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Original Article

Standardization of *Kirāmpu kutinīr* Decoction and Extract Granules using Pharmacognostic, Physicochemical and HPTLC Studies

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ABSTRACT

Introduction: Siddha being one of the ancient systems of medicine, has been counted on by most of the population during the outbreak of pandemics in recent times. The decoctions like *nilavempu kutinir* and *kapacura kutinir* have been authorized for prescription for conditions like dengue, Covid-19 etc. *Kirampu kutinir* (KK) is one such decoctions which has been found efficacious in Covid patients with respiratory tract infections. The current study is aimed at standardizing KK curnam and two of its dosage forms like *Kutinir* and extract granule employing pharmacognostic and chemical analyses. **Methods:** *Kirampu kutintr* (KK) and *Kirampu kutinir* extract granules (KEG) were analysed for pharmacopoeial standards following standard procedures. **Results:** The macroscopy and powder microscopy correlated with standards and matched with their characters. Both HPTLC photo documentation and densitometric scan revealed that the KEG comprises of the said ingredients. It also divulges that KEG and KK are of same bands and same pattern. **Conclusion:** The reported results will be supportive for standardization and future studies of KK.

Key words: Herbal medicine, Polyherbal formulation, Respiratory infection, Siddha COVID care, Quality control, Vector-borne diseases.

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INTRODUCTION

The search for remedies for new emerging diseases is a challenge to every healthcare system. WHO estimates that, 80% of populations from underdeveloped realm rely mostly on the traditional medicines.[1] Furthermore, the World Health Organization (WHO) identified approximately 21,000 plants with therapeutic potential around the world, of which 2500 varieties are found in India, including 150 species with large-scale commercial use.[1] Traditional medical systems like Siddha, from its history to present day scenario, had proved its success in dealing many sorts of sufferings to humanity particularly that from epidemic origin.[2] Siddha formulations, such as *kapacura kutinīr* and *nilavēmpu kutinīr*, are used to combat vector-borne diseases etc. and were observed to reduce neuraminidase.[3]

Recently a polyherbal decoction, *Kirāmpu kutinīr* (KK) was found out to be successful in managing COVID-19, specifically in those presenting respiratory symptoms. KK is a combination of 6 herbal ingredients which are mostly used as spices, prepared as decoction, well indicated for symptoms of respiratory tract infections attended with fever.[4] The decoction is prescribed to be taken internally at frequent intervals at standard dosage of 40 to 60 ml. With experience, the usage was found to improve lung functions, oxygen saturation, mucosal clearance, cough and chest congestion.[4] Because of the growing popularity of this formula, a standardization study has been taken up as a step further to control quality of this traditional Siddha medicine. The current study is aimed at standardizing KK curnam and two of its dosage forms like *Kutinīr* and extract granule employing pharmacognostic and chemical analyses.

MATERIALS AND METHODS

Procurement of raw drug

The raw drugs were procured from market in Chennai, Tamilnadu. All the drugs were authenticated by Research Officer and HOD (Department of Pharmacognosy), Siddha Central Research Institute (SCRI). All the drugs matched the standard samples stored in SCRI museum, Chennai. The botanical details of the six herbal ingredients used in KK and the proportion used in the formulation is detailed in Table 1 and Figure 1.

Sample preparation for pharmacognostic, physiochemical and HPTLC studies

All the procured raw drugs were physically cleaned and checked for any foreign materials and taken for macroscopy studies. The drugs were sun dried and powdered for powder microscopic, and HPTLC studies individually. KEG and one sample of decoction were also studied for HPTLC and physiochemical parameters.

Preparation of KK decoction

Outer skin of *Z. officinale* was scrapped off, washed well in potable water and cut into small slices.[3] The other ingredients were cleaned, dried and pounded coarsely.[5] The ingredients were taken as per the formula composition (Table 1), mixed and added with 16 parts of water, boiled well. The decoction was prepared by reducing the water level to 1/4th, filtered and preserved for further studies.[5,6]

Table 1: Details of Ingredient Composition KK.

SN	Ingredient	Botanical name	Part used	Quantity
1.	*Kirāmpu*	*Syzygium aromaticum* (L.) Merr. and L.M.Perry	Flower bud	1 part
2.	*Ōmam*	*Trachyspermum ammi* (L.) Sprague	Fruit	2 parts
3.	*Mañcal*	*Curcuma longa* L.	Rhizome	1 part
4.	*Milaku*	*Piper nigrum* L.	Fruit	1 part
5.	*Iñci*	*Zingiber officinale* Roscoe	Rhizome (fresh)	1 part
6.	*Atimaturam*	*Glycyrrhiza glabra* L.	Root	2 parts

Figure 1: Ingredients of KK.

Preparation of KEG granules

From KK decoction granules were prepared by mixing it with equal ratio of fine powder, dried well in hot air oven at 60°C for 5 hr.[7]

Macroscopy

Macroscopical characters of were observed and characters were documented.

Powder microscopy

The finely powdered formulation of five drugs (1 to 4 and 6 in the proportion mentioned in Table 1) in the proportion mentioned in Table 1 was passed through sieve no. 60. A pinch of the sample was taken and mounted in glycerin after treating with 20% KOH.[8] The characters were identified and labeled.

