



Antipyretic activity of Nilavembu Kudineer – A Siddha System of Medicine

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Authors' contributions

This work was carried out in collaboration among all authors. Author AJSJS guided and designed the study. Author AAAS performed the pharmacological studies. Author AGKAV and SR helped in the statistical analysis and drafting the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i25A31450

Editor(s):

(1) Dr. Amal Hegazi Ahmed Elrefaei, Hot Lab and Waste Management Center, Atomic Energy Authority, Egypt.

Reviewers:

(1) Yusransyah, STIKes Salsabila Serang, Indonesia.

(2) Ruqaiya Hasan, University of Karachi, Pakistan and Umm Al Qura University, KSA.

(3) Hasta Handayani Idrus, Universitas Muslim Indonesia, Indonesia.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/67412>

Original Research Article

Received 06 February 2021

Accepted 13 April 2021

Published 20 April 2021

ABSTRACT

Aim: To evaluate the antipyretic activity of Nilavembu kudineer against yeast induced pyrexia in Albino rats.

Study Design: Experimental study

Place and Duration: Research lab, Department of Siddha Medicine, Tamil University, Thanjavur, India and KPJ Healthcare University College, Nilai, Malaysia between March 2018 and July 2019.

Methodology: The Nilavembu kudineer powder was extracted by using acetone, methanol and aqueous solvents. The acute toxicity study was carried on swiss albino mice using acetone, methanolic and aqueous extracts of Nilavembu kudineer. From this, the LD₅₀ value was determined and 1/10th of the LD₅₀ value was taken as ED₅₀ value and selected for the antipyretic studies. The

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Pyrexia was induced by 20% suspension of Brewers' yeast at a dose level of 20 mg/kg on Albino rats. The test extracts (200mg/kg), Standard Paracetamol (150 mg/kg) and control saline vehicle were administered orally. The phytochemical parameters such as carbohydrates, proteins, lipid, oil, amino acid, glycosides, tannins, phenolic compounds, triterpenoids, flavones, flavanones and alkaloids were tested using standard procedures. Statistical analysis, the values were subjected to one way analysis of variance (ANOVA) followed by Dennett's test.

Results: LD₅₀ value of various extracts of Nilavembu kudineer was 2000 mg/kg and 1\10th of ED₅₀ as 200 mg/kg was selected for screening of various pharmacological activities. The treatment with methanolic extract of Nilavembu kudineer at a dose of 200mg/kg significantly ($p < 0.001$) decreased the elevated rectal temperature after 2 hr of administration. Yeast-instigated pyrexia rodents had been controlled with Nilavembu kudineer at a dose of 200 mg/kg to decide the Tamil traditional claim about this plant for its antipyretic property.

Conclusion: The methanolic extract of Nilavembu kudineer (200 mg/kg) possess potent fever reducing agent in various types of fever. The phytoconstituents such as Flavonoids, Alkaloids, Glycosides, Tannins and Phenolic compounds may be responsible for controlling the elevation of body temperature.

Keywords: Nilavembu kudineer; antipyretic activity; siddha; traditional medicine.

1. INTRODUCTION

The siddha system of medicine is an ancient traditional system of medicine. There are 64 types of medications has been used for the treatment of different ailments. One among the 64 types of medications is 'Kudineer'. The important characteristics of kudineer such as, Easily Absorbing capacity, Good digestible property and Easily preparable. Each of these kudineer's drugs has antipyretic and immunomodulatory properties, making them very effective for fever and other vector-borne diseases such as dengue, malaria, chikungunya and COVID. Plants have been used by mankind as a source of medicines since time immemorial. Information on the ancient uses of plant materials as medicines can be found in archaeological records, old literature, history books, and pharmacopeia. In fact, in the Quran and the Bible, about 20 and 125 plants are mentioned, respectively, as being used as medicinal agents to treat various ailments [1]. Over 35,000 plant species have been accounted for to be utilized in different human societies throughout the world for clinical purposes [2]. In any case, the number could be a lot higher as information on the indigenous uses of plants was for the most part given orally starting with one age then onto the next. The utilization of spices and therapeutic as the principal medications is a universal phenomenon. Each culture on earth through-composed or oral custom has depended on the immense of natural chemistry found in healing plants for their therapeutic properties. All medications of the past re-substances with a specific remedial activity extracted from plants.

