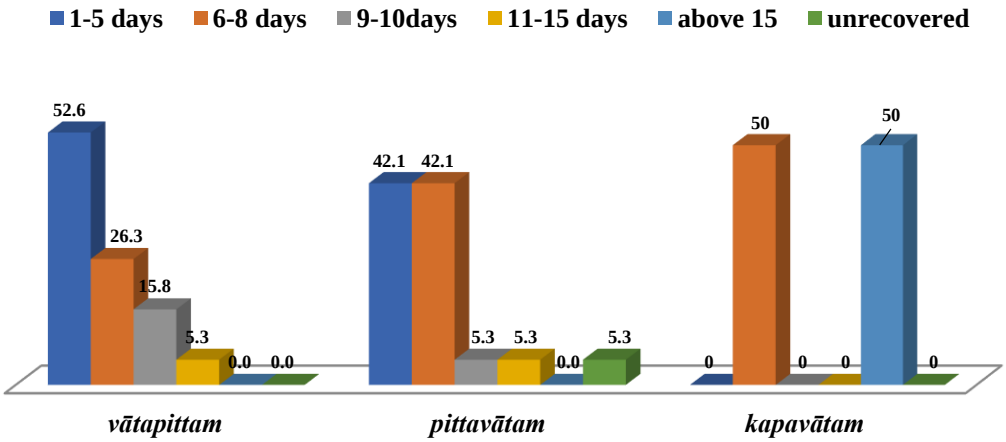

Figure 5.11: Effectof PDC in normalising the disparity in *nāṭi*

Most of the affected individual showed *vātapittam* and *pittavāta nāṭi and* most of the subjects recovered within 8 days. Among the 2 subjects with *kapavātamnāṭi*, one took more than 15 days to recover. One subject with*pittavāta* remains unrecovered

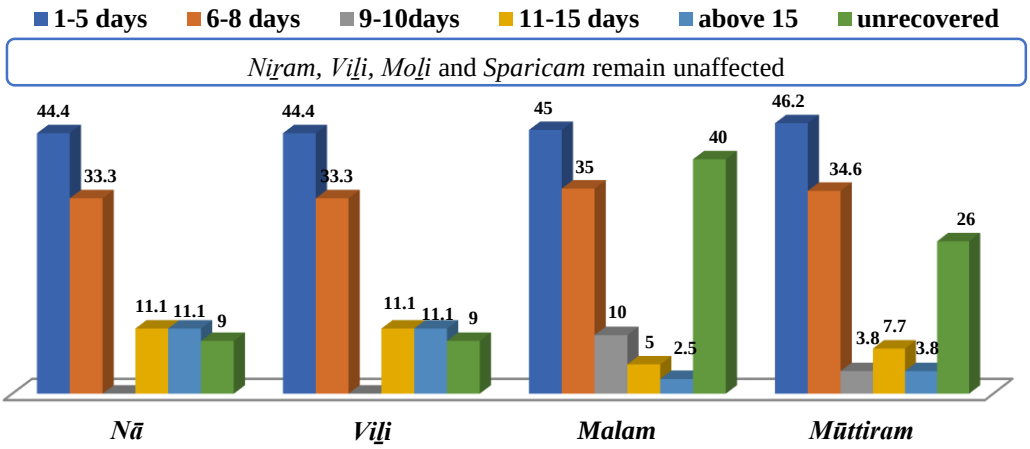

Figure 5.12: Effect of PDC in normalising *Sparicam*, *Nā*, *Niṟam*, *Moḷi*, *Viḷi*, *Malam* and *Mūttiram* among the subjects affected by *āma kaḷiccal* n = *Nā*(9), *Niṟam*(0), *Moḷi*(0), *Viḷi*(9), *Sparicam*(0), *Malam*(40)and*Mūttiram*(26)

In Envagai thervugal, malam, *Mūttiram*, *Nā*, *ViḷI* were affected and remaining unaffected.

Signs and symptoms:

Among 40 subjects, 77% subjects recovered from abdominal pain within 8days. (Figure.4.6).However 3% took above 15 days to recover and 3% subjects did not recover during the course of PDC therapy.

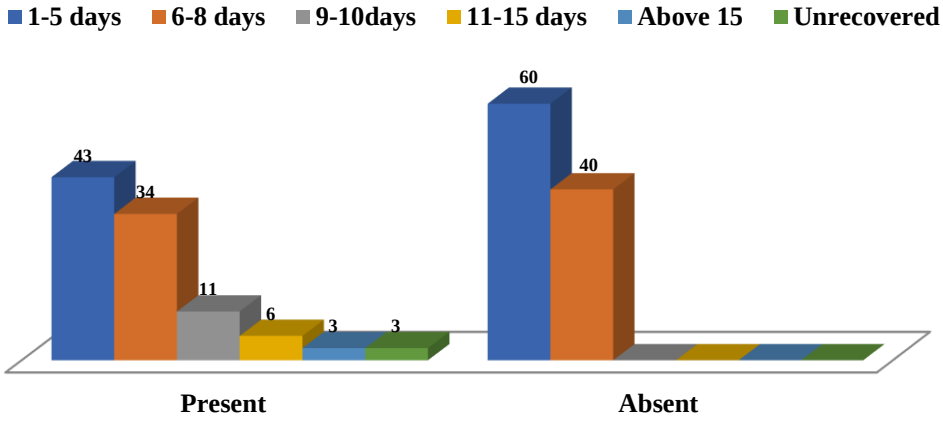

Figure 5.13: Effect PDC in reducing abdominal pain among the subjects affected by *āma kaḷiccal* n=35 (present), 5 (absent)

Most of the subjects recovered from anal irritation, flatulence and vomiting within 8 days (Figure 5.15). However, considerable number of subjects took around 9-15 days to

recover from hyperperistalsis. One subject did not recover during the course of PDC therapy from hyperperistalsis and vomiting.

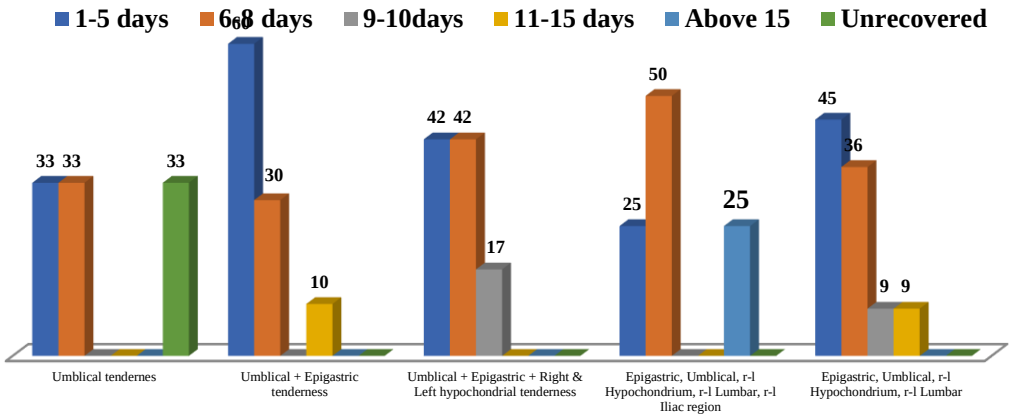

Figure 5.14: Effect of PDC in reducing the abdominal tenderness in subjects affected by *āma kaḻiccal*

Most of the subjects with different types of abdominal tenderness recovered within 8 days. However, few subjects with tenderness in umbilical, epigastric, hypochondrial and lumbar regions took more than 8 days to recover. One subject with umblical tenderness fail to recover.

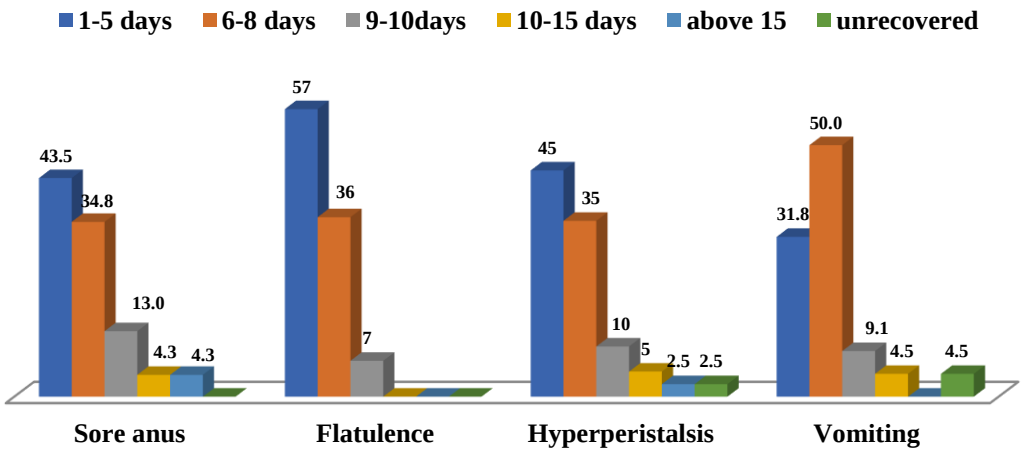

Figure 5.15: Effect of PDC reducing Sore anus, flatulence, hyperperistalsis and vomiting among the subjects affected by *āma kaḻiccal* n = Sore anus (23), flatulence (14), Hyperperistalsis (40), Vomiting (22)

Significant percentage of subjects at various stages of dehydration recovered within 8 days (Figure 5.16). However, one subject with moderate dehydration took around 15 days to recover and one subject did not recover during the course of PDC therapy from dehydration.

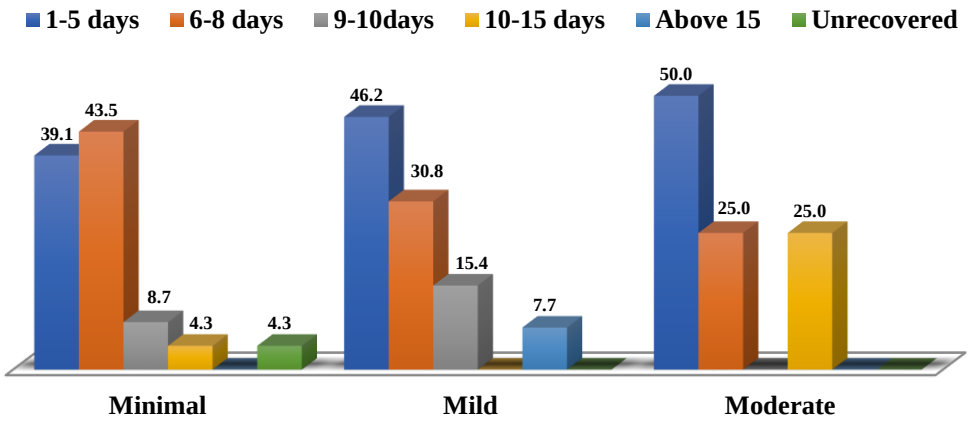

Figure 5.16: Effect of PDC in improving the dehydration status of subjects affected by *āma kaḻiccal* n= 23 (minimal), 13 (mild), 4 (moderate)

Causative factors:

Most of the subjects affected due to indigestion, infection, seasonal variation, fear and antibiotic intake recovered within 6-8 days. One among the three reported subjects with *AK*after antibiotic intake took more than 15 days to recover. One infant with *AK* during teething did not recover with PDC therapy.

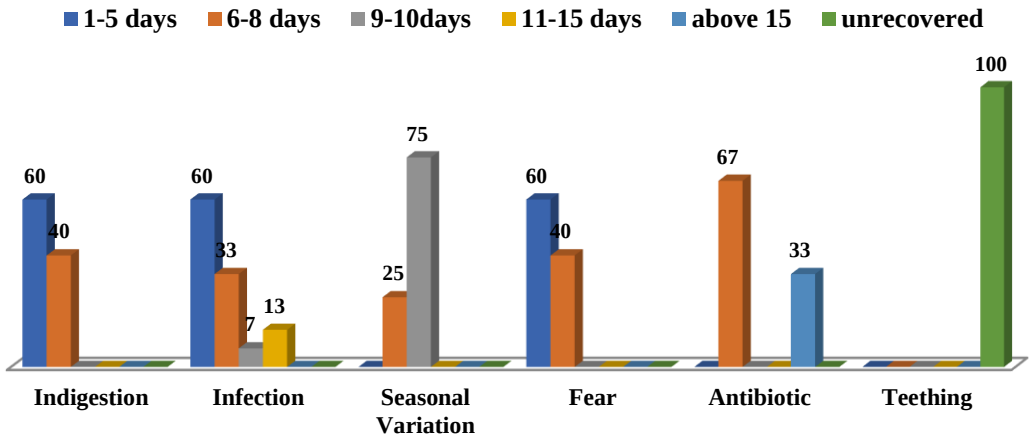

Figure 5.17: Effect of PDC therapy on *āma kaḻiccal* with respect to the causative factor

Nature of stools:

Most of the stools were of green and yellow colour and bloody stools is found only in 4 subjects. Apart from two subjects, all other subjects recovered within 15 days.

