

## CLINICAL SIGNIFICANCE OF NILAVEMBU KUDINEER -A REVIEW

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### ABSTRACT

*Nilavembukudineer* is a well-known popularized Siddha drug in southern part of India especially for dengue fever. *Andrographispaniculata* is known as 'kirayat' in Ayurveda is one of the chief ingredients of *Nilavembukudineer* which is used as a unique drug for dengue fever and other related viral febrile condition. This plant has got a multifaceted therapeutic efficiency in treating various type of illness in human body such as skin disorders, hepato biliary illness, diabetes mellitus, and other immune deficiency disorders of the body. According to *Agathiyargunavagadam*,<sup>6</sup> this *Nilavembukudineer* is a more potent therapeutic drug in treating diseases like *vathasuram*, *suranoigal* (Febrile illness), *neercovai* (sinusitis), *mayakam* (syncope, or shock). The intake of *Nilavembukudineer* gives physical and mental relief after the convalescence period.

**KEYWORDS:** Dengue, *Nilavembu*, *Suranoigal*, Viral fever.

### 1. INTRODUCTION

Siddha system of medicine is one of the oldest system belongs to traditional system of medicine in India especially practiced in Tamil Nadu and nearby states. Nowadays health awareness by using herbal medicines is highly appreciable one. Siddha system of medicine is using herbals to prepare medicine, in addition to that metals, minerals and animal products are also used.<sup>[1]</sup> For recent epidemic of dengue fever in TamilNadu, *Nilavembukudineer* is one of the contributions from this system to prevent and control of this epidemic. This paper aimed to review the various activities of *Nilavembukudineer* (NV *Kudineer*) and discussed elaborately.

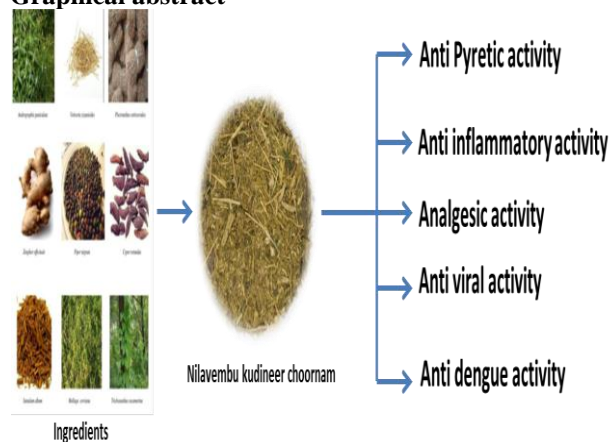
#### 1.1. Ingredients (Pharmacopoeia of Hospital of Indian Medicine, 1995)<sup>[2]</sup>

1. Nilavembu (*Andrographispaniculata*)
2. Vettiver (*Vetiveriazizanioidas*)
3. Vila MichanVer (*Plectransthusvettiveroides*)
4. SanthanaThool (*Santalum album*)
5. Peyippudal (*Trichosantheslobata*)
6. Koraikilangu (*Cyperusrotundus*)
7. Cukku (*Zingiberofficinale*)
8. Milagu (*Piper nigrum*)
9. Parpadagam (*Hedyotiscorymbosa*)

#### 1.2. Purification of drug

All the herbal ingredients purified as per the traditional validation and illustration (Siddha formulary of India, 1992)<sup>[3]</sup>

### Graphical abstract



#### 1.3. Process (Siddha formulary of India, 1992)<sup>[3]</sup>

All the nine ingredients are purified and grind into a coarse powder by using machineries, this mixer of powder 100 g mix with 800 ml of water and boiled it. It is reduced into 100 ml then filtered it.