Thus, medicinal plants may be defined as any plant that can be put to culinary or medicinal use. The therapeutic plants produce numerous substances to shield themselves from microbial disease and decay including peptides, Unsaturated long-chain aldehydes, alkaloids, and some fundamental oils and phenols. These mixtures have potential critical remedially application against human microorganisms including microbes, parasites, and infections. Therapeutic plants being the viable wellspring of both conventional and present-day, are valuable in essential medical services. Throughout the long term, the World Health Organization (WHO) pushed customary medicines as protected solutions for sicknesses of both microbial and non-microbial origins. The utilization of alternative medicinal therapy has expanded the interest of pharmacologists and cultivators over the previous decade. Traditionally the plants have given a wellspring of motivation to novel medication compounds as plant inferred medicines have made a huge commitment to human health and wellbeing. On the other hand, there is a high use of herbal products all over the world [3].

Fever is the rise of core body temperature heat level better than average; in typical grown-ups, the normal oral temperature is 37°C (98.6°F). In oncology practice, a single temperature of more than 38.3°C (101°F) or three readings (at least 1 hour apart) of more than 38°C (100.4° F) are considered as significant [4]. The basic "endogenous pyrogens" engaged with delivering an exceptionally directed provocative reaction to tissue injury and contamination are polypeptide

cytokines. Pyrogenic cytokines, for example, interleukin-1 β (IL-1 β), tumour necrosis factor (TNF), and interleukin-6 (IL-6) are those that act straightforwardly on the nerve centre to influence a fever reaction. Exogenous pyrogens, like microbial surface segments, evoke pyrexia most regularly through the incitement of pyrogenic cytokines. The gram-negative bacterial outer membrane lipopolysaccharide (endotoxin), however, is equipped for working at the level of the nerve centre, similarly as IL-1 β [5]. Nilavembu kudineer is a combination of 9 herbal plants which are mixed and grained together with equal proportion. *Andrographis paniculata* – Tamil name (Nilavembu), Roots of *Plectranthus vettiveroides* – Tamil name (Vilamichamver), Dried *Zingiber officinale* - Tamil name (Sukku), Stem of *Cyperus rotundus* -Tamil name (Koraikizhangu), whole plant of *Trichosanthes cucumerina* – Tamil name (Pei pudal), Roots of *Vetiveria zizanioides* - Tamil name (Vetiver), Seed of *Piper nigrum* – Tamil name (Milagu), Whole plant of *Oldenlandia corymbosa* – Tamil name (Kattucayaver), Wood of *Santalum album* – Tamil name (Sandanam), The most significant of these bioactive constituents of plants are steroids, terpenoids, carotenoids, flavonoids, alkaloids, tannins, and glycosides. Plants in all features of life have filled in as a significant beginning material for drug improvement [6].

The significance of alkaloids, saponins, and tannins in different anti-toxins utilized in treating regular pathogenic strains [7-8] reports alkaloids in 12 verdant vegetables contemplated [9] had before recorded that bitter leaf contains an alkaloid which is fit for lessening migraines related with hypertension. More than 3/4th of the complete world, the populace relies for the most part upon plants and their concentrates for wellbeing concerns. Roughly, the World Market for plant-inferred medications may well record for about Rs. 2, 00,000 crores; of which the Indian commitment is under Rs.2000 crores. Also, 2,50,000 higher plant species are found on the earth, more than 80,000 are having medicinal uses. [10]. The famous *Kannusamiyam* text says that the combination of three tastes viz. *Karppu* (acid), *Thuvappu* (astringent), and *Kaippu* (bitter) will neutralize the increased kabam, another combination of three tastes *Thuvappu* (astringent), *Innipu* (sweet), and *Kaippu* (bitter) will neutralize Pitham (fire). When the observation shows the predominant taste such as Bitter, Acid, Astringent and Sweet from nine ingredients will reduce or neutralize increased

Kabam and Pitham related disorders. By this inference, the Nilavembu kudineer can be correlated better to cure fevers associated with Kabam and Pitham [11]. The present study was carried out to evaluate the Antipyretic activity of Nilavembu kudineer to assess the claim of the traditional practices of this formulation used as a fever remedy.