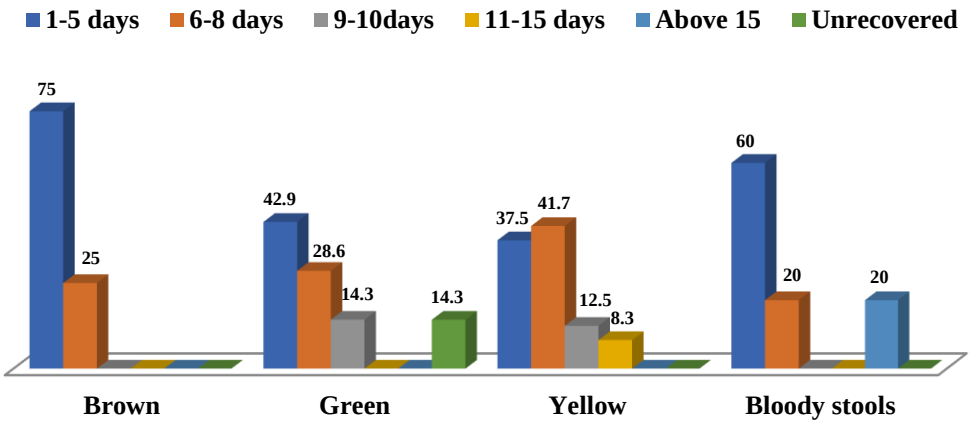

Figure 5.18: Effect of PDC in management of *āma kaḻiccal* with respect to colour of the stools. n = Brown, green, yellow, bloody

Significant number of subjects with diarrhoea, foul smelling stools, mucus in stools and mucus with blood in stools recovered within 8 days (Figure 5.19). Considerable number of subjects took 9-15 days to recover from foul smelling and mucus containing stools. 20% of subjects with blood and mucus in stools took more than 15 days to recover.

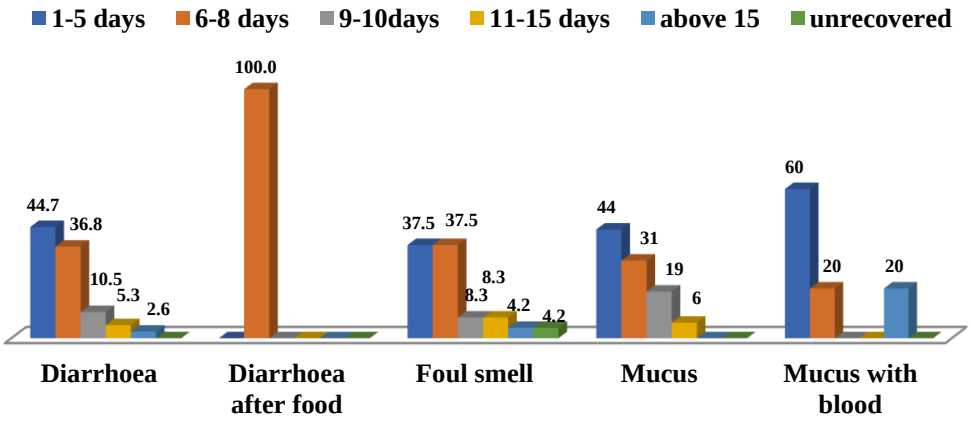

Figure 5.19 : Effect of PDC in management of diarrhoea, diarrhoea after food, foul smell, mucus and mucus with blood in subjects affected by *āma kaḻiccal*

Significant number of subjects with bowel movements of 1-4 times per day, 5-6 times per day and above 6 times per day recovered within 8 days (Figure. 5.20). However, approximately 30% of subjects with bowel movements of 5-6 times per day took more than 10 days to recover. One subject with bowel movements of 4 times a day did not recover.

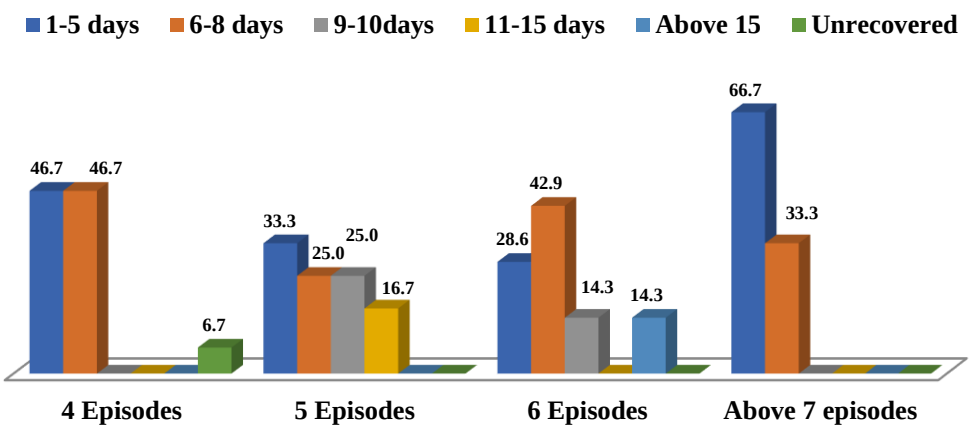

Figure 5.20: Effect of PDC in frequency of stools per day among subjects affected by *āma kaḻiccal.* n= 4 episodes (15), 5 episodes (12), 6 episodes(7), above 6 episodes (6).

Most of the subjects with past history of diarrhoea within 2 months before present illness recovered within 8 days (Figure. 5.21). One subject with past history of diarrhoea before 2 weeks took 15 days to recover.

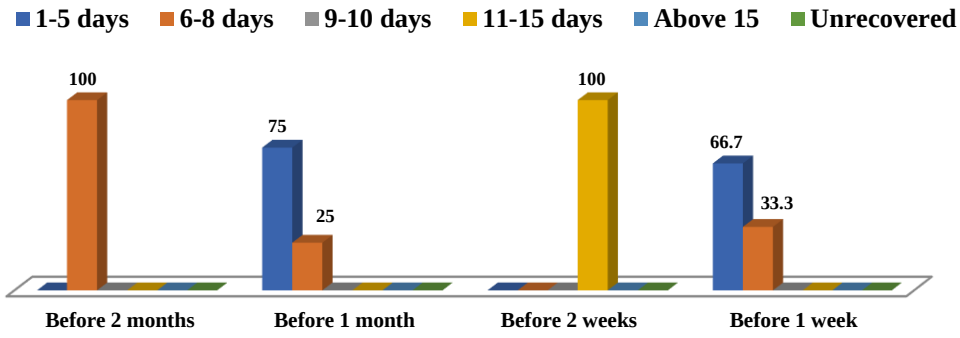

Figure 5.21: Effect of PDC in the treatment of *āma kaḻiccal* with respect to the past history of diarrhoea.

Subjects treated within 5 days showed fast recovery within 8 days. (Figure. 4.15).One subject with disease duration more than 6 days took above 15 days to recover. In subjects with disease progression after consumption of protein diet, spicy food and cow's milk, there is 100% recovery within 8 days (Figure. 5 .22).

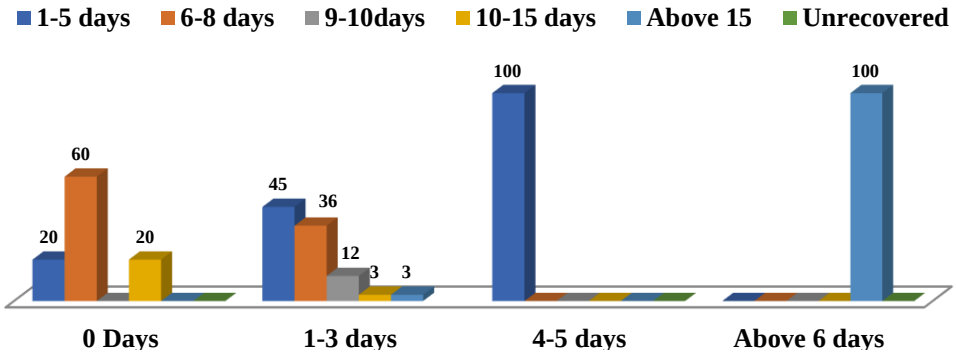

Figure 5.22: Effect of PDC in treatment of subjects affected by *āma kaḻiccal* with respect to duration of the disease food (6)

Significant number of subjects with disease progression after consuming fast food took around d 9-15 days to recover. One subject with normal diet history did not recover during the course of PDC therapy.

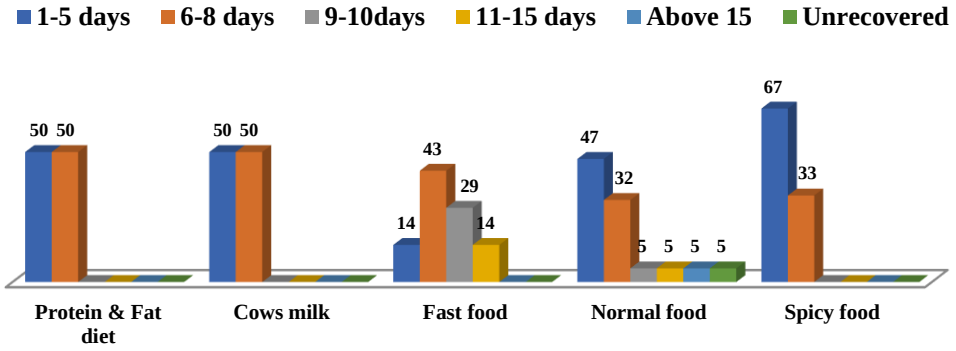

Figure 5.23: Effect of PDC in management of *āma kaḻiccal* with respect to recent food history .n=Protein (6), Cow's milk(2), Fast food (7), Normal food(19), Spicy

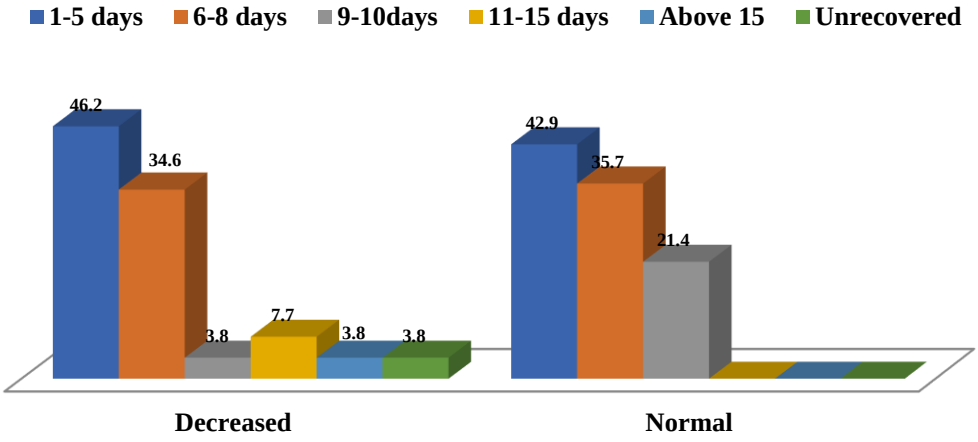

Figure 5.24: Effect of PDC in maintaining urine output among subjects affected by *āma kaḻiccal.*

80% with decreased urinary output recovered within 8 days and 3.8 % remains did not recover during the course of study (Figure. 5.24).

Discussion:

Despite the high incidence of AK in male compared with female, recovery was faster in male. Effect of psychological stress related hormones would have played a major role in better effect of PDC in males. Our study also showed that PDC therapy was also effective in diarrhoea due to fear and anxiety. It is a well-established fact that psychological stress can modulate the gastrointestinal and immune systems through the hypothalamus-pituitary-adrenal (HPA) axis. Huges *et al* showed that acute psychological stress was directly related to symptoms of gastrointestinal dysfunction. PDC is found to be more effective in children of 3-10 years and was not much better in age group below 3 years and above 11 years. This could possibly due to the underdeveloped HPA axis in children below 3 years and disturbed HPA axis from 11-17 years. As the effect of ingredients of PDC on HPA is not well established in literature, this study provides new information on the benefit of PDC (and its individual ingredients) therapy on HPA axis in young children. Few of the vātam, pittam and kapam subtypes are imbalanced in AK subjects but most of the imbalances were compared within 8 days. As mentioned in Siddha texts, our study demonstrated that 80% of AK cases were reported only during *muṉpaṉi*, *piṉpaṉi* during which pitta humour gets naturally aggravated. Moreover few cases reported during *kārkālam, kūtirkālam* and *mutuvēṉil*, in which *pitta* humour remains normal recovered within 5 days. This clearly shows that AK was primarily due to aggravated *pittam*, and initially the aggravated humour should be balanced before treatment. This also substantiate the statement Dr. Sampasivampillai in his dictionary which dictates the predisposing cause to this disease are the changing period from hot weather into the damper season of the monsoon. In pranathi vaayukal, the disparity is seen in pirāṇaṉ, apāṉaṉ, viyāṉaṉ, utāṉaṉand camāṉāṉ. It may be due to change in physiological function. One among the function of pranan is the digestion of food which is altered in loose stools. In apāṉaṉ, the normal function is expulsion of stool and urine and helps in contraction of anal sphincter which is affected in AK. Viyāṉaṉ which is paravukaal functions both in voluntary and involuntary muscles which also helps in

flexion and extension of organs. As utāṉaṉ is melnokkungaal, vomiting and low pitched voice indicates the disparity of utāṉaṉ. Loss of appetite among subjects indicates disparity in kirukaran. Though most of the cases of AK are reported from *marutam* region, it could not be concluded that AK is predominant in *marutam* as the study centre was primarily located in *marutam* and chances of affected subjects reporting from *Neytal, Pālai, kuṟiñci, mullai* will be relatively rare. Hence a multi-cantered trail is required to confirm this. Among the reported subjects only few subjects were vegetarians and they recovered within 5 days which shows the disease management was much easier in vegetarians compared with subjects in mixed food habits.