#### 1.4. Shelf Life

3 hours

#### 1.5. Discription of NilavembuKudineer (VDH, 2017)

##### 1.5.1. Nilavembu (*Andrographispaniculata*)

Nilavembu is widely known as the king of bitter herbs. It is a natural antipyretic herb reduces body temperature. It eliminates toxic metabolites brought by the pathogens by stimulating liver detoxification.<sup>[4]</sup>

**1.5.2. Vettiver (*Vetiveria Zizanioides*)**

Vettiver is a small grass variety popularly known for its aroma. Its peculiar refreshing aroma regains health. Its cooling property provides enough hydration inside the body and relieves thirst. It helps in eliminating pathogenic waste materials through sweat and urine.<sup>[4]</sup>

**1.5.3. Vilamiccamver (*Plectranthusvettiveroides*)**

This is an exceedingly coolant herb helpful in reducing the body heat both internally and externally. It reduces fever by inducing perspiration. It is also best known for its anti-inflammatory action that relieves pain and burning sensation associated with fever.<sup>[4]</sup>

**1.5.4. Santanam (*Santalumalbum*)**

Sandal wood is a sacred herb useful in therapeutic as well as spiritual activities. Its bitter and cooling properties reduces body temperature in fever. It elevates the mood and creates sense of wellbeing thus helps in speedy recovery from fever.<sup>[4]</sup>

**1.5.5. Peypudal (*Trichosanthes cucumerina*)**

This bitter herb is best known for its liver protection. Along with fever reduction it helps in detoxing the blood for infective organisms.<sup>[4]</sup>

**1.5.6. Korakilanku (*Cyperusrotandus*)**

Dried rhizomes of this herb controls systemic inflammations and reduce fever. Its psycho somatic stimulant action elevates mental and physical wellbeing to tolerate the ill effects of fever.<sup>[4]</sup>

**1.5.7. Cukku (*Zingiberofficinale*)**

Dried rhizomes of ginger increases saliva secretion and provide antibacterial protection to entire digestive system. It stimulates the secretion of gastric enzyme to recover appetite and digestion.<sup>[4]</sup>

**1.5.8. Milaku (*Pipernigrum*)**

Black pepper one of the cooking spices of India holds tremendous healing qualities. It neutralizes the endotoxins and detoxifies pathogenic remnants from liver and blood. Its hot potency deactivates microbes and enhances body immunity to prevent recurrence of fever.<sup>[4]</sup>

**1.5.9. Parpatakam (*Mollugocerviana*)**

It is an antiseptic herb counteracts septic inflammations with in the body. It induces sweating to lower the body temperature. It helps in digestion and proper elimination of bowels to complete the body cleansing.<sup>[4]</sup>

Therapeutic efficacy of ingredients of *Nilavenbukudineerchoornam* based on *panchabhutas* (panchabhootham) and taste (*suvai*) is represented in Table 1.

Table 1: Ingredients of NV Kudineer.<sup>[5]</sup>

Sl. No.	Ingredients	Taste	Panchabootham	Action	Indications as per literature
1	<i>Andrographispaniculata</i> (Nilavembu)	Bitter	Air+Space	Stomachic, Tonic, Alterative Stimulant	Fever, Sinusitis
2	<i>Vetiveriazizanioides</i> (Vetiver)	Sweet	Earth+Water	Tonic, Stimulant, Antispasmodic, Diaphoretic, Diuretic, Emmenagogue, Febrifuge	Thirst, Jaundice, Hypertension, Fever, Cervical problem, Impotence, Psychiatric Eye disease, Burns, Delirium
3	<i>Plectranthusvettiveroides</i> (Vilamichuver)	Bitter	Air+Space	Refrigerant, Anti pitha	Diabetic mellitus, Hypertension, Sweating Psychiatric, Delirium Dropsy, Migrain
4	<i>Zingiberofficinale</i> (Chukku)	Acrid	Fire+Air	Stimulant, Stomachic, Carminative	Indigestion, Hyperthermia Asthma, Cough, Diarrhoea Sinusitis, Peptic ulcer, Ascitis, Anaemia
5	<i>Piper nigrum</i> (Milagu)	Bitter +Acrid	Air+Space Fire+Air	Acrid, Carminative Anti-periodic, Rubefacient, Stimulant, Resolvent Antivatha, Antidote	Fever with rigor, Anaemia Cold, Diarrhoea, Peptic ulcer, Gastritis, Loss of taste – sensation, Psychiatric Plies, Delirium, Cough, Hemiplegia, Ear problem, Indigestion, Jaundice
6	<i>Cyperrotundus</i> (Korai)	Astringent	Earth+Air	Astringent, Stimulant, Tonic, Diuretic, Diaphoretic, Demulcent, Emmenagogue Diaphoretic, Vermifuge	Fever with rigor, Hypertension All type of fever, Thirst, Delirium, Diarrhoea, Psychiatric, Cold, Calcaneus spur, Tuberculosis
7	<i>Santalum album</i> (Chandanam)	Bitter +Little Astringent	Air+Space Earth+Air	Alternative, Diuretic, Diaphoretic, Stimulant, Disinfectant, Astringent, Cooling	Delirium, Confusion Fever, Leucorrhoea Thirst, Itching
8	<i>Mollugocerviana</i> (Parpatakam)	Bitter	Air+Space	Laxative, Stomachic, Antiseptic, Fabrifuge, Diaphoretic	Fever, Psychiatric, Thirst
9	<i>Trichosanthuscucumerina</i> (Pudal)	Bitter	Air+Space	Refrigerant, Aphrodisiac	Aphrodisiac, Cold, sychiatric