2. MATERIALS AND METHODS

2.1 Collection of Nilavembu kudinner Powder

1 Kg of Nilavembu kudinner powder was purchased from the locally available store at Thanjavur.

2.2 Preparation of Extracts

The purchased Nilavembu kudinner powder (1kg) was taken in an aspirator bottle and extracted successively by cold maceration technique with solvents like acetone, methanol, and water respectively for six days. At the end of each extraction, the extracts were filtered using filter paper and were concentrated using a rotary vacuum evaporator. The colour, consistency, and percentage yield of all extracts were recorded [12].

2.3 Phytochemical Studies

A spectrum of natural compounds like glycosides, volatile oils, alkaloids, tannins, and similar other secondary metabolites which possess physiological activity are synthesized in the plant. The different qualitative chemicals tests were performed for establishing a profile of the extracts of Nilavembu kudineer for their phytoconstituents [13].

2.4 Pharmacological Evaluation

2.4.1 Animals

Healthy adult albino rats of Wistar strain weighing 150-200 gm and healthy adult Swiss albino mice weighing 20-25 gm were obtained from the animal house. The animal house was well ventilated and the animals had 12 \pm 1 hr day and night schedules with a spacious, hygienic cage during the experimental period. The animals were fed pellet feed and water *ad libitum*.

Table 1. Detection of alkaloids

50 mg of extracts of Nilavembu kudinneeer was stirred separately with two ml of dilute hydrochloric acid and filtered. The filtrates were tested carefully with various reagents for detection of alkaloids as follows.

Name of the Test	Procedure	Observation	Inference
Mayer's test	In one ml of filtrate, two drops of Mayer's reagent were added along the sides of the test tube.	Cream coloured precipitate appeared	Presence of alkaloids
Dragendroff's test	In one ml of filtrate, two drops of Dragendroff's reagent were added	Reddish orange precipitate appeared	Presence of alkaloids
Hager's test	In one ml of filtrate, two drops of Hager's reagent were added	Yellow precipitate appeared	Presence of alkaloids
Wagner's test	In one ml of filtrate, two drops of Wagner's reagent were added	Brown precipitate appeared	presence of alkaloids

Table 2. Detection of carbohydrates and glycosides

100 mg of all the extracts were dissolved in 5 ml of distilled water separately and filtered. The filtrate was subjected to the following tests.

Name of the Test (for Carbohydrates)	Procedure	Observation	Inference
Molisch's test	Two ml of filtrate was added with two drops of alcoholic solution of α -naphthol. The mixture was shaken well and one ml of concentrated sulphuric acid was added along the sides of the test tube and allowed to stand.	Formation of A violet or purple ring	Presence of carbohydrates.
Fehling's test	One ml of filtrate was boiled on a water bath with one ml each of Fehling's solutions A and B	A red precipitate appeared	presence of carbohydrates
Barfoed's test	One ml of filtrate, one ml of Barfoed's reagent was added and heated on a boiling water bath for 2 mins	A red precipitate appeared	presence of carbohydrates
Benedict's test	One ml of filtrate, one ml of Benedict's reagent was added. The mixture was heated in a boiling water bath for 2 mins.	Yellow to red precipitate appeared	presence of carbohydrates
Test for Glycosides			
Borntranger's test	Two ml of filtered hydrolysate was treated with three ml of chloroform and shaken well. The chloroform layer was separated and 10% ammonia solution was added	The pink colour appeared	Presence of glycosides

Name of the Test (for Carbohydrates)	Procedure	Observation	Inference
Legal's test	to it. 50 mg of the extracts were dissolved in pyridine. To this sodium nitroprusside solution was added and made alkaline using 10% sodium hydroxide solution	The pink colour appeared	Presence of glycosides

Table 3. Detection of proteins and amino acids

100 mg of all the extracts were dissolved in 10 ml of distilled water and filtered through filter paper and the filtrates were subjected to tests for proteins and amino acids.

Name of the test (for proteins)	Procedure	Observation	Inference
Biuret test	An aliquot of two ml of filtrate was treated with one drop of 2% copper sulfate solution. To this one ml of (95%) ethanol was added, followed by an excess of potassium hydroxide pellets	The pink colour in the ethanolic layer appeared	Presence of proteins
Test for Amino acids			
Ninhydrin test	Two drops of Ninhydrin solution were added to two ml of aqueous filtrate	A characteristic purple colour	Presence of amino acids.