As far as the cause is concerned, only T. V. Sambasivampillai, cite AK as Tamil description of catarrhal enteritis. Modern texts refer enteritis as a pathological condition with a decrease in the consistency of stools and an increase in the frequency of evacuations (typically more than 3 in 24 hours), with or without fever or vomiting. This can be caused due to various factors such as infection, indigestion, drugs, auto-immune disorders, fear and some normal physiological processes such as teething. Other secondary factors such as geographical location, seasonal variation, age, sex and dietary habits play an important role in regulating these factors in an indirect way. As descriptions of AK in Siddha texts were very similar to the symptoms of enteritis, all the above-mentioned factors were considered carefully in this study. The primary cause of enteritis due to infection among infants and children worldwide is viral gastroenteritis caused by rotavirus. Other causes include bacterial pathogens such as *E.coli, Vibrio cholerae, Shigella*, and *Salmonella* and protozoa such as *Entamoeba histolytica*, *Cryptosporidium parvum* and *Giardia lambli*. Seasonal change and immune status of the child play an important role in prognosis of the disease. In the present study, PDC therapy was found to be more effective in gastritis due to infection. Anti-microbial and anti-oxidant properties of various extract of *Mangifera indica* (MI) kernel, *Murraya koenigii* (MK) [46, 47], *Solanum torvum* (ST) [48], *Carum copticum* (CC) and *Trigonellum foenum graecum* (TFG) is well established in literature. Sibanarayanan *et al.*reported that methanolic extract of CC, TFG andMI inhibited the growth of various Multiple Drug resistance strains (*Enterococcus, Staphylococcus, Acinetobacter, Citrobacter, Enterobacter, E.coli, Klebsiella, Proteus and Pseudomonas*) isolated from

urinary tract infections in a significant way. [49] *Kabuki et al*. reported antimicrobial activities of an ethanolic extract from MI kernels against 18 bacterial species including food- borne pathogens. These anti-bacterial activities were reported to be due to the presence of hydrolysable tannins in them. Furthermore, MK was reported for its anti-tuberculosis effect [47], analgesic and anti-inflammatory property [50]. Methyl caffeate, a compound isolated from ST is found to have antimicrobial activity particularly against gram negative bacteria species (*Salmonella, Pseudomonas, Proteus, Bacillus and Klebseilla*) and few fungal species (*Candida albicans and Aspergillus flavus*)[48]. CC has antiviral activity against hepatitis C virus and Japanese encephalitis.[51]and found to inhibit the growth of *Staphylococcus aureus Shigella flexneri* and *pseudomonas auerginosa*..[52]. TFG extract was able to prevent the proliferation of acanthameobiasis [53] and inhibits *H pylori* by enhancing alpha-amylase activity[54]. However, [55] Rachel O Mahony *et al* claim that only the TFG sprouts were effective against *H.pylori* and not the TFG seeds. Methanolic fractions of TFG have anti-fungal activity against *Botrytis cinerea, Fusarium graminearum, Alternaria sp., Pythium aphanidermatum,* and *Rhizoctinia solani*. [56]. These reports vouch the significant effect of PDC therapy in cases of enteritis due to infections. As, PDC has ingredients which has anti-microbial sensitivity against broad group of bacteria, virus and protozoans, this can be used in management of all kind of infections leading to gastroenteritis. However, the synergistic effect of all these ingredients should be clinically evaluated for better understanding.

In present study, the subjects treated with therapy within 5 days of onset of disease recovered within short period of time. However subjects treated 5 days after onset of disease took longer time to recover and this result was irrespective of the people with past history of diarrhoea within a period of 2, 3 months. This shows that PDC therapy is also very promising in management of gastritis due to indigestion.Apart from its anti-microbial properties; ingredients of PDC also possess anti-inflammatory and anti-oxidant properties. Most of the patient were presented with abdominal pain and hyperperistalsis and significant number of patients were reported with sore anus, flatulence and vomiting. This could possibly due to the systemic inflammation of large intestine as described by various authors in siddha literature. Effect of PDC was very significant in addressing all these symptoms within 8 days. MI kernel extracts were also found to inhibit the

prostaglandin secretion and in turn will reduce the electrolyte permeability in gut. Aqueous extract ofST shows anti-inflammatory and analgesic activity by inhibition of prostaglandin. Effect of carbazole alkaloids isolated from MK viz., namely koenimbine and kurrayam were proved to be effective in decreasing the peristaltic movements in rats [57]. *Arque-Ajeeb,* a Unani formulation with CC as main ingredient was found to inhibit serotonin-induced diarrhoea in a dose dependent manner*[58]*.TGF seed fractions were reported to protect against the gastric ulcer induced by ethanol in rats [59]. In addition, CC is able to increase the gastric acid secretion time and the amount of gastric acid. Moreover, it was shown that the CC can reduce the transit time of food in the digestive system of mice. Inhibitory effect of CC on the contractions of the digestive tract smooth muscle, especially the intestines, increased activities of digestive enzymes and bile secretion was reported, which support its effect on gastrointestinal tract.[45] . TFG enhances lipase and chymotrypsin action in liver and intestine of rats[60]. Moreover, MI kernel extract was reported to be a strong anti-oxidant which even has the capacity to neutralise the viper venom.This could be the primary reason for the enhanced activity of PDC therapy in gastritis with indigestion. Though, PDC therapy did not show any effect in enteritis during teething and moderate effect in enteritis due to anti-biotic intake, as the sample size was small, further studies are required to confirm this.

Conclusion:

Though the preclinical effects of various ingredients of PDC is already documented in literature, synergistic effect of PDC is not reported till date. This study is a step towards understanding the synergistic effects of all the ingredients of PDC in human subjects. As this study was performed with limited number of subjects, only little information could be made out of it. However, this could be taken as a lead and further trials should be performed with large scale to understand the activity of PDC in management of AK. PDC was found to be more effective inAK due to infection and indigestion. But the effect of PDC on AK due to antibiotic intake and physiological process such teething could not be established due to small sample size. Hence specific studies based on causative factors should be performed with large sample size to have a better understanding on PDC. Furthermore, long term studies should be performed to understand the influence of

season and geographical location in cause, progression and manifestation of AK. Once we have that information, we will have a complete contemporary understanding of PDC activity in humans.

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Summary and conclusion

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This study was primarily designed to understand the nature of AK described in Siddha literature through Siddha and biomedical parameters. Moreover, the effect of PDC in management of AK affected subjects is also evaluated. Briefly, the raw materials required for the preparation of PDC was collected from palayamkottai and authenticated by taxonomist in GSMCH, Palayamkottai. After authentication, the collected raw materials were sun dried, pulverised and mixed together. This is sieved in a cotton cloth (vasthirakayam) and very fine powder is obtained. The prepared drug was then characterised by various qualitative and instrumental analysis. Preliminary analysis showed the presence of calcium, sulphate, chloride, starch, ferrous form of iron and amino acid and absence of carbonate, ferric form of iron, phosphate, albumin, tannic acid, zinc and reducing sugar. The standardisation parameters were determined as per PLIM guidelines. Degradation temperature of PDC was found to be around 350- 400 ^{o}C. After characterisation, the acute toxicity of the drug was assessed in rats as per OECD 425 guidelines and was found to be safe upto 2000mg /kg body weight. With this information from the acute toxicity study, a 28 day repeated dose toxicity was performed and no observable toxicity is noted up to 100 times the therapeutic equivalent dose indicated for humans in Siddha texts. Preliminary antimicrobial activity study on *Streptococcus pneumonia, Pseudomonas aeruginosa, Staphylococcus aureus* and *Klebsiella pneumoniae* reveals that PDC was effective only against *Straptococcus pneumoniae*. Any subjects reporting with mucoid stools or stools with blood and mucus were included in the study. Clinically, AK was predominant during the month of December to April (*mu̲npa̲ṉi*, *pi̲npa̲ṉ)* and the prevalence in vegetarian subjects is very low. This study revealed that PDC was

significantly effective in AK due to infection and indigestion. However, the effect of PDC on AK due to antibiotic intake and physiological process such teething could not be established due to small sample size. Hence specific studies based on causative factors should be performed with large sample size to have a better understanding on PDC. Furthermore, long term studies should be performed to understand the influence of season and geographical location in cause, progression and manifestation of AK. Once we have that information, we will have a complete contemporary understanding of PDC activity in subjects affected by AK.

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References:

1. Subbarayappa, B.V., *The roots of ancient medicine: an historical outline.*
2. Sujatha, V., *Pluralism in Indian medicine: Medical lore as a genre of medical knowledge.* Contributions to Indian, 2007. **2**: p. 169–202.
3. sebastia, B., *Government institutions vs. associations. The multifaceted expression of Siddha medicine in Tamilnadu.*http://hal.archives-ouvertes.fr/index.php?halsid=873g1ltelqedm6n6r6a0bknrh3&view_this_doc=halshs-00408677&version=1, 2009.
4. Sébastia, B., *Competing for medical space Traditional Practitioners in the Transmission and Promotion of Siddha Medicine.* 2011.
5. *citta maruṭuvāṅka curukkam,* ed. D.k.s. Uthamarayan. 1983, chennai: Indian medicine and homeopathy.
6. *Nōy nāṭal nōy mutal nāṭal tiraṭṭu,* ed. D.M. Sanmugavelu. 1967, Chennai: Indian Medicine and Homeopathy.
7. pillai, T.V.S., *Siddha medical dictionary*. 1998, Chennai: Department of Indaian medicine- Homeopathy.
8. *pāla vākaṭam (kuḻantai maruttuvam)*. 1933, chennai-600 002: sri venkateshwara enterprises.
9. *matalai nōy pākam 2*. 2008, Kanyakumari: A.T.S.V.S SIDDHA MEDICAL COLLEGE munsirai, pudhukadai. 349.
10. Wang, D.H., *Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality,1980–2015: a systematic analysis for the Global Burden of Disease Study 2015.* Lancet, 2017.
11. Claudio F. Lanata, C.L.F.-W., Ana C. Olascoaga, Carla X. Torres, Martin J. Aryee, Robert E. Black, *Global Causes of Diarrheal Disease Mortality in Children <5 Years of Age: A Systematic Review.* Plos one, 2-13. **8**(9).
12. Lora L Iannotti, I.T., Kathryn L Clitheroe and Mark J Manary, *Diagnosis and treatment of severely malnourished children with diarrhoea.* journal of paediatrics and child health, 2014.
13. Metcalf, C., *Chronic diarrhoea:investigation, treatment and nursing care.* 2006.
14. Radbill, S.x., *Teethings as a Medical Problem - Changing Viewpoints Through the Centuries.* Clinical pediatrics. **4**(9).
15. Childs, p., *dietary fat, dyspepsia, diarrhoea, and diabetes.* The british journal of surgery, 1972. **59**(9).
16. Olivier Chassany, A.M.a.J.F.B., *Drug-Induced Diarrhoea.* Drug Safety, 2000. **22**(1).
17. Shira Idit Doron, P.L.H.a.S.L.G., *Probiotics for Prevention of Antibiotic-associated Diarrhea.* J Clin Gastroenterol, 2008. **42**: p. S58-S63.
18. McFarland, L.V., *Antibiotic associated diarrhea: Epidemiology trends and treatment.* Future microbiol 2008. **3**(5).
19. mushtaq, S.a.a.M., *Antibiotic Associated Diarrhea in Children.* Indian pediatrics, 2009. **46**.