Table 2: NV Kudineer- Pharmacognosy & Ethno pharmacological aspect<sup>[6,7,8,9,10,11,12,13,14,15]</sup>

Sl. No.	Ingredient	Family	Habit	Part used	Phytochemical constituents
1	<i>Andrographispaniculata</i>	Acanthaceae	Erect, annual herb, <sup>[9]</sup>	Leaves, Stem	Leaves-sitosterol,glucoside; Andrographolide and panicolide, polyphenols, caffeic& chlorogenic acids and mixture of dicaffeoylquinicacids.Roots flavones, andrographin &panicolin & sitosterol. <sup>[8]</sup>
2	<i>Vetiveriazizanioides</i>	Poaceae	Habit- Perennial herb. <sup>[9]</sup>	Root	Isobisabolene, khusol, khusinol, khusilal, khusinol oxide, isokhusimol, khusillrol, khusimene, khusenic acid, sokhusenic acid, khusimone, cyclocopa, carnphenol epicyclocopacampheno1 (C-IIepimer), vetiselinenol and zizanol, zizanenelevojunenol, epikhusinol, ketones. <sup>[8]</sup>
3	<i>Plectranthusvettiveroides</i>	Lamiaceae	Habit- aromatic herb, Roots -deep straw-coloured aromatic. <sup>[9]</sup>	Root	Flavonoids, glycosides, phenolic compounds,volatile, constituents,hydrocarbons, alcohols, aldehydes, ketones, esters,Diterpenoids,essential oil, forskolin, alpha-tocopherol and ascorbic acid. <sup>[8]</sup>
4	<i>Zingiberofficinale</i>	Zingiberaceae	Habit- Perennial, erect herbwith horizontal tuberous rhizome. <sup>[9]</sup>	Rhizome	Starch(50%), lipids, Tryglycerides, phosphatidic acid, lecithins, free fatty acids (e.g., palmitic acid, oleic acid, linoleic acid, lauric acid, stearic acid, linolenic acid); oils.Other chemicals - cineole, gingerene, zingiberol;gingediol, methyl gingediol, gingediaceate & methylgingediacetate, paradol. <sup>[8]</sup>
5	<i>Piper nigrum</i>	Piperaceae	Habit- slender,aromatic& climber <sup>9</sup>	Fruit	Long chain of hydrocarbon, mono& sesquiterpene, caryophyllene, piperine, pipartine, piperlongumine, perlongumine&itsdihydro-derivative, pipernonaline, piperundecalidine, pipericide&guineensine, sesamin, diuedesmin, sitosterol & dihydrostigmasterol. <sup>[8]</sup>
6	<i>Cyperrotundus</i>	Cyperaceae	Habit-perennial shrub. <sup>[9]</sup>	Rhizome	Pinene, trace of cineole, sesquiterpenes&iso-cyperol;fatty oil-glycerol ,linolenic ,linolic, oleic, myristic&stearicacids;tubers-oleanolic acid & its glycosides, sitosterol. <sup>[8]</sup>
7	<i>Santalum album</i>	Santalaceae	Habit- small evergreen Tree. <sup>[9]</sup>	Wood	Santalac acid, palmiticacid, oleic acid, linoleic acid and glucose, fructose, n-octacosanol, n-triacontanol,palmitonce, alpha-beta santalences, santenol. Terpenoids, saponin, phenolics and tannins. <sup>[8]</sup>
8	<i>Mollugocerviana</i>	Molluginaceae	Habit- Erect, slender, branched herbs <sup>[9]</sup>	Whole plant	Phenols, tannins, flavonoids, flavone-c-glycoside orientin, vitexin, saponins, steroids, terpenoids, and alkaloids. <sup>[8]</sup>
9	<i>Trichosanthiscucumerina</i>	cucurbitaceae	Habit-Annual climber. <sup>[9]</sup>	Fruit	Phenolics and flavonoids, Vitamin C and E. <sup>[10]</sup> , mineral-potassium and phosphorus, sodium, Magnesium and Zinc, triterpenes. <sup>[11]</sup> dihydroisocucurbitacin B, 23,24-dihydrocucurbitacin E,sterols 2 $\beta$ -sitosterol stigmasterol, <sup>[12]</sup> galactose-specific lectin, trichoanguin, isoflavoneglucoside. <sup>[13]</sup>