Table 4. Detection of sterols

After saponifying the lipid fraction of plant tissue and extracting the resulting soap solution with petroleum ether, the unsaponifiable fraction containing sterols will be obtained.

Name of the Test	Procedure	Observation	Inference
Liebermann sterol test	In a solution of glycoside or steroid aglycones in glacial acetic acid, one drop of concentrated sulphuric acid was added.	A play of colour was observed starting with rose, red, violet, blue to green.	Presence of Sterols
Liebermann Burchard's test	Five ml of the unsaponifiable fraction was dissolved in two ml chloroform and two ml of acetic anhydride. After this, two drops of concentrated sulphuric acid were added to the above solution	A strong blue colouration changing gradually to green	Presence of steroids
Salkowski's test	Two ml of extract was dissolved in three ml of chloroform and two drops of concentrated sulphuric acid were added along the sides of the test tube.	The formation of the red-coloured ring at the junction and green-coloured fluorescent layer at the bottom	Presence of cholesterol

Table 5. Detection of fixed oils and fats

Name of the test (for fixed oils)	Procedure	Observation	Inference
Spot test	10 mg of extract was pressed between two filter papers	Oil stain on the paper appeared	Presence of fixed oil.
Test for fats			
Saponification test	0.5 ml of 0.5 N alcoholic potassium hydroxide solution was added to 10 mg of extract along with a drop of phenolphthalein. The mixture was heated in a water bath for 2 hrs	The formation of soap or the partial neutralization of alkaline solution	Presence of both fixed oils and fats.

Table 6. Detection of phenolic compound and tannins

Name of the test	Procedure	Observation	Inference
Lead acetate test	50 mg of extract was dissolved in distilled water, and to this, three ml of 10% lead acetate solution was added	A bulky white precipitate appeared	Presence of phenolic compounds
Ferric chloride test	50 mg of extract was dissolved in distilled water, and to this, 0.5 ml of neutral 5% ferric chloride solution was added.	A dark green colour appeared	Presence of tannins.

Table 7. Detection of triterpenoids

Name of the test	Procedure	Observation	Inference
Tin and thionyl chloride test	25 mg of the extract is treated with tin and thionyl chloride	The formation of purple colour	Presence of triterpenoids.

Table 8. Detection of saponins

Name of the test	Procedure	Observation	Inference
Foam test	100 mg of extract was diluted with distilled water to 20 ml. The suspension was shaken in a graduated cylinder for 15 mins	The formation of 2 cm layer foam	Presence of saponins.
Blood hemolysis test	A drop of human blood was placed over a slide and a drop of drug extract was added and mixed well, visualize through a microscope	Hemolysis in the blood cells appeared	Presence of saponin

Table 9. Detection of gums and mucilage

Name of the test	Procedure	Observation	Inference
Precipitation test	100 mg of extract was dissolved in 10 ml of distilled water and to this 25 ml of absolute alcohol was added with constant stirring	White precipitate appeared	Presence of gums
Test for mucilage			
Ruthenium red test	50 mg of extract was soaked in water, and two drops of ruthenium red were added	Pink colour appeared	Presence of mucilage

Table 10. Detection of flavones and flavanones

Name of the test	Procedure	Observation	Inference
Aqueous sodium hydroxide	20 mg of extract was added to 2 ml of aqueous sodium hydroxide solution	Blue to the violet colour appeared Yellow to the orange colour appeared Orange to the crimson colour appeared	Presence of anthocyanins Presence of flavones Presence of Flavanones
Concentrated sulphuric acid	20 mg of extract was added to one ml of concentrated sulphuric acid	Yellowish-orange colour appeared Yellow to the orange colour appeared orange to the crimson colour appeared	Presence of anthocyanins Presence of flavones Presence of flavanones
Shinoda's test	50 mg of extract was dissolved in alcohol; few magnesium turnings and concentrated hydrochloric acid (dropwise) were added	The appearance of the magenta colour	Presence of flavonoids