20. Dominique Turck, J.-P.B., Jacques Marx, Hélène Kempf, Patrick Giard,Olivier Walbaum, André ,Lacombe, Françoise Rembert, Francis Toursel, Paul Bernasconi, Frédéric Gottrand, Lynne V. McFarland, and Karine Bloch, *Incidence and Risk Factors of Oral Antibiotic-Associated Diarrhea in an Outpatient Pediatric Population.* Journal of Pediatric Gastroenterology and Nutrition, 2003. **37**: p. 22-26.
21. Friedman, G., *The Role of Probiotics in the Prevention and Treatment of Antibiotic-Associated Diarrhea and Clostridium Difficile Colitis.* Gastroenterol Clin, 2012. **41**: p. 763-779.
22. Carla Massignan, M.C., André Luís Porporatti, Secil Aydinoz, GrazielaDe Luca Canto, Luis Andre Mendonça Mezzomo, Michele Bolan,, *review article Signs and Symptoms of Primary Tooth Eruption: A Meta-analysis.*Pediatrics, 2016. **137**(3).
23. Michael L. Macknin, M.P., Jonathan Jacobs, MD and Christine Skibinski, *Symptoms Associated With Infant Teething: A Prospective Study.* Pediatrics, 2000. **105**(4).
24. Maria Rosaria A. Muscatello , A.B., Gianluca Pandolfo ,Umberto Mico, Simona Stilo , Mariagrazia Scaffidi , Pierluigi Consolo, Andrea Tortora , Socrate Pallio , Giuseppa Giacobbe , Luigi Familiari ,Rocco Zoccali, *Depression, Anxiety and Anger in Subtypes of Irritable Bowel Syndrome Patients.* J Clin Psychol Med Settings, 2010. **17**: p. 64-70.
25. E Guthrie, F.C., L Fernandes, J Ratcliffe, J Van der Jagt, J Martin, S Howlett, N Read, J Barlow, and B.T. D Thompson, *Cluster analysis of symptoms and health seeking behaviour differentiates subgroups of patients with severe irritable bowel syndrome.* GUT, 2003. **53**: p. 1616–1622.
26. Spiller, R., *Serotonin and GI clinical disorders.* elsilver, 2008.
27. *WHO/UNICEF statement clinical management of acute diarrhea.*
28. A.D. Alan´ıs , F.C., J.A. Cervantes , J. Torres G.M. Ceballos, *Antibacterial properties of some plants used in Mexican traditional medicine for the treatment of gastrointestinal disorders.* Journal of ethnopharmacology, 2005: p. 153–157.
29. Metcalf, C., *Continuing professional development Gastroenterology.* royal college of nursing, 2002.
30. *piḷḷaippiṇi maruttuvam 2*. 2006.
31. *citta vaittiya tiraṭṭu*, ed. D.k.c.u. Dr.ka.nā. kuppucāmi mutaliyār. 2006, chennai: Indian medicine and homeopathy.
32. *yūki muṉivar vaittiya cintāmaṇi*, ed. rā.tiyākarācaṉ. 1896, chennai: indian directorate of medicine
33. LOHAR, D.D.R., *Protocol For Testing Ayurvedic, Siddha & Unani Medicines (PLIM).*
34. Rosalen, I., *Alternative Animal and Non-Animal Models for Drug Discovery and Development: Bonus or Burden?* Pharm Res, 2016: p. 11095-016-2069.
35. Ramamurthy Murugan, T.V., Manickavasakam Kumarswamy, *Toxicological Study of a Siddha Sastric Formulation Arumuga Chendhuram in Rat Model.* 2016. **6**(03): p. 081-087.

36. M Sudha, P.P., Kanagavalli *Acute - Sub Acute Toxicity Studies on Siddha Drug Velvanga Parpam.* International Journal of Pharmacy and pharmaceutical research, oct 2015. **4**(3).
37. B. Chitra, R.S.R.a.V.S., *Toxicity Evaluation of P.rn. a Cantirotaya Cent.ram, a Siddha Medicine in Wistar Rats.* Hindawi Publishing Corporation, 2014: p. 10 pages.
38. Robert B. Saper, R.S.P., Anusha Sehgal, and R.B.D. Nadia Khouri, , Janet Paquin, Venkatesh Thuppil, and Stefanos N. Kales, , *Lead, Mercury, and Arsenic in US- and Indian-Manufactured Ayurvedic Medicines Sold via the Internet.* NIH public accessv JAMA, 2008. **300**(8): p. 915-923.
39. *OECD guideline for testing of chemicals.* 2001.
40. *OECD guidelines for the testing of chemicals 407.* 2008.
41. Sunday A. Ejeh, P.O.a.S.E.A., *Anti-diarrhea activity of the aqueous root bark extract of Byrsocarpus coccineus on castor oil-induced diarrhea in Wistar rats.* Veterinary World, 2017. **10**.
42. Ghader Jalilzadeh-Amin, M.M., *Antidiarrheal activity and acute oral toxicity of Mentha longifolia L. essential oil.* Avicenna journal of phytomedicine, 2014. **5**: p. 128-137.
43. *kuḻantai maruttuvam*.
44. *citta vaittiya tiraṭṭu*, ed. k.n.k.m.H.P.I.M. de, dr.ka.cu.uttamarāyaṉ H.P.I.M. 1998, chennai: Indian and Homeopathy.
45. Mohammad Hossein Boskabady, S.A., and Azam Alavinezhad, *Review Article Carum copticum L.: A Herbal Medicine with Various Pharmacological Effects.* BioMed Research International, 2014. **2014**.
46. Thilahgavani Nagappan , P.R., Mohd Effendy Abdul Wahid ,Thirukanthan Chandra Segaran and Charles S. Vairappan *Biological Activity of Carbazole Alkaloids and Essential Oil of Murraya koenigii Against Antibiotic Resistant Microbes and Cancer Cell Lines.* Molecules, 2011. **16**: p. 9651-9664.
47. Sumanta Kumar Naik, S.M., Avinash Padhi, Rashmirekha Pati and Avinash Sonawane, *Evaluation of antibacterial and cytotoxic activity of Artemisia nilagirica and Murraya koenigii leaf extracts against mycobacteria and macrophages.* BMC Complementary and Alternative Medicine, 2014. **14**(87).
48. Chandrasekhar Balachandran , V.D., Naif Abdullah Al-Dhabi ,K. Balakrishna ,Nitin Pal Kalia,Vikrant Singh Rajput , Inshad Ali Khan , Savarimuthu Ignacimuthu, *Antimicrobial and Antimycobacterial Activities of Methyl Caffeate Isolated from Solanum torvum Swartz. Fruit.* Indian J Microbiol, 2012. **52**(4): p. 676-681.
49. Toshihide Kabuki , H.N., Megumi Arai , Shigeko Ueda , and S.i.D. Yoshiharu Kuwabara *Characterization of novel antimicrobial compounds from mango (Mangifera indica L.) kernel seeds.* Food Chemistry, 2000: p. 61-66.
50. Shailly Gupta, M.G., Manmohan Singhal, Ganesh N. Sharma, and Vikas Garg, *Leaves extract of murraya koenigii linn for antiinflammatory and analgesic activity in animal models.* Journal of Advanced Pharmaceutical Technology & Research, 2010. **1**(1): p. 68-77.
51. Soumen Roy, P.C., and Abhay Chowdhary, *Evaluation of antiviral activity of essential oil of Trachyspermum Ammi against Japanese encephalitis virus.* Pharmacognosy Research, 2015. **7**(3): p. 263-267.

52. Arora, G.J.K.a.D.S., *Antibacterial and phytochemical screening of Anethum graveolens, Foeniculum vulgare and Trachyspermum ammi.* BMC Complementary and Alternative Medicine, 2009. **9**(30).
53. Yasemin Kaya , A.B., Ülkü Karaman , Nilay Ildız ,Yeliz Kasko Arıcı , Gamze Kaçmaz , Zeynep Kolören ,Yusuf Konca, *Amebicidal effects of fenugreek (Trigonella foenum-graecum) against Acanthamoeba cysts.* Wiley food science and nutrition, 2018.
54. Shetty, R.R.a.K., *Improved α-amylase and Helicobacter pylori inhibition by fenugreek extracts derived via solid-state bioconversion using Rhizopus oligosporus.* Asia Pac J Clin Nutr, 2007. **16**(3): p. 382 - 392.
55. Rachel O'Mahony, H.A.-K., Deepaka Weerasekera, Neluka Fernando, Dino Vaira, John Holton, Christelle Basset, *Bactericidal and anti-adhesive properties of culinary and medicinal plants against Helicobacter pylori.* World Journal of Gastroenterology, 2005. **11**(47): p. 7499 - 7507.
56. R. Haouala, S.H., A. El-Ayeb, R. Khanfir, N. Boughanmi, *Aqueous and organic extracts of Trigonella foenum-graecum L. inhibit the mycelia growth of fungi* 2008.
57. Suvra Mandal , A.N., Manoj Kar , Samir K. Banerjee , Ashes Das , S.N. Upadhyay ,R.K. Singh , Avijit Banerji , Julie Banerji *Antidiarrhoeal activity of carbazole alkaloids from Murraya koenigii Spreng (Rutaceae) seeds.* Elsevier B.V, 2010. **81**: p. 72-74.
58. Mohd Aleem Khan, N.A.K., Iqbal Ahmad Qasmi, and G.A.a.S. Zafar, *Research article Protective effect of Arque-Ajeeb on acute experimental diarrhoea in rats.* BMC Complementary and Alternative Medicine, 2004. **4**(8).
59. R. Suja Pandian, C.V.A., P. Viswanathan *Gastroprotective effect of fenugreek seeds (Trigonella foenum graecum) on experimental gastric ulcer in rats.* Journal of Ethnopharmacology, 2002. **81**: p. 393- 397.
60. Platel/Srinivasan, *Influence of dietary spices and their active principles on pancreatic digestive enzymes in albino rats.* Nahrung, 2000.

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List of transliterated words

Transliterated form	Tamil form
ēlam	*ஏலம்*
karuñcīrakam	*கருஞ்சீரகம்*
lavaṅkakapaṭṭai	*லவங்கபட்டை*
Āmai	*ஆமை*
Āmaiyōṭṭu Paṟpam	*ஆமையோட்டு பற்பம்*
ĀmakkaḻIccal	*ஆமக் கழிச்சல்*
Aṉṉak Kuṭinīr	*அன்ன குடிநீர்*
Aṉṉapēti Centūram	*அன்னபேதி செந்தூரம்*
Aṉupava Vaittiya Tēva Rakaciyam	*அனுபவ வைத்திய தேவ ரகசியம*
Aṉupava Vaittiya Tēva Rakaciyam	*அனுபவ வைத்திய தேவ ரகசியம்*
Apiṉi	*அபினி*
Arttarā Kirāṇi	*அர்த்தர கிராணி*
Aticāra	*அதிசார*
Aticāra Tōṭam	*அதிசார தோடம்*
Ativiṭaya Kuṭinīr	*அதிவிடய குடிநீர்*
Ativiṭayam	*அதிவிடயம்*
Ātmaraṭcāmirtam Eṉum Vaittiya Cāracaṅkirakam	*ஆத்மரக்ஷாமிர்தம் என்னும் வைத்திய சாரசங்கிரகம்*
Calak	*சலக்*
Caṅkarak	*சங்காரக்*
Caṅkirakak Kirāṇi	*சங்கிராக் கிராணி*
Caṉṉipāta Aticāram	*சன்னிபாத அதிசாரம்*
Caṇṭamārutam	*சண்டமாருதம்*
Carapēntirar Vaittiya Muṟaikaḷ	*சரபேந்திரர் வைத்திய முறைகள்*

Cātikkāy	*சாதிக்காய்*
Cātikkāy Lēkiyam	*சாதிக்காய் லேகியம்*
Cātikkāy Meḻuku	*சாதிக்காய் மெழுகு*
Cātipattiri	*சாதிபத்திரி*
Cemparutti Maṇapāku	*செம்பருத்தி மணப்பாகு*
Ceriyāppaṭuvaṉ	*செரியாப்படுவன்*
Cilācattu Paṟpam	*சிலாசத்து பற்பம்*
Cilēttuma Aticāram	*சிலேத்தும அதிசாரம்*
Cilēttuma Kirāṇi	*சிலேத்தும கிராணி*
Cītak	*சீதக்*
Cītapēti Cūraṇam	*சீதபேதி சூரணம்*
Cītapēti Cūraṇam	*சீதபேதி சூரணம்*
Cōpak	*கோபக்*
Cukku Poṭi	*சுக்கு பொடி*
cūkkuma uṭal	*சூக்கும உடல்*
Cuḻimāntam	*சுழிமாதம்*
Cuṇlai Vaṟṟal Cūraṇam	*சுண்டைவற்றல் சூரணம்*
Cura	*சுர*
Cura Aticāram	*சுர அதிசாரம்*
Iñci Lēkiyam	*இஞ்சி லேகியம்*
Intuppu	*இந்துப்பு*
Irai	*இறை*
Iraimāntam	*இரைமாதம்*
Īraṟpaṭuvaṉ	*ஈரற்படுவன்*
Irattam	*ரத்தம்*
Kācukaṭṭi Cūraṇam	*காய்ச்சுக்கட்டி சூரணம்*
Kaṇa	*கண*