## 2. Chemical Constituents of Nilavembu

Several active constituents reported to be present in *Andrographispaniculata* include flavonoids, flavonoid glycosides, diterpenes glycosides, lactones and diterpenes are the major active constituents. Flavonoids are existing mainly in the root, but have also been isolated from the leaves. Bitter principle andrographolide in pure form was first isolated by Gorter<sup>16</sup> where andrographolide was found to be high in leaves and hence most of the study is reported for leaves, compared to other parts of the plant (Gorter MK., 1911).

## 3. Nilavembu Kudineer's Preventative Medicine

*NilavembuKudineer* is one of the decoction variety used in Siddha OPDs as important medicine for fever. This Siddha product has antimicrobial properties that help it to counter fevers that arise due to a variety of causes. This medicine is used for preventive aspect for Chikungunya, Swine Flu and Dengue fever.

## 4. Pharmacological Activity of Nilavembu Kudineer

(Assessed from. [www.elsevier.com/locate/apjtm](http://www.elsevier.com/locate/apjtm) assessed on 09.10.2017)<sup>31</sup>

### 4.1. Antipyretic activity (Brewer's yeast induced pyrexia)

Administration of EENKC 200mg/kg and paracetamol 150mg/kg was significantly ( $p < 0.01$ ) reduced pyrexia at 1 to 5 h compared to 0h at the same group animals. At a dose of 400mg/kg EENKC did not show significant reduction in pyrexia at 1 and 2h compared 0h. But it reduced pyrexia significantly ( $p < 0.01$ ) at 3,4 and 5h compared to 0h of the same group animals the EENKC 200mg/kg has equal and consistent efficacy to reduced pyrexia compared to paracetamol 150mg/kg at 1 to 5h (Amaryan et al., 2003, Anbarasu et al., 2014, Madav et al., 1995).<sup>[17,18,19]</sup>

### 4.2. Anti – inflammatory activity (Carragenam induced rat raw oedema)

The efficacy of the EENKC 400mg/kg was not significant at 1h, but it showed significant activity at 3 h ( $p < 0.01$ ) and 5h ( $p < 0.01$ ). The EENKC 200mg/kg showed more significant ( $p < 0.01$ ) anti-inflammatory activity at 1h. Compared to control group than standard drug indomethacin 10mg/kg was more consistent and significant ( $p < 0.01$ ) the EENKC 400mg/kg. the higher level of inhibition of inflammation with EENKC 200mg/kg revealed the greater efficacy than indomethacin but there is no statically significant efficacy. (Warisara et al., 2010, Zhang et al., 2013, Lie et al., 2011).<sup>[20,21,22]</sup>