2.4.2 Acute toxicity study of extracts of Nilavembu kudineer

The acute toxicity study was carried on albino mice as per guidelines No.423 given by the organization for Economic Co-operations and Development, Paris. Albino mice were fasted overnight and divided into four groups of 3 animals each. The entire test samples such as acetone, methanolic and aqueous extracts were given orally at a starting dose of 5mg/kg. Animals were observed for two hours, then occasionally for 4 hrs for the severity of any toxic signs and mortality. Since no mortality was observed, the same dose was repeated with one more animal. Since no mortality was observed, the procedure was repeated using higher doses of 50, 300, and 2000mg/kg in another separate group of animals. From this, the LD₅₀ value was determined and 1/10th of the LD₅₀ value was taken as ED₅₀ value and selected for the pharmacological studies. Behaviour as well as other toxic symptoms if any was observed for 24, 48, and 72 hrs. The animals were kept under observation up to 14 days after drug administration to find out delayed mortality if any [14].

2.4.3 Screening of antipyretic activity by Brewer's yeast induced method

Albino rats were divided into five groups of six rats each. Fever was induced by injecting 20 mg/kg (subcutaneous) of 20% suspension of Brewer's yeast in normal saline below the nape of the neck [15]. Initial rectal temperature was recorded. After 18 hr, animals that showed an increase of 0.3-0.5°C in rectal temperature were selected for antipyretic studies. The test extracts (200mg/kg) reference standard Paracetamol (150 mg/kg) and control saline vehicle were administered orally. The rectal temperature was measured with the clinical thermometer at 1,2,3,4 and 5 hours of post-dosing [16].

2.4.4 Statistical analysis

Results were expressed as mean \pm SEM. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Dennett's test [17]. The values of P <0.05 were considered statistically less significant and P < 0.001 considered as more significant.

3. RESULTS

3.1 Nature and Yield of Extracts

The successive solvent maceration of Nilavembu Kudineer was carried out. The colour,

consistency, and percentage yield of various extracts were recorded in Table 11.

3.2 Qualitative Phytochemical Screening

The different qualitative chemical tests were performed to assess the chemical nature of the various extracts. The results were presented in Tables 12. The qualitative phytochemical screening of the Nilavembu kudineer showed the presence of alkaloids, carbohydrates, glycosides, proteins, amino acids, steroids, phenolic compounds, triterpenoids, mucilage, saponins, and flavones, flavanone and fixed oils.

3.3 Acute Toxicity Study for the Various Extracts of Nilavembu Kudineer

Table 13 represents the results of acute toxicity studied in albino mice administered with various extracts of the plant by the oral route. The test extracts were suspended in 0.5% Carboxymethylcellulose (CMC) and administered orally. No acute mortality was observed even at 2 g/kg of test extracts of Nilavembu kudineer. All the animals were found to be normal and there were no gross behavioural changes till the end of the observation period (14 days). From these results, LD₅₀ or the maximum tolerated dose was found to be 2000mg/kg. From this, 1/10th of the maximum tolerated dose (200 mg/kg) was selected for the screening of antipyretic activity.

3.4 Antipyretic Effects

Extracts of Nilavembu kudineer showed significant antipyretic activity by reversing yeast-induced pyrexia in albino rats. Methanolic extract of Nilavembu kudineer at a dose of 200 mg/kg significantly (P<0.05) decreased the elevated rectal temperature after 2 hours of administration. The highly significant antipyretic activity (P<0.001) was observed after 4 hr of administration in the groups of rats treated with acetone, methanol and water extracts. These findings were well comparable with standard drug paracetamol 150 mg/kg. The results are presented in Table 14.

4. DISCUSSION

In the present study, Nilavembu kudineer was evaluated for an antipyretic agent on Yeast induced pyrexia using Albino rats. Yeast-induced pyrexia rodents had been controlled with Nilavembu kudineer of 200 mg/kg shows

better antipyretic impacts. Fever might be because of contamination or one of the spin-offs of tissue harm, irritation, joint dismissal, or other sickness states [18-19].

Antipyretics are the specialists, which decrease raised internal heat level. Guideline of internal heat level requires a sensitive harmony among creation and loss of warmth, and the nerve centre manages the set point where internal heat level is kept up. In fever, this set point lifts, and a medication like paracetamol doesn't impact internal heat level when it is raised by the variables like exercise or an expansion in surrounding temperature.

Yeast-actuated fever is called pathogenic fever. Its etiologic remembers the creation of prostaglandins for the focal sensory system

which is the last regular pathway liable for fever acceptance [18]. From the outcome, the methanolic extract showed a stamped decline in the raised rectal temperature of pyretic rodents. By and large, NSAIDS produce their antipyretic activity through the restraint of prostaglandin synthetase inside the nerve centre [20-21].