Kaṇai	*கணை*
Kāntam	*காந்தம்*
Kapam	*கபம்*
Kapāṭa Māttirai	*கபாட மாத்திரை*
Kapitāṣṭaka cūraṇam	*கபிட்டாஷ்தக சூரணம்*
Karppa Kirāṇi	*கருப்பக் கிராணி*
Kaṭuppu	*கடுப்பு*
KaṭuppukkaḷIccal	*கடுப்புக் கழிச்சல்*
Kīḻānelli Vēr Kaṟkam	*கீழாநெல்லி வேர் கற்கம்*
Kirāmpu	*கிராம்பு*
Kirāṇi	*கிராணி*
Kōpāla Paṇikkar Ācāṉ Pāla Vākaṭam	*கோபால பணிக்கர் ஆசான் பால வாகடம்*
Kuṉma Kirāṇi	*குன்ம கிராணி*
Kuṉṟi Kaṟkam	*குன்றி கற்கம்*
kuru-cīṭaṉ	*குரு சித்தன்*
Liṅka Meḻuku	*லிங்க மெழுகு*
Liṅkatuvar	*லிங்கதுவர்*
Mānta	*மாத*
Manta Aticāram	*மாந்த அதிசாரம்*
Maramañcaḷ Kuṭinīr	*மரமஞ்சள் குடிநீர்*
Matalai Noy 2	*மதலை*
Mātuḷam Paḻattōl	*மாதுளம் பழத்தோல்*
Mātuḷampiñcu Cūraṇam	*மாதுளம்பிஞ்சு சூரணம்*
Mūlakkotippu	*மூலக்கொதிப்பு*
Mūlavāyu Kirāṇi	*மூலவாயு கிராணி*
Muttu Paṟpam	*முத்து பற்பம்*
Nāka Paṟpam	*நாக பற்பம்*

Naṟcīrakam	நற்சீரகம்
Nattai Paṟpam	நத்தை பற்பம்
Niṇa	நிண
NiṇakkaḻIccal	நிணக்கழிச்சல்
Nīrpaṭuvaṉ	நீர்படுவன்
Nīrppāṭu	நீர்ப்பாடு
Ōmac Cūraṇam	ஓமச் சூரணம்
Oṭṭu Kirāṇi	ஒட்டு கிராணி
Paccilai	பச்சிலை
Pāl	பால்
Pal Muḷaikkum Pōtu Kaḻiccal	பல் முளைக்கும்போது கழிச்சல்
Pāla Cañacīvi Māttirai	பாலசஞ்சீவி மாத்திரை
Pāla Vākaṭa	பால வாகடம்
Palakaṟai Paṟpam	பலகரை பற்பம்
Panjadeepakni Cūraṇam	பஞ்சதீபாக்கினி சூரணம்
Paṭikaliṅkkatuvar	படிகலிங்கதுவர்
Pavaḻa Paṟpam	பவள பற்பம்
Payam Aticāram	பயம் அதிசாரம்
PeruṅkaḻIccal	பெருங்கழிச்சல்
Peruṅkāyam	பெருங்காயம்
Piḷḷai Piṇi Maruttuvam	பிள்ளை பிணி மருத்துவம்
Piraḷi	பிரளி
pirāṇaṉ	பிராணன்
Pitta Aticāram	பித்த அதிசாரம்
Pitta Kirāṇi	பித்தக் கிராணி
Pittakapam	பித்தம்
Pittam	பித்தம்

Porumal	*பொருமல்*
Puḷiyārai Cāru	*புளியாரை சாறு*
Ratta	*ரத்த*
Ratta	*இரத்த*
Ratta Aticāram	*ரத்த அதிசாரம்*
Rattak	*ரத்தக்*
Rattapaṭuvaṉ	*இரத்தபடுவன்*
stūla uṭal	*ஸ்தூல உடல்*
Tāmarai Vaḷaiya Ēlātk Kuḷikai	*தாமரை வளைய குளிகை*
Tayircuṇṭi Cūraṇam	*தயிர் சுண்டி சூரணம்*
Tippiliyāti Kuṭinīr	*திப்பிலியாதி குடிநீர்*
Tirikaṭuku	*திரிகடுகு*
Tiritōca Aticāram	*திரிதோட அதிசாரம்*
Tiritōca Kirāṇi	*திரிதோட கிராணி*
Toṅkal Kaḻiccal	*தொங்கல் கழிச்சல்*
Tonta Kirāṇi	*தொந்த கிராணி*
Tōṣā Aticāram	*தோஷ அதிசாரம்*
Tōṭa	*தோட*
Tukka Aticāram	*துக்க அதிசாரம்*
Uppili Ney	*உப்பிலி நெய்*
Uppu	*உப்பு*
Uṣṇavāyu Kirāṇi	*உஷ்ணவாயு கிராணி*
Vaccira Māttirai	*வச்சிர மாத்திரை*
Vāḻaippottik Kuḷikai	*வளைப்பொட்டி குளிகை*
Vānti	*வாந்தி*
Varaḷ	*வறள்*
Vāta Aticāram	*வாத அதிசாரம்*

Vātak Kirāṇi	*வாதக் கிராணி*
Vātak Kirāṇi	*வாதக் கிராணி*
Vātam	*வாதம்*
Vaṭṭattiruppi Ney	*வட்டத்திருப்பி நெய்*
Vayirrruk	*வயிற்றுக்*
Vayirrrukkaṭuppu	*வயிற்றுக்கடுப்பு*
Vayirrrukkotippu	*வயிற்றுக்கொதிப்பு*
Vayirrruḷaivu	*வயிற்றுளைவு*
Vāyuviṉāl Uṇṭākum Kirāṇi	*வாயுவினால் உண்டாகும் கிராணி*
Vēliparutti Ney	*வேலிப்பருத்தி நெய்*
Veḷḷuṭaik	*வெல்லுடைக்*
Ventaya Cūraṇam	*வெந்தய சூரணம்*
Ventaya Cūraṇam	*வெந்தய சூரணம்*
Veppu	*வெப்பு*
Vilvāti Maṇapāku	*வில்வாதி மணப்பாகு*
Vilvāti Cūraṇam	*வில்வாதி சூரணம்*
Vilvāti Cūraṇam	*வில்வாதி சூரணம்*
Vilvāti Lēkiyam	*வில்வாதி லேகியம்*
Viṭā	*விட*
Yūkimuṉi Vaittiya Cintāmaṇi	*யூகிமுனி வைத்திய சிந்தாமணி*
Yūkimuṉi Vaittiya Kāviyam	*யூகிமுனி வைத்திய காவியம்*
	லிங்கம்

ANNEXURE:

The Tamil Nadu Dr.M.G.R.Medical University

69, Anna Salai, Guindy, Chennai - 600 032.

This Certificate is awarded to Dr/~~Mr~~/~~Mrs~~ A.R.KARTHIKA

For participating as ~~Resource Person~~ / Delegate in the Twenty Fifth Workshop on

"RESEARCH METHODOLOGY & BIOSTATISTICS"

For AYUSH Post Graduates & Researchers

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University From 3rd to 7th July 2017.

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PROF & HEAD, DEPT.OF SIDDHA

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GOVERNMENT SIDDHA MEDICAL COLLEGE
PALAYAMKOTTAI

SCREENING COMMITTEE

DEPARTMENT OF KUZHANTHAI MARUTHUVAM

Candidate Registration No.....

This is to certify that the dissertation topic **An open clinical study to evaluate the Clinical fficacy of Siddha Sasthric Formulation PANCHA DEEPAKINI CHOORANAM for the reatment of AAMA KALICHAL** has been approved by the screening committee.

anch	Department	Name	Signature
1	Pothu Maruthuvam	Prof. Dr.A.Manoharan. MD(s).,	
2	Gunapadam	Dr.A.Kingsly MD(s)., Associate Professor	
3	Sirappu Maruthuvam	Prof. Dr.A.S.Poongodi Kanthimathi MD(s).,	
4	Kuzhandhai Maruthuvam	Prof. Dr.D.K.Soundararajan. MD(s).,	
5	Noi Nadal	Prof. Dr.S.VictoriaMD(s).,	for
6	Nanju Nool Maruthuvam	Prof. Dr.M.Thiruthani. MD(s).,	For

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Arulmigu Kalasalingam College of Pharmacy

(Approved by AICTE, PCI, New Delhi and Affiliated to The Tamil Nadu Dr.M.G.R. Medical University, Chennai)
Anand Nagar, Krishnankoil - 626 126. Srivilliputtur (Via), Virudhunagar Dist., Tamil Nadu
Phone: 04563-289006 Email: akcpprl@yahoo.com Website: www.akcp.ac.in

"Kalvivallal"
T.Kalasalingam, B.Com.,
Founder

"Ilayavallal"
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Er.S.Arjun Kalasalingam, M.S., (USA)
Director

Dr.N.Venkateshan, M.Pharm., Ph.D.,
Principal

CERTIFICATE

INSTITUTIONAL ANIMAL ETHICS COMMITTEE APPROVED BY CPCSEA, NEW DELHI.

Name of the principle investigator : Dr. Ar.Karthika

Title of the Project : Anti diarrhoeal & Anti spasmodic activity of *Panchadeepakini chooranam*

Proposal Number : AKCP/IAEC/95/2018-19

Date of received after modification (if any) : Nil

Date of received after second Modification : Nil

Approval date : 27.04.2019

Animals : Rat

Expiry Date : Nil

Name of IAEC Chairperson : Dr.N.Venkateshan

Signature of IAEC Chairperson

GOVERNMENT SIDDHA MEDICAL COLLEGE

PALAYAMKOTTAI

Certificate of Botanical Authentication

Certified that the following plant drugs used in Siddha formulation of***Panchadeepakinichooranam*** (Internal) for the management of ***Aamakalichal*** taken up for the Post Graduate Dissertation Studies by **Dr.Karthika.Ar**PG Dept. of KuzhanthaiMaruthuvam, is correctly identified and authenticated through Visual Inspection / Organoleptic Characters / Experience, Education & Training / Morphology/Microscopical& Taxonomical methods.

S.NO	DRUG	BOTANICAL NAME	FAMILY	PART USED
1.	Maankottai paruppu	Mangifera indica	Anacardiaceae	Seed
2.	Karuvepilai ilai	Muraya koenigii	Rutaceae	Leaf
3.	Sundaikai vatral	Solanum torvum	Solanaceae	Fruit
4.	Vendhayam	Trigonellafoenum graecum	Fabaceae	Seed
5.	Omam	Carum copticum	Apiaceae	Fruit

Station: Palayamkottai

Date: 20.9.18.

Authorized Signature

CERTIFICATE

This Certifies that

Dr. Karthika. Ar 3rd year *PG Scholar*

has actively participated in the continuing medical education training program held on 20th February 2019 at Government Siddha Medical College, Palayamkottai

---

ORGANISED BY

Post graduate department of Kuzhanthai maruthuvam, Government Siddha Medical College, Palayamkottai

Prof. Dr. S. K. Soundararajan, MD (s)	*Dr. K. Shyamala, MD (s)*	*Prof. Dr. R. Neelavathy, MD (s) PhD*
HEAD OF THE DEPARTMENT	CO-ORDINATOR	PRINCIPAL

WORLD BREASTFEEDING WEEK

CERTIFICATE

This Certifies that

Dr. Ar. Karthika 2nd Year PG Scholar

[illegible]

Government Siddha Medical College, Palayamkottai

ORGANISED BY

Post graduate department of Kuzhanthai maruthuvam, Government Siddha Medical College, Palayamkottai

Dr. K. Shyamala, MD (s)	*Prof. Dr. S. K. Soundararajan, MD (s)*	*Prof. Dr. R. Neelavathy, MD (s) PhD*
CO-ORDINATOR	HEAD OF THE DEPARTMENT	PRINCIPAL

INTERNATIONAL JOURNAL OF REVERSE PHARMACOLOGY AND HEALTH RESEARCH

ISSN 2589 - 3343 A Peer Reviewed Interdisciplinary Medical Journal

CERTIFICATE OF PUBLICATION

The board of "International Journal of Reverse Pharmacology and Health Research''
(ISSN 2589-3343, www.ijrphr.com) is herby awarding this certificate to Co-author

Dr Karthika Ar

in recognition of the publication of the Research/Review Paper entitled

Biochemical analysis of Siddha polyherbal drug Ilagu seena chooranam

CODENJ: IJRPHR

Published in Volume **2** , Issue **3** , Jul-Sep, **2019**

Editor-in-Chief
(Dr. Vijila Chandrasekar)

Member, Editorial Board

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Karthika Ar

in recognition of the publication of the Research/Review Paper entitled

Qualitative chemical analysis of Siddha polyherbal drug Panchadeepakini chooranam

CODENJ: IJRPHR

Published in Volume **2** , Issue **3** , Jul-Sep, **2019**

Editor-in-Chief
(Dr. Vijila Chandrasekar)

Member, Editorial Board

FULL DETAILS (Read-only) -> Click Here to Create PDF for Current Dataset of Trial