### 4.3. Analgesic activity (Acetic acid induced writhing in mice)

Both the dose (200 and 400mg/kg) of EENKC and aspirin (100mg/kg) Pretreatment animals significantly ( $P < 0.01$ ) reduced the painful response produced acetic acid, manifested as writhing compared to the control group animals. (Ghosh et al., 1981, Lin et al., 2009).<sup>[23,24]</sup>

## 4.4. Anti- Viral Activity

*Andrographispaniculata* reported for anti- viral activity against herpes simplex virus (HSV-1) Flavivirus, and pestviruses and dengue virus (DENV1) Tang et al. Investigated anti- viral activity for methanol extract of medicinal plants viz. *Andrographispaniculata*, citrus lemon, *Momaradicacharantia*, *Ocimum sanctum* and *Pelargonium citrosum* on dengue virus serotypes 1 (DENV1). Anti-viral assays based on cytopathic effects (CPE) denoted by degree of inhibition upon treating (DENV1) interested vero E6 cells with MNTD of six medicinal plants showed that *Andrographispaniculata* has the most anti-viral inhibitory effects followed by *Momaradicacharantia* Lin et al. Reported on inhibition of the epstanbarr virus lytic cycle of andrographolide, *Andrographispaniculata* is a medicinal plant that is commonly used in Asia.<sup>[25]</sup> (Lin et al., 2013).

## 4.5. Anti-Dengue activity

Tang et al., (2012)<sup>[26]</sup> reported anti-dengue activity in methanol extract of medicinal plants of *Andrographispaniculata*, citrus lemon, *Cymbopogon citrates*, *Momaradicacharantia*, *Ocimum sanctum* and *Pelargonium citrosum* on dengue virus serotype 1 (DENV1). Authors reported methanol extract of *Andrographispaniculata* and *Momaradicacharantia* possesses the ability of inhibiting the activity of DENV1 whereas *C.limon* and *Pelargonium citrosum* did not prevent cytopathic effect or cell death of DENV1. Kalaiarasi et al., (2013)<sup>[27]</sup> reported that administration of combination of Nilavempukudineer and Adathodamanapagu for scheduled period of 7 days in twenty cases revealed satisfactory symptomatic relief and significant improvement in the management of dengue fever,<sup>[28]</sup> (Tang et al., 2012, Kalaiarasi et al., 2013).

## 5. DENGUE - A SIDDHA REVIEW

Siddha system classifies fever into 64 types based on the cause, the affected biological humour, altered physical constituents and presenting clinical features. Hence each type of suram as mentioned in Siddha literatures can be considered as single disease rather than a symptom itself. Therefore dengue fever can be correlated to *Pithasuram* which is mentioned in a text named *Agasthiyarsuranool* 300 and another one text *Suravagadam*<sup>28</sup> (Kalaiarasi et al., 2013, Kuppasamudaliyar, 2007). The symptoms mentioned in literature can be correlated with Dengue and Dengue haemorrhagic fever which is shown in Table 1.

### 5.1. Dengue prevalence in India

Dengue virus is a mosquito-borne virus (Flavivirus) spreads through *Aedes aegypti* mosquito. These small (50 nm) viruses contain single-strand RNA. The virion consists of a nucleocapsid with cubic symmetry enclosed in a lipoprotein envelope. The virus infects over 50 million people worldwide, resulting in over many more deaths annually of people remain exposed to the disease across Africa, Eastern Mediterranean, Southeast Asia

and Western Pacific region. It has 4 serotypes; infection with 1 serotype provides lifelong homotypic immunity, but there is only short-term cross-protective immunity against heterotypic serotypes. India's population is twice that of Southeast Asia, these regions show the most dengue-related deaths. Dengue virus-specific antibodies, types IgG and IgM, can be useful in confirming a diagnosis in the later stages of the infection despite comparable environmental risk conditions, the number of

reported cases and deaths in India is only a fraction of that reported in south-east Asia. In many regions of India, an increasing number of suspected cases of dengue are seropositive for IgM and IgG antibodies. Our study highlight that alternative system of medicine are to provide medicine or siddha herbal product which can cure dengue and should not be adversely affected the human body and kill the virus of dengue.