Hence, apparently the antipyretic activity of concentrates of Nilavembu kudineer may likewise be identified with the restraint of prostaglandin blend in the nerve center by the presence of flavonoids in the extracts of Nilavembu kudineer. The pharmacological exercises give the remedial adequacy of Nilavembu kudineer, the outcomes got recommend that the utilization of this plant in the treatment of fever is critical. These findings confirmed the Indian folklore claim.

Table 11. The colour, consistency and percentage yield of different extracts of Nilavembu kudineer

S. No.	Extract	Nilavembu kudineer		
		Colour	Consistency	% of extract
1.	Acetone	Slightly yellowish	Sticky mass	1.79
2.	Methanol	Brownish	Sticky Powder	4.73
3.	Water	Dark Brown	Mucilagenous	38.02

Table 12. Qualitative analytical test of Nilavembu kudineer

S. No.	Qualitative Test	Acetone extract	Methanol extract	Water extract
1.	Alkaloids	-	+	+
2.	Carbohydrates and glycosides	-	+	+
3.	Proteins and amino acids	+	+	+
4.	Sterols	+	+	-
5.	Fixed oils and fats	+	-	-
6.	Tannins-phenolic compounds	-	+	+
7.	Triterpenoids	-	+	-
8.	Saponins	-	+	+
9.	Gum and mucilage	-	+	+
10.	Flavones and flavanones	-	+	+

+ = Positive; - = Negative

Table 13. Acute toxicity study of various extracts of Nilavembu kudineer

Sl. No	Solvents used	LD ₅₀ or MTD (mg/kg)	ED ₅₀ or 1/10 th of LD ₅₀ (mg/kg)
1.	Acetone extract of Nilavembu kudineer	2000	200
2.	Methanolic extract of Nilavembu kudineer	2000	200
3.	Water extract of Nilavembu kudineer	2000	200

MTD - Maximum Tolerated Dose; LD₅₀ - Lethal dose producing lethal effect in 50% population; ED₅₀ - Effective dose producing pharmacological effect in 50% population

Table 14. Effects of Nilavembu kudineer extracts on yeast-induced pyrexia rats

Groups Dose(mg/ml)	Groups Dose(mg/ml)	Average rectal temperature (°C)					
		0h	1h	2h	3h	4h	5h
Control	---	38.23±0.48	39.41±0.54	38.62±0.63	38.14±0.11	38.62±0.48	38.48±0.72
Aqueous Extract	200mg/kg	38.43±0.26	38.23±0.54	38.61±0.62	37.33±0.78 ^b	37.03±0.29 ^a	38.19±0.18
Methanol Extract	200mg/kg	39.21±0.38	38.96±0.61	37.62±0.33 ^b	36.41±0.41 ^a	36.23±0.58 ^a	38.76±0.31
Acetone Extract	200mg/kg	38.36±0.19	38.28±0.68	38.01±0.48	37.09±0.81 ^b	36.19±0.41 ^a	37.22±0.64
Paracetamol	150mg/kg	38.68±0.42	36.42±0.56 ^a	36.08±0.41 ^a	36.08±0.18 ^a	36.19±0.41 ^a	37.22±0.64

Values are expressed as mean ± S.D aP<0.001, bP<0.01, cP<0.05; significantly different from control; Dennett's test, N=6

5. CONCLUSION

The present study concluded that the methanolic extract of Nilavembu kudineer (200mg/kg) possesses a potent fever-reducing agent in various conditions like infective fever, etc. The various crude drugs present in Nilavembu kudineer had important Phytoconstituents such as flavonoids, alkaloids, glycosides, tannins, and phenolic compounds which helps in the control of elevated body temperature. This study also helps to standardize and confirm the folklore claim.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study protocol was approved by ethical committee, KPJ healthcare University college, Malaysia (KPJUC/SOP/EC/F029/03).