CTRI No	**CTRI/2018/05/014263** [Registered on: 31/05/2018] **Trial Registered Prospectively**
Acknowledgement Number	REF/2018/05/019976
Last Modified On:	30/05/2018
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Drug Siddha
Study Design	Other
Public Title of Study Clarification(s) with Reply Modification(s)	To evaluate the therapeutic efficacy of siddha formulation Panchadeepakini chooranam in the treatment of Aama kalichal(Dysentry in children)
Scientific Title of Study	An open clinical study to evaluate the clinical efficacy of Siddha Sasthric Formulation Pancha Deepakini Chooranam for the treatment of Aama Kalichal
Trial Acronym	
Secondary IDs if Any	Secondary ID: Nil — Identifier: NIL
Details of Principal Investigator or overall Trial Coordinator (multi-center study)	**Name**: ARKARTHIKA **Designation**: PG Scholar **Affliation**: Govt Siddha Medical College Hospital **Address**: Op No-7, Department of Kuzhanthai Maruthuvam, Govt Siddha Medical College Hospital, Palayamkottai. Tirunelveli TAMIL NADU 627002 India **Phone**: **Fax**: **Email**: drkarthikarajendran92@gmail.com
Details Contact Person Scientific Query	**Name**: DKSoundara rajan **Designation**: Professor **Affliation**: Govt Siddha Medical College Hospital **Address**: Op No-7, Department of Kuzhanthai Maruthuvam, Govt Siddha Medical College Hospital, Palayamkottai. Tirunelveli TAMIL NADU 627002 India **Phone**: **Fax**: **Email**: dr.dks2012@gmail.com

Details Contact Person Public Query	**Name** ARKARTHIKA **Designation** PG Scholar **Affliation** Govt Siddha Medical College Hospital **Address** Op No-7, Department of Kuzhanthai Maruthuvam, Govt Siddha Medical College Hospital, Palayamkottai. Tirunelveli TAMIL NADU 627002 India **Phone** **Fax** **Email** drkarthikarajendran92@gmail.com
Source of Monetary or Material Support	AR.KARTHIKA Op No-7, Department of Kulanthai Maruthuvam, Govt Siddha Medical College Hospital, Palayamkottai.
Primary Sponsor	**Name** ARKARTHIKA **Address** Op No-7, Department of Kulanthai Maruthuvam, Govt Siddha Medical College, Palayamkottai. **Type of Sponsor** Other [PG Scholar Stipend]
Details of Secondary Sponsor	Name: Nil; Address: NIl
Countries of Recruitment	India
Sites of Study Clarification(s) with Reply Modification(s)	No of Sites = **1** Name of Principal Investigator: ARKarthika; Name of Site: Govt Siddha Medical College Hospital; Site Address: Op No-7, Department of Kuzhanthai Maruthuvam, Govt Siddha Medical College Hospital, Palayamkottai. Tirunelveli TAMIL NADU; Phone/Fax/Email: 2572736 drkarthikarajendran92@gmail.com
Details of Ethics Committee	No of Ethics Committees= **1** Name of Committee: IEC Govt Siddha Medical College Palayamkottai; Approval Status: Approved; Date of Approval: 29/05/2017; Approval Document: Approval File; Is IEC?: No
Regulatory Clearance Status	Status | Date | Aproval Document

from DCGI	Not Applicable | No Date Specified | No File Uploaded
Health Condition / Problems Studied Clarification(s) with Reply	**Health Type**: Patients; **Condition**: Patients suffering from Dysentry,
Intervention / Comparator Agent	**Type**: Comparator Agent; **Name**: Nil; **Details**: Nil **Type**: Intervention; **Name**: Panchadeepakini Chooranam; **Details**: Panchadeepakini Chooranam-oral route twice daily. Dose-500mg-1to5 years 1gm - 6to12 years
Inclusion Criteria	**Age From**: 1.00 Year(s) **Age To**: 12.00 Year(s) **Gender**: Both **Details**: 1. Mild and moderate dehydration 2. Blood tinged motion or mucoid stools 3. Increased Temperature 4. Low pitch voice 5. Loss of appetite 6. Nausea 7. Vomiting 8. Patients who are willing to stay in IPD Ward for 7 days or willing to attend OP Dept. 9. Children who are willing to undergo blood and urine and stool samples for laboratory investigation. 10. Patient's informant / Parent willing to sign the informed consent stating that he/she will consciously stick to the treatment during 7 days but can opt out of the trial of his / her own conscious discretion.
Exclusion Criteria	**Details**: 1. Children above 12 years. 2. Severe Dehydration 3. Diarrhoea due to other causes 4. Acute life threatening cases 5. Abdominal distension due to any other serious illness
Method of Generating Random Sequence	Not Applicable
Method of Concealment	Not Applicable
Blinding/Masking	Open Label
Primary Outcome	**Outcome**: To evaluate the clinical efficacy of the drug "Panchadeepakini Chooranam" to reduce Dysentry and its presentations like abdominal pain, nausea and vomiting, rapid dehydration, weight loss,headache, muscle pain, etc….; **TimePoints**: 7 days

Secondary Outcome	<table><tr><th>Outcome</th><th>TimePoints</th></tr><tr><td>To correlate the signs and symptoms of Aama kalichal with modern aspect. To study the chemical and pharmacological action of the drug towards the efficacy of the medicine. Along with the analysis Siddha investigatory techniques such as envagai thervu, neerkuri, neikuri are also done.</td><td>7 days</td></tr></table>
Target Sample Size	**Total Sample Size=**"40" **Sample Size from India=**"40" **Final Enrollment numbers achieved (Total)=** "Applicable only for Completed/Terminated trials" **Final Enrollment numbers achieved (India)=**"Applicable only for Completed/Terminated trials"
Phase of Trial	Phase 2
Date of First Enrollment (India) Clarification(s) with Reply Modification(s)	04/06/2018
Date of Study Completion (India)	Applicable only for Completed/Terminated trials
Date of First Enrollment (Global)	No Date Specified
Date of Study Completion (Global)	Applicable only for Completed/Terminated trials
Estimated Duration of Trial	**Years=**"2" **Months=**"0" **Days=**"0"
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Not Yet Recruiting
Publication Details	None Yet
Brief Summary	**STUDY ENROLLMENT** In this study, patients reporting at the OPD with the clinical symptoms of • Regurgitation of milk • Diarrhoea with mucus or blood • abdominal pain • nausea and vomiting • head ache

- Anaemia (due to blood loss in motion)
- Loss of appetite
- Fever
- Chillness of extremities
- Low pitched voice etc.

Patient will be examined clinically for enrolling in the study based on inclusion and exclusion criteria.

- The patients who are to be enrolled patients would be informed (Form IV) about the study, trial drug, possible outcomes and the objectives of the study in the language and terms understandable to them and to their informants.
- After ascertaining the parent's willingness, informed consent would be obtained in writing from them in the consent form (Form IV-A).
- All these patients will be given unique registration card in which patient's registration number of the study address, phone number and Doctor's phone number etc. will be given, So as to report easily if any complications arise.
- Complete clinical history, complications and duration, examination findings – all would be recorded in the prescribed proforma in the history and clinical assessment forms separately. Screening form- I will be filled up; Form I-A, Form II and Form III will be used for recording the patient's history, clinical examination of symptoms, signs and laboratory investigations respectively.
- Patients would be advised to take the trial drug and appropriate dietary advice (Form IV-D) would be given according to the patient's perfect understanding.

CONDUCT OF THE STUDY:

The trial drug "***Panchadeepakini Chooranam***" will be given for 7 days (twice a day), Op patients should visit the hospital once in 2 days. At each clinical visit clinical assessment is done and prognosis should be noted. For IP patients the drug will be given for 3 days and followed up till 7 days and the clinical assessment will be done daily. Laboratory investigations will be done 0 day, 03rd day, 07th day of the trial. For IP patients who are not in a situation to stay in the hospital for a long time they will be advised to attend the OPD for further follow up.

Siddha investigations like *Neerkuri* and *Neikuri* will be carried over. After the end of the treatment the patient will be advised to visit the OPD for another 1 week for follow up. If any trial patients who fail to collect the trial drug on the

prescribed day but wants to continue in the trial from the next day or two, he/she will be allowed, but defaulters of the week and more will not be allowed to continue and be withdrawn from the study with a fresh case being included.

DATA MANAGEMENT:

After enrolling the patient in the study, a separate file for each patient will be opened and all forms will be kept in the file. Study number, patient number will be entered on the top of file for easy identification. Whenever study patient visits OPD during the study period, the respective patient's file will be taken and necessary recording will be made at the assessment form or other suitable form. The screening forms will be filled separately. The Data entries will be monitored for completion and adverse event by HOD and pharmaco-vigilance committee. All forms will be further scrutinized in presence of investigations by HOD for logical errors and incompleteness of data to any bias. No modification in the results is permitted for unbiased reports.

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL

PALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*"-**

A PEDIATRIC

DISORDER AND THE DRUG OF CHOICE IS***PAÑCATĪPĀKKIṆI CŪRAṆAM***

Form I-SCREENING & SELECTION PROFORMA

S.I.No: ……. OP/IP No: ……. Name: ……

Age: ……. Gender: ……..Date of Enrollment: …….

Date of Completion :……. Informant:……Reliability : ……

INCLUSION CRETERIA:	**YES**	**NO**
• Age 1-12 years	☐	☐
• Loose stools with blood or mucus	☐	☐
• Pyrexia	☐	☐
• Low pithched voice	☐	☐
• Loss of appetite	☐	☐
• Nausea	☐	☐
• Vomiting	☐	☐

EXCLUSION CRITERIA:

• Severe dehydration	☐	☐
• Acute life threatening disease	☐	☐
• Abdominal distension due to any other serious illness	☐	☐

Signature of Guide: **Signature of Principal Investigator:**

Signature of HOD:

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL

PALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*".** A PEADIATRIC DISORDER AND THE DRUG OF CHOICE IS

PAÑCATĪPĀKKIṆI CŪRAṆAM

FORM IA – HISTORY PROFORMA ON ENROLLMENT

Patient id:	**OP/IP NO.**	**VISIT DATE (___/____/_____)**
NAME :		
AGE:		
Gender: MALE FEMALE		**Date Of Birth :(____/____/_____)**
Fathers/Mother/Guardian name :		
Fathers Occupation:		
Fathers Monthly income:		
Religion:		
Socioeconomic status:		
Patient informant :		

Postal Address Contact no:

1. **Complaints and duration**

2. Present illness

History of past Illness

History /Symptoms /Signs	Yes	No	if, Yes Details
Any Similar Complaints	☐	☐	_____
Bronchial Asthma	☐	☐	_____
Dust Allergy	☐	☐	_____
Hospitalization	☐	☐	_____
Any Other	☐	☐	_____

Family History

Any hereditary familial Disease **Yes** **No**

If yes, details……..

Immunization History

Proper Immunization given **Yes** **No ……..**

Food Habits:

1. **Veg** ☐ **2. Non-Veg** ☐ **3. Mixed** ☐

General assessment	Yes	No
1. Picca	☐	☐
2. Nail Biting	☐	☐
3. Bowel Movements	☐	☐

General Examination	Yes	No
1. Pallor	☐	☐
2. Jaundice	☐	☐
3. Cyanosis	☐	☐
4. Clubbing	☐	☐
5. Pedal oedema	☐	☐
6. Lymph adenopathy	☐	☐

Vital signs:-

1. **Pulse rate / mint**

2. **Heart rate / mint**
3. **Respiratory Rate / mint**
4. **Temperature**
5. **BP**

Anthropometry:

Height

Weight

Head Circumference

Chest Circumference

Mid Arm Circumference

CLINICAL EXAMINATION:

	Normal	Affected
Cardio Vascular system:	☐	☐
Gastro intestinal system:	☐	☐
Musculo skeletal system:	☐	☐
Central nervous system:	☐	☐
Endocrine system:	☐	☐

CLINICAL EXAMINATION OF SKIN:

1. Site:

   ……

   ……..