**Table 3: Comparison of Pithasuram with Dengue (Kalaiarasi et al., 2013).**

Sl. No.	Inference	
	Siddha	Modern medicine
1.	<i>Edaividamalathigasuramkaithal</i> (High grade fever)	Hyperpyrexia
2.	<i>Neervetkai</i> (Thirst)	Dehydration
3.	<i>Okaalam</i> (Sensation of vomiting)	Nausea
4.	<i>Vairukazlithal</i> (Loose stools)	Dysentery
5.	<i>Udalsigappuniramadaithal</i> (Red spots on the body)	Petechial haemorrhage
6.	<i>Siruneersigappuniramadaithal</i> (Red colour urine)	Hematuria
7.	<i>Malamsigappuniramadaithal</i> (Blood in faeces)	Melaena
8.	<i>Manakalakam, mayakam, Padukaiyelthangamai</i> (Anxiety, loss of consciousness and restlessness)	Dengue encephalitis symptoms of Restlessness and altered sensorium

### 5.2. Siddha perspective-*Nilavembukudineer*

According to saint *Theriyar* "*Kudalthannilseethamala thusuramumvarathu*" which implies accumulation of *Kabam* (water) in the intestine predisposes to the development of fever and more "*Asseranamindraru ramvarathu*" which explains that the indigestion may leads to the development of fever. The indigestion may be due to increased *Kabam* in the digestive mechanism in the gastro intestinal tract. It has been observed from the above said prose the increased *Kabam* is the primary cause for the evolution of fever.<sup>[7]</sup>

The famous *Kannusamiyam* text says that the combination of three tastes viz. *Karppu* (acidic),

*Thuvarppu* (astringent) and *Kaippu* (bitter) will neutralize the increased *Kabam*, another combination of three tastes *Thuvarppu* (astringent), *Innipu* (sweet) and *Kaippu* (bitter) will neutralize *Pitham* (fire). When we observe the tastes of these nine ingredients the predominant tastes are Bitter, Acrid, Astringent and Sweet which will reduce or neutralize increased *Kabam* and *Pitham* related disorders.<sup>[8]</sup>

### 5.3 Duration of treatment

Generally, 7 days treatment with this combination is sufficient in all cases. If muscle or joint pains continue, then this combination can be taken for 4 to 6 weeks<sup>4</sup> (Jagdev Singh, 2016).

The general dosage of <i>NilavembuKudineer</i> Decoction is as follows.	
Infants (Age: Up To 12 Months)	2.5 to 5 ml
Toddler (Age: 1 – 3 yrs)	5 ml
Preschooler (3 – 5 yrs)	5 to 7.5 ml
Grade-schooler (5 – 12 yrs)	7.5 to 15 ml
Teenager (13 -19 yrs)	15 to 30 ml
Adults (19 to 60 yrs)	30 to 60 ml
Geriatric (above 60 yrs)	30 to 60 ml
Pregnancy	15 to 30 ml
Lactation	30 to 60 ml
Maximum Possible Dosage	180 ml Per Day (in divided doses)
* Twice a day	
<b>Best Time to Take:</b> Before Food	

### 5.4. Chikungunya

*Nilavembukudineer* is a drug of choice for the management of Chikungunya. *Andrographispaniculata* is considered to be responsible for its action against Chikungunya and the pain associated with it. It shows positive results within few days. The antipyretic, analgesic and anti-inflammatory properties of

*Nilavembukudineer* give relief from fever, joint pain, joint swelling, headache, muscle pain and rash<sup>4</sup>.

### CONCLUSION

In future more interest must be given to the clinical documentation. Based on this literature survey the

*Nilavembukudineer* can be used for preventative as well as curative for any type of fevers. As per the order of State Government of Tamil Nadu, the primary and tertiary health centres provide *Nilavembukudineer* for Dengue fever which yields good results. These results must reach globally to combat such outbreaks.

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