ACKNOWLEDGEMENTS

The authors would like to thank Department of Siddha Medicine, Faculty of Science, Tamil University, Thanjavur and Department of Pharmacy and KPJ healthcare University college, Nilai, Malaysia for providing facilities and guidance to carry out the research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Arokyaraj DM, Rathiga G. Phytochemicals and pharmacological activities of kabhasura kudineer, nilavembu kudineer, adathodai kudineer-a review. *Int J Trans Res Ind Med.* 2020;2(3):41-51.
2. Musselman LJ, Holy Pharmacy. *Modern Medical Uses of some Plants of the Quran and the Bible. Its Relation to Biodiversity;* 1999.
3. Lewington A. *Medicinal plants and plant extracts: A review of their importation into Europe.* Cambridge, United Kingdom, Traffic International; 1993.
4. David MA, Eric GN. Antipyretics mechanisms of action and clinical use in fever suppression. *The American Journal of Medicine.* 2011;111(4):304–315.
5. Pan SY, Litscher G, Gao SH, Zhou SF, Yu ZL, Chen HQ, Zhang SF, Tang MK, Sun JN, Ko KM. Historical perspective of traditional indigenous medical practices: The current renaissance and conservation of herbal resources. *Evidence-Based Complementary and Alternative Medicine;* 2014.
6. Clark VL, Kruse JA. Clinical methods: The history, physical, and laboratory examinations. *Jama.* 1990;264(21):2808-9.
7. Abiramasundari G, Sreepriya M. *Research Journal of Pharmaceutical, Biological and Chemical Sciences;* 2014.
8. Kubmarawa D, Ajoku GA, Enworem NM and Okorie DA. *African Journal of Biotechnology.* 2007;6:1690-1696.
9. Mensah JK, Okoli RI, Ohaju-Obodo JO and Eifediyi K. *African Journal of Biotechnology.* 2008;7: 2304-2309.
10. Ayitey-Smith E and Addae-Mensah IW. *West African Journal of Pharmacology and Drug Research.* 1977;4:7-8.
11. Naqvi SA, Khan MS, Vohora SB. Antibacterial, antifungal and anthelmintic studies on ochrocarpus longifolius. *Planta Medica.* 1976;29:98-100.
12. Shanmugavelu M. *Noi Naadi Noi Mudal Naadi Part-1.4th edition,* Chennai: Directorate of Indian Medicine & Homeopathy. 2006;25.
13. Anbu JS, Jayaraj P, Varatharajan R, John T, James J, Muthappan M. Analgesic and Antipyretic Effects of *Sansevieria Trifasciata* Leaves. *African Journal of Traditional, Complementary and Alternative Medicines.* 2009;6(4):529-533.
14. Ramanathan M, Subramanian L, Poongodi T, Manish S, Muneeswari E, Pavithra P, Pugalendran S. Formulation and evaluation of Nilavembu Kudineer capsules. *Asian Journal of Pharmaceutical*

- Research and Development. 2019;7(1):41-5.
15. Maithili V, Dhanabal SP, Mahendran S, Vadivelan R. Antidiabetic activity of ethanolic extract of tubers of *Dioscorea alata* in alloxan induced diabetic rats. Indian journal of pharmacology. 2011; 43(4):455-459.
 16. Somezeet P, Choudhury NSK, Jagannath PV, Dipti KP, Goutam KJ. Analgesic, Antipyretic and Anti-inflammatory Effect of the Whole Plant Extract of *Desmostachya bipinnata* Stapf (Poaceae) in Albino Rats. DIT. 2009;1(2):150-153.
 17. Uma SS, Umesh KS, Abhishek S, Niranjan S, Puspak JS. Screening of *Terminalia Bellirica* Fruits Extracts for its Analgesic and Antipyretic Activities. Jordan Journal of Biological Sciences. 2010;3(3):21-124.
 18. Moltz H. Fever: Causes and consequences. Neuroscience & Biobehavioral Reviews. 1993;17(3):237-69.
 19. Paschapur MS, Patil S, Patil SR, Kumar R, Patil MB. Evaluation of the analgesic and antipyretic activities of ethanolic extract of male flowers (inflorescences) of *Borassus flabellifer* (L. arecaceae). International journal of pharmacy and pharmaceutical sciences. 2009;1(2):98-106.
 20. Clark WO, Cumby HR. The antipyretic effect of Indomethacin. The Journal of Physiology. 1975; 248:625-38.
 21. Zeal R, Krupp P, Schorbaum E, Lomax P, Jacob J. Temperature regulation and drug action. 1975;233-41.

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