2. Colour: Normal ☐ Reddish ☐ Black ☐ Pallor ☐
3. Itching: No ☐ Mild ☐ Moderate ☐ Severe ☐

EXAMINATION OF NAILS:

1. Pallor: Present ☐ Absent ☐
2. Koilonychia: Present ☐ Absent ☐

Nilam:

Kuṟiñci ☐ *Mullai* ☐ *Marutam* ☐ *Neytal* ☐ *Pālai* ☐

KaalaIyalbu

Kārkālam	☐	*Kūtirkālam*	☐	*MuṉPaṉI*	☐
Piṉpaṉi	☐	*iḷavēṉil*	☐	*mutuvēṉil*	☐

Yaakai

Vātam	☐	*Vātapittam*	☐	*Vātakapam*	☐
Pittam	☐	*Pittavātam*	☐	*Pittakapam*	☐
Kapam	☐	*Kapavātam*	☐	*Kapapittam*	☐

UyirThathukkal

Vātam	Normal	Affected	Remarks
Pirāṇaṉ	☐	☐	
Apāṉaṉ	☐	☐	
Utāṉaṉ	☐	☐	
Viyāṉaṉ	☐	☐	
Camāṉāṉ	☐	☐	
Nākaṉ	☐	☐	
Kūrman	☐	☐	
Kirukaraṉ	☐	☐	
Tēvatattaṉ	☐	☐	
Taṉañceyaṉ	☐	☐	

Pittam	Normal	Affected	Remarks
Aṉaṟpittam	☐	☐	
Irañcakappittam	☐	☐	
Cātakappittam	☐	☐	
Ālōcakam	☐	☐	
Pirācakam	☐	☐	

Kapam	Normal	Affected	Remarks
Avalampakam	☐	☐	
Kilētakam	☐	☐	
Pōtakam	☐	☐	
Pōtakam	☐	☐	
Cantikam	☐	☐	

Udalthathukkal	Normal	Affected	Remarks
Cāram	☐	☐	
Cennīr	☐	☐	
Ūṇ	☐	☐	
Koḻuppu	☐	☐	
Eṉpu	☐	☐	
Mūḷai	☐	☐	
Cukkilam	☐	☐	

Envagai Thervugal	Normal	Affected	Remarks
Nā	☐	☐	
Niṟam	☐	☐	
Moḻi	☐	☐	
Viḻi			
Sparicam	☐	☐	

Malam	Normal	Affected	Remarks
Niṟam	☐	☐	
Nurai	☐	☐	
Iḷakal	☐	☐	
Iṟukal	☐	☐	

Moothiram

Neerkuri:	Normal	Affected
Niṟam	☐	☐
Eṭai	☐	☐
Nurai	☐	☐
Maṇam	☐	☐
Eñcal	☐	☐

Neikuri:	Normal	Affected
Vātam	☐	☐
Pittam	☐	☐
Kapam	☐	☐
Others	☐	☐

Naadi:

ThaniNadi

Vātam ☐ *Pittam* ☐ *Kapam* ☐

ThonthaNadi

Vātapittam ☐ Pittavātam ☐ *Pittakapam* ☐ *Kapapittam* ☐

Sparism

Diagnosis_____

Admitted to trial : 1. Yes 2. No.

if yes, S.No: 1IP 2.OP

Diagnosis

DRUGS ISSUED:_____

Date :_____

Station _____

Date :

Signature of the Guide **Signature of Principal Investigator:**

Signature of the HOD

GOVERNMENT SIDDHA MEDICAL COLLEGE AND HOSPITAL

BRANCH IV – KUZHANTHAI MARUTHUVAM

PALAYAMKOTTAI - 627 002.

FORM-IB:CASE SHEET PROFORMA-" *ĀMA KAḶICCAL*"

I.P.No. :

Bed. No. :

Name of the Medical unit:

Name :

Age/Sex:

Permanent Address:

Temporary Address:

PG-Pediatric Ward, Government Siddha Medical College & Hospital, Palayamkottai.

Informant:

Invesitgator:

Nationality:

Religion:

Occupation(Parents):

Income:

Date of Admission:

Date of Discharge:

Diagnosis:

Medical Officer:

Complaints and duration :

History of present illness :

History of past illness :

Personal History:

Family History:

Consanguinity :
Ataxia :
Blindness :
CP :
MR :
Seizure :
Movement disorder :
Deafness :

Socio-Economic Status:

Habits:

Bowel and micturation habit :
Sleep :
Enuresis :
Thumb sucking :
Nail biting :
Pica :

Diet History :

Appetite :
Types of diet :

Antenatal History :

Medication :
Infection (STARCH) :
Irradiation :
Toxaemia :

Hemorrhage :

Severe Anaemia :

Eclampsia :

H/o Decreased foetal Movements :

Maternal malnutrition :

Maternal Diabetes Mellitus(DM) :

Maternal Hypertension :

Natal:

Breech presentation :

Forceps / - C- Section :

Home / Hospital :

H/o prolonged labour :

Post Natal

Post partum Haemorrhage :

Sepsis :

Neonatal History:

Birth Weight :

Term / Pre term baby :

Congenital malformations :

Birth Asphyxia – APGAR – Score :

Neonatal convulsions :

Kernicterus :

Diarrhoea :

Birth injury / Head injury / Activity of the child

a) at birth :

b) after birth :

Time of cry after birth :

Resuscitation done or not :

(if done nature of resuscitation)

Respiratory distress / cyanosis :

Fever / altered sensorium :

Feeding after birth :

Lymphadenopathy :

Developmental History :

Immunization History :

General Examination

Anthropometry:

Height :

Weight :

Head Circumference :

Chest Circumference :

Mid Arm Circumference :

1. Consciousness :
2. Decubitus :
3. Anemia :
4. Jaundice :
5. Cyanosis :
6. Clubbing :
7. Pedal oedema :
8. Lymphadenopathy :
9. Nourishment :
10. Skin changes :
11. Edema :
12.JVP :
13.Pulse Rate :
14.Heart Rate :
15.Respiratory Rate :
16.Temperature :
17.Blood Pressure :
18.Spine :
19.Skin :

Systemic Examination

Cardio Vascular System :

Respiratory System :

Gastro Intestinal System :

Genito Urinary System :

Nervous System :

Consciousness:

Temper Tantrum: Sociable- Irritable - Playful

Memory :

Orientation :

Speech :

Intelligence (I.Q) :

Handedness :

Cranial Nerve Examination:

Motor System:

Power :

Tone :

Reflex :

Grip :

Gate :

Sensory Examination:

Superficial Sensation:

Touch :

Pain :

Temperature :

Deep Sensation:

Position sense :

Joint sense :

Vibration sense:

Cortical Sensation:

Cerebellar Signs:

Autonomic System:

Siddha Systems – Clinical Examination:

Nilam

Kuṟiñci,:

Mullai:

Marutam:

Neytal:

Pālai :

ParuvaKaalam

Iḷavēṉil

Mutuvēṉil

Kārkālam

Kūtirkālam

MuṉPaṉi

PiṉPaṉi

Uyirthathukal:

Vatham

Pirāṇaṉ

Apāṉaṉ

Viyāṉaṉ

Utāṉaṉ

Camāṉāṉ

Nākaṉ

Kūrman

Kirukaraṉ

Tēvatattaṉ

Taṉañceyaṉ

Pitham

Aṉaṟpittam

Irañcakappittam

Cātakappittam

Ālōcakam

Pirācakam

Kabam

Avalampakam

Kilētakam

Pōtakam

Taṟpakam

Cantikam

UdalKattugal

Cāram

Cennīr,

Ūṇ

Koḻuppu

Eṉpu,

Mūḷai

Cukkilam

EnvagaiThervugal

Nāṭi

Sparicam

Nā

Niṟam

Moḻi

Viḻi

Malam

Mūttiram

Neerkuri

Niṟam,

Nurai

Eṭai

Maṇam

Eñcal

Neikuri

Malakuri

Nirami

Nura

Iḷakal

Iṟukal

Lab Investigations

1. Blood

TC :

DC :

Hb :

ESR :

2. Urine

Albumin :

Sugar :

Deposits :

3. Motion

Ova :

Cyst :

Occult blood :

DIFFERNTIAL DIAGNOSIS :

PROGNOSIS :

MARUTHUVAMURAI :

ADVICE :

DAILY PROGRESS :

Date	Symptoms	Medicine

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL

PALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*"**-A PEDIATRIC DISORDER AND THE DRUG OF CHOICE IS ***PAÑCATĪPĀKKIṆI CŪRAṆAM***

FORM - II&IIA

CLINICAL ASSESMENT ON ENROLLMENT DURING AND AFTER TRIAL

S.I.No: ……. OP/IP No: …… Name: ……

Age: ……. Gender: …….. Date of Enrollment: ……

Date of Completion :……. Informant: ……. Reliability : ……

SIDDHA SYSTEM OF EXAMINATION

I.ENVAGAI THERVU: [EIGHT-FOLD EXAMINATION]

1.NAADI: [PULSE PERCEPTION]

2.SPARISAM: [SENSITIVITY]

3.NAA:[TONGUE]

4.NIRAM: [COMPLEXION]

5.MOZHI: [VOICE]

6.VIZHI: [EYES] (Lower palpebral conjunctiva)

7.MALAM: [BOWEL HABITS / STOOLS]

	1st Day	05th Day	7th Day
Colour	Dark/Yellow/ Red/ Pale	Dark/Yellow/ Red/ Pale	Dark/Yellow/ Red/ Pale
Consistency	Solid/ Semisolid/ Watery	Solid/ Semisolid/ Watery	Solid/ Semisolid/ Watery
Stool bulk	Normal/ Reduced	Normal/ Reduced	Normal/ Reduced
Constipation	Present/ Absent	Present/ Absent	Present/ Absent
Diarrhoea	Present/ Absent	Present/ Absent	Present/ Absent

8.MOOTHIRAM[URINE EXAMINATION]:

NEERKURI	1st Day	05th Day	7th Day
Niṟam [Colour]	White/ Yellowish/ Straw coloured/ Crystal clear	White/ Yellowish/ Straw Coloured/ Crystal clear	White/ Yellowish/ Straw coloured/ Crystal clear
Maṇam [Odour]	Present/ Absent	Present/ Absent	Present/ Absent
Nurai [Froth]	Nil/Reduced/ Increased	Nil/Reduced/ Increased	Nil/Reduced/ Increased
Eṭai [Sp.gravity]	Normal/ Increased/	Normal/ Increased/R	Normal/ Increased/R
Eñcal [Deposits]	Present/ Absent	Present/ Absent	Present/ Absent
Volume	Normal/ Increased/	Normal/ Increased/R	Normal/ Increased/R

NEIKURI	1st Day	05th Day	7th Day
Serpentine fashion			
Annular/Ringed fashion			
Pearl beaded fashion			
Mixed fashion			

II.THEGI: [TYPE OF BODY CONSTITUTION]

III.NILAM: [LAND WHERE PATIENT LIVED MOST]

Kurinji ☐ Mullai ☐ Marutham ☐ Neithal ☐ Palai ☐

IV.KAALAM:

Kaarkalam - ☐ Pinpanikalam - ☐

Koothirkalam - ☐ Ilavenil - ☐

Munpanikalam - ☐ Muthuvenil - ☐

V.MUKKUTRAM:[AFFECTION OF THREE HUMORS]

A)VATHAM:

	1st Day	05th Day	7th Day
Pirāṇaṉ			
Apāṉaṉ			
Viyāṉaṉ			
Utāṉaṉ			
Camāṉān			
Nākaṉ(Higher intellectual function)			
Kūrman (airway of yawning)			
Kirukaraṉ (Air of salivation/nasal secrection)			
Tēvatattaṉ (Air of laziness)			
Taṉañceyaṉ(this air that acts on death)			

B.PITHAM:

	1st Day	05th Day	7th Day
Aṉaṟpittam (Gastric juice)			
Irañcakappittam(Haemoglobin)			
Cātakappittam (Life energy)			
Pirācakam (Bile)			
Ālōcakam			

C.KABAM:

	1st Day	05th Day	7th Day
Avalampakam (Serum)			
Kilētakam (saliva)			
Pōtakam (lymph)			
Taṟpakam (cerebrospinal fluid)			
Cantikam(synovialfluid)			

VI.SEVEN DHATHUS: (7 SOMATIC COMPONENTS)

	1st Day	05th Day	7th Day
Cāram ***[Chyme]***			
Cennīr [Blood]			
Ūṇ [Muscle]			
Koḻuppu[Fat]			
Eṉpu [Bones]			
Mūḷai [Bonemarrow]			
Cukkilam [Genital discharges]			

1.SYSTEMIC EXAMINATION:

	1st Day	05th Day	7th Day
1)Gastrointestinal System			
2) Respiratory System			
3)Cardiovascular System			
4)Central Nervous System			
5)Urogenital System			

Anthropometry:

Height :

Weight :

Head Circumference :

Chest Circumference :

Mid Arm Circumference :

2. GENERAL EXAMINATION:18th

	1st Day	03th Day	7th Day
Height (cms)			
Weight (kg)			
Temperature (F^0)			
Pulse rate (per min)			
Heart rate (per min)			
Respiratory rate(per min)			
Blood pressure (mm/Hg)			
Anaemia			

3.CLINICAL SYMPTOMS:

COMPLAINTS	1-3days	6-8 days	9-10 days	11-15 days	Above 15 days	Unrecovered
Loose stools with blood or mucus						
Abdominal pain						
Sore anus						
Flatulence						
Colour and smell of stools						
Vomiting						
Loss of appetite						
Urinary retention						

Date:

Station

Signature of the Investigator:

Signature of the Guide **Signature of the HOD**

GOVERNMENT SIDDHA MEDICAL

COLLEGE&HOSPITALPALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF

KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON "***ĀMA KAḶICCAL***"A PEDIATRIC DISORDER AND THE DRUG OF CHOICE IS***PAÑCATĪPĀKKIṈI CŪRAṆAM***

S.I.No: ……. OP/IP No: …… Name: ……

Age: ……. Gender: ……..Date of Enrollment: …….

Date of Completion :……. Informant:……Reliability : ……

FORM III – LABORATORY INVESTIGATION

Routine blood investigations		**Normal values**	**Before TMT date:**	**After TMT date:**
Hb (gms%)		**11.5- 14.5**		
T.RBC (milli/cu.mm)		**4-4.9**		
ESR(mm)	**½ hr.**	**0-4**		
	1hr.	**0-13**		
T.RBC (milli/cu.mm)		**5000-14500**		
DIFFERENTIAL COUNT (%)	**Polymorphs**	**40-75**		
	Lymphocytes	**28-48**		
	Monocytes	**3-6**		
	Eosinophils	**0-3**		
	Basophils	**0-1**		

Urine Investigation	**Before TMT Date :**	**After TMT Date :**
Albumin		
Sugar		
Deposits		

Stools Investigation	**Before TMT Date :**	**After TMT Date :**
OVA		
Cyst		
Occult blood		

Date :

Signature of Guide: **Signature of Principal Investigator:**

Signature of HOD:

அரசுசித்தமருத்துவகல்லூரி மற்றும்

பாளையங்கோட்டைமருத்துவமனைபட்டமேற்படிப்புகுழந்தைமருத்துவத்துறை

பேர்ச்செங்காய் கிருதம் பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவஆய்வு.

ஒப்புதல் படிவம்

சான்றாளரால் சான்றளிக்கப்பட்டது

நான் இந்த மருத்துவ ஆய்வை குறித்த அனைத்து விபரங்களையும் நோயாளியின் பெற்றோருக்குபுரியும் வகையில் எடுத்துரைத்தேன் எனஉறுதிஅளிக்கிறேன்.

தேதி : கையொப்பம் :

இடம் : பெயர் :

நோயாளியின் பெற்றோர் ஒப்புதல் படிவம்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும்,மருந்தின் தன்மைமற்றும் மருத்துவ வழிமுறைபற்றியும், இந்த மருத்துவத்தை தொடர்ந்து எனது குழந்தையின் உடல் இயக்கத்தைக் கண்காணிக்கவும்,அதனைப் பாதுகாக்க பயன்படும் மருத்துவ ஆய்வுக்கூடப் பரிசோதனைகள் பற்றியும் திருப்தி அளிக்கும் வகையில் ஆய்வுமருத்துவரால் விளக்கிக் கூறப்பட்டது.

நான் இந்த மருத்துவ ஆய்வின் போதுகாரணம் எதுவும் கூறாமல் எப்போது வேண்டுமானாலும் என் குழந்தையை விடுவித்துக் கொள்ளும் உரிமையைத் தெரிந்திருக்கிறேன்.

நான் என்னுடைய சுதந்திரமாக தேர்வு செய்யும் உரிமையைக் கொண்டு **ஆமக் கழிச்சல்** நோய்க்கான மருந்து **பஞ்ச்சதீபாக்கினி சூரணம்** பரிகரிப்புத் திறனை கண்டறியும் மருத்துவ ஆய்வுக்கு எனது குழந்தையை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

இந்த ஆராய்ச்சிக்குதங்கள் விருப்பத்தின் பேரில் குழந்தையை உட்படுத்தும் பட்சத்தில் உளமருந்தாக பேர்ச்செங்காய் கிருதம் 5ml, 18 நாட்கள் உட்கொள்ள வேண்டும்.

இந்த ஆராய்ச்சியில் நோயினராக சேர்ந்த பிறகு உங்களுக்கு விருப்பம் இல்லையெனில் எப்பொழுது வேண்டுமானாலும் தங்களது குழந்தையை விலக்கிகக் கொள்ளலாம்.

மேலும் இந்த ஆராய்ச்சிக்குIEC (நிறுவனநீதிநெறிகுழு) சான்றுபெறப்பட்டுள்ளது.

இந்தமருந்து சிறப்பாக **ஆமக் கழிச்சல்** நோய்க்காக அங்கீகரிக்கப்பட்ட சித்தமருத்துவ நூலில் கூறப்பட்டுள்ளது. இது வரை நோயாளிகளிடம் எந்தவித பக்கவிளைவுகளை ஏற்படுத்தவில்லை.

மேலும் உணவுமுறையில் பத்தியம் காக்குமாறுஅறிவுறுத்தப்படுகிறது.

தேதி : பெற்றோர் பெயர் :

இடம் : கையொப்பம்

சாட்சிக்காரர் பெயர் :

கையொப்பம் :

உறவுமுறை :

GOVT SIDDHA MEDICAL COLLEGE AND HOSPITAL

PALAYAMKOTTAI

PG. DEPT. OF KUZHANTHAI MARUTHUVAM

CONSENT FORM

An open clinical study to evaluate the safety and efficacy of Siddha sasthric Formulation **"*Pañcatīpākkiṉi cūraṇam*"** for the management **"*ĀMA KAḶICCAL*"**

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all the details about the study in the terms readily understood by the parent.

Date ……. **Signature……..**

place ……. **Name ……**

CONSENT OF INFORMANT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial, and the nature of drug treatment and follow-up including the laboratory investigations to be performed to monitor and safeguardmy Son / Daughter body functions.

I am aware of my right to opt out of the trial at any time during the courseofthe trial without having to give the reasons for doing so.

I am, exercising my free power of choice; hereby give my consent to be included as a subject in the clinical trial of "*Pañcatīpākkiṉi cūraṇam*"for the treatment of "*Āma kaḷiccal*"

Informant Signature:…….

Date: **Informant Name: …….**

Place: **Patient Name:…….**

Signature of Witness **Relationship:……**

GOVERNMENT SIDDHA MEDICAL COLLEGE&HOSPITAL

PALAYAMKOTTAIPOST GRADUATE DEPARTMENT OF

KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*"**-A PEDIATRIC DISORDER AND THE DRUG OF CHOICE IS ***PAÑCATĪPĀKKIṆI CŪRAṆAM***

S.I.No: ……. OP/IP No: …… Name: ……

Age: ……. Gender: …….. Date of Enrollment: …….

Date of Completion :……. Informant: ……. Reliability : ……

FORM IVB – WITHDRAWAL

Date of Trial commencement :

Date of withdrawal from trial :

Reason (s) for withdrawal : Yes /No

Long absence at reporting : Yes /No

Irregular treatment : Yes /No

Shift of locality : Yes /No

Complication adverse reactions if any: Yes /No

Exacerbation of symptoms : Yes /No

Pt. not willing to continue : Yes /No

Date :

Signature of Guide: **Signature of Principal Investigator:**

Signature of HOD:

FORM IV-C – PATIENT INFORMATION SHEET

Name of the principal investigator:

…….

Name of the institution : GOVERNMENT SIDDHA MEDICAL COLLEGE&HOSPITAL, Palayamkottai

Information sheet for patients participating in the open clinical, trial

1, _____ Studying as PG Scholar at **GOVERNMENT SIDDHA MEDICAL COLLEGE&HOSPITAL, PALAYAMKOTTAI** is doing a trail on the study **"*ĀMA KAḶICCAL*"**.It is a most common disease in children. In this regard, I am in a need to ask you few questions. I will maintain confidentially of your comments and data obtained. There will be no risk of disclosing your identity and no physical, psychological or professional risk is involved by taking part in this study. Taking part in this study is voluntary. No compensation will be paid to you for taking part in this study.

You can choose not to take part. You can choose not to answer a specific question. There is no specific benefit for you if you take part in the study. However, taking part in the study may be of benefit to the community, as it may help us to understand the problem of defaulters and potential solutions.

If you agree your child to be a participate in this study, he/she will be included in the study primarily by signing the concern form and then you will be given the internal medicine "***PAÑCATĪPĀKKIṈI CŪRAṆAM***" (250 – 300 mg) for 7 days.

Date :

Signature of Guide: **Signature of Principal Investigator:**

Signature of HOD:

GOVERNMENT SIDDHA MEDICAL COLLEGE&HOSPITAL

PALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*"**-A PEDIATRIC DISORDER AND THE DRUG OF CHOICE IS ***PAÑCATĪPĀKKIṆI CŪRAṆAM***

FORM IVD- DIETARY ADVICE FORM

S.I.No: ……. OP/IP No: …… Name: ……

Age: ……. Gender: …….. Date of Enrollment: ……

Date of Completion :…… Informant: ……. Reliability : ……

The following diet to be taken:	The following food should be avoided
• Drink adequatewater • Apple • Orange • Pomegranate • Nuts	• Avoid bitter and sour taste foods • Milk and milk products • Agathi greens • Spicy foods • Chicken

Date:

Station:

Signature of the Investigator:

Signature of the Guide :

Signature of the HOD

Form – IVE

NATIONAL PHARMACOVIGILANCE PROGRAMME FOR SIDDHA DRUGS

Reporting Form For Suspected Adverse Reactions to Siddha Drugs

Please Note: i. All Consumers/Patients and reporters information will remain confidential.

ii. It is requested to report all suspected reactions to the concerned, even if it does not have complete data, as soon as possible.

Peripheral centre code : State :

. Patient /Consumer Identification (Please complete or tick boxes below as appropriate)

Name	Father Name	Patient record no
Ethnicity	Occupation	
Address Village/Town Post/Via District /State		Date of Birth/Age
		Sex: Male /Female Weight: Degam:

2. Description of the suspected adverse reactions please complete boxes below

Date and time of initial observation		Season:
Description of reaction		Geographical area:

3. List of all medicines/Formulations including drugs of other systems used by the patient during the reporting period:

Medicine	**Daily dose**	**Route of administration Vehicle – Adjuvant**	**Date**		**Diagnosis for which medicine taken**
			Starting	**Stopped**	
Siddha					
Any other system of medicines					

4. Brief details of the Siddha Medicine which seems to be toxic :

Details	Drug
a) Name of the Medicine	
b) Manufacturing unit and batch no. and date	
c) Expiry date	
d) Purchased and obtained from	
e) Composition of the formulation / part of the drug used	

2) Dietary restrictions if any

3) Whether the drug is consumed under institutionally qualified medical supervision or used as self medication

4) Any other relevant information

5. Treatment provided for adverse reaction:

6. The result of the adverse reaction /side effect / untoward effects (Please complete the boxes below)

Recovered	Not recovered:	Unknown	Fatal	If fatal Date of death:
Severe Yes /No	Reaction abated after drug stopped or dose reduced			
	Reaction reappeared after re introduction :			
Was the patient admitted to hospital? If yes, give name and address of hospital				

7. Any laboratory investigation done to evaluate other possibilities? If yes specify:

8. Whether the patient is suffering with any chronic disorders?

9. H/O previous allergies /Drug reactions:

10. Other illness (please describe):

Type (please tick):Nurse/Doctor/Pharmacist/Health worker/Patient/Attendant/Manufacturer/Distribution /Supplier /Any other (please Specify)

Name :
Address:
Telephone /E-mail if any:

Signature of the reporter **Date :**

Please send the completed from to

To,
The co-ordinator pharmacovigilence,
Govt., Siddha Medical College and Hospital,
Palayamkottai,
Tirunelveli.

From

Government Siddha Medical College &Hospital, Palayamkottai, Post Graduate Department of Kuzhanthai Maruthuvam

This Filled- in ADR report may be send within one month of observation / occurrence of ADR

Who can report?

- Any health care professionals like Siddha Doctors /Nurses /Siddha Pharmacists /Patients Etc.,

What to report?

- All reactions, Drug interactions

Confidentiality

- The patient's identify will be held in strict confidence and protected to

Date :

Station:

Signature of Investigator:

Signature of Guide: **Signature of HOD**

GOVERNMENT SIDDHA MEDICAL COLLEGE AND HOSPITAL

BRANCH IV – KUZHANTHAI MARUTHUVAM

PALAYAMKOTTAI - 627 002.

Form IVF -ADMISSION – DISCHARGE SHEET

Name of the medical unit	:	Nationality	:
I.P.No	:	Religion	:
Bed No	:	Informant	:
Name	:	Date of Admission	:
Age/Sex	:	Date of Discharge	:
Occupation(parents)	:	No. of days treated	:
Income(parents)	:	Diagnosis	:

S.No	Clinical Features	During admission	During discharge
1	Loose stools with mucus or blood		
2	Abdominal pain		
3	Flatulence		
4	Sore anus		
5	Loss of appetite		
6	Colour and smell of stools		
7	Vomiting		
8	Urinary retention		

Place:

Date:

Signature of the Medical Officer

GOVERNMENT SIDDHA MEDICAL COLLEGE&HOSPITAL

PALAYAMKOTTAI

POST GRADUATE DEPARTMENT OF KUZHANTHAI MARUTHUVAM

PRECLINICAL AND CLINICAL STUDY ON **"*ĀMA KAḶICCAL*"**-A PEDIATRIC DISORDER AND THE DRUG OF CHOICE IS ***PAÑCATĪPĀKKIṆI CŪRAṆAM***

FORM V-DRUG COMPLIANCE

S.I.No: ……. OP/IP No: …… Name: ……

Age: ……. Gender: …….. Date of Enrollment: …….

Date of Completion :……. Informant:……..Reliability : ……

NAME OF THE DRUG : ***PAÑCATĪPĀKKIṆI CŪRAṆAM***

FORM OF THE DRUG : ***CŪRAṆAM***

ADMINISTRATION &ADJUVANT : PER ORAL

DOSE & DURATION : 250-300mg (based on duration and requirement)

NO OF DRUG PACKS GIVEN : _____

NO OF DRUG PACKS RETURNED : _____

DAY	DATE OF DRUG INTAKE	MORNING	EVENING
DAY 1			
DAY 2			
DAY 3			
DAY 4			
DAY 5			
DAY 6			
DAY 7			

Date : **Signature of Principal Investigator:**

Signature of the Guide:

Signature of HOD :