Organoleptic studies of Formulation

The formulation was checked for organoleptic characters like colour, odour and taste and the observations were recorded.[9]

Physicochemical evaluation

The formulations, both granule form and decoction, were tested for physicochemical parameters like loss on drying at 105°C, total ash, water soluble ash, acid insoluble ash, water soluble extractives, alcohol soluble extractives, total solid, specific gravity and pH values as per the standard protocol.[10]

TLC/HPTLC Analysis

One gram of the sample was taken separately in a conical flask and 10 ml of methanol was added, boiled for few minutes, cooled, filtered and then concentrated to 2 ml. The mobile phase used was *Toluene*: *Ethyl acetate*: *Formic acid* (8:2:0.5, *v/v/v*). Six and 10 µl of the samples were applied on silica gel (60 F_{254}) pre-coated TLC plate using CAMAG (Muttenz, Switzerland) ATS4 applicator. The plate was placed in a TLC chamber (CAMAG)(10 x 10 cm size) presaturated with the selected mobile phases. It was monitored for development till the mobile phase rises to a height of 90 cm from the bottom of the plate. Then the plate was viewed under UV at 254 nm and 366 nm and the images were captured. Subsequently the plate was scanned at 254 nm using deuterium lamp in absorption mode and at 366 nm using mercury lamp in fluorescence mode respectively for development of fingerprint profile. For visualization, the plate was sprayed with vanillin sulphuric acid reagent and heated over a plate heater till the appearance of coloured spots. Immediately the derivatized plate was photo documented and scanned at 520 nm using tungsten lamp in absorption mode for generating fingerprint profiles.[11]

RESULTS

Macroscopy

***Syzygium aromaticum* (L.) Merr. and L.M.Perry:** The flower bud consisted of two parts, a head and stalk. Stalk is dark brown coloured cylindrical, longitudinally wrinkled measuring about 10 to 11 mm in length, surmounted by 4, spreading thick acute sepals about 3 mm in length. The head portion is globular pale brown 4 to 5 mm in diameter surrounded by four imbricated petals and rests on the stalk.[12]

***Trachyspermum ammi* (L.) Sprague:** Fruit is entire cremocarps. The dorsal surface of the mericarp is convex with five distinct longitudinal ridges in each mericarp, surface warty, commissural surface flat, showing two darker longitudinal bands representing the vittae with or without pedicel attached at the base. A bifid stylopod is found at the apex, broadly ovoid, 1.5 to 3 mm in length and 1.2 to 2.8 mm in width, yellowish green.[13]

***Curcuma longa* L.:** Rhizome is round ovate-oblong, conical to pear shaped 3 to 7 cm long 2 to 3 cm wide longitudinally wrinkled and marked with rows of circular 3 to 5 large depression scars left by removal of lateral branches. Secondary lateral branches arising from the primary rhizomes are known as fingers or long turmeric are cylindrically curved and nearly straight pieces, tapering bluntly at the end, occasionally branched 4 to 10 cm in length and 1 to 1.5 cm in diameter longitudinally wrinkled and exhibit encircling leaf scars placed at longer distance and occasional lateral root scars, short fracture, yellowish orange in colour, internally dull yellowish.[12]

***Piper nigrum* Linn.:** Fruit is globose, ovoid to oblong, 3.5 to 6 mm in diameter hard surface is rough, coarsely deeply reticulately wrinkled, shows remains of sessile stigma on the tip and a basal scar showing point of attachment to the axis, greyish black in colour.[12]

***Zingiber officinale* Roscoe:** Rhizome consists of branched laterally compressed pieces of horizontally growing rhizomes 5 to 12 cm in length, 3 to 5 cm in height and 1 to 2 cm in thickness, the surface is marked with circular placed leaf scars, and small circular root scars at places clearly visible on unpeeled or partially peeled pieces of rhizomes, surface is rough, longitudinally striated and slightly fibrous, fracture short and fibrous, hard, pale buff or brownish in colour.[12]

***Glycyrrhiza glabra* L.:** Roots are cylindrical 14 to 20 cm in length and 5 to 20 cm in length, surface rough, longitudinally wrinkled at places shows scars left by removal at the lateral roots fracture outer fibrous and inner splintery, externally dark brown, internally golden yellow, transversely cut surface exhibits wide central xylem, cambium ring, outer narrow phloem and wide radiating medullary rays.[14]

Powder microscopy

Results from powder microscopy showed parenchymal cells with contents, cells from scaly leaves from *Curcuma longa*, fibrous layer cells, schizolysigenous oil glands from *S. aromaticum*, papilla and striated cuticle from *T. ammi*, perisperm cells and bearer cells from *P. nigrum* and crystal fibres from *G. glabra* (Figure 2).

Physiochemical parameters of KK and KEG

The reports of physiochemical analysis of both KK and KEG are given in Table 2 and Table 3.

TLC/HPTLC Analysis

KK and KEG (methanolic extract) were developed in *Toluene*: *Ethyl acetate*: *Formic acid* (8:2:0.5, *v/v/v*) solvent system. TLC photodocumentation and HPTLC 3D chromatogram of KK, KEG granules and Kirāmpu kutinīr formulation along with ingredients are presented in Figure 3. The R_f values and color of spots in different conditions are presented in Table 4.

At shortwave length of 254 nm, corresponding to the ingredient *C. longa*, *G. glabra*, *P. nigrum, S. aromaticum, T. ammi*, *Z. officinale,* there was observation of 10, 5, 8, 7, 7 spots and 1 spot respectively. The R_f values of KEG were recorded at 0.11, 0.19, 0.26, 0.31 and 0.37 (green). The R_f values of extract of KK was recorded at 0.07, 0.11, 0.14, 0.19, 0.23, 0.28, 0.31, 0.37, 0.42, 0.49, 0.55, 0.62 and 0.72 (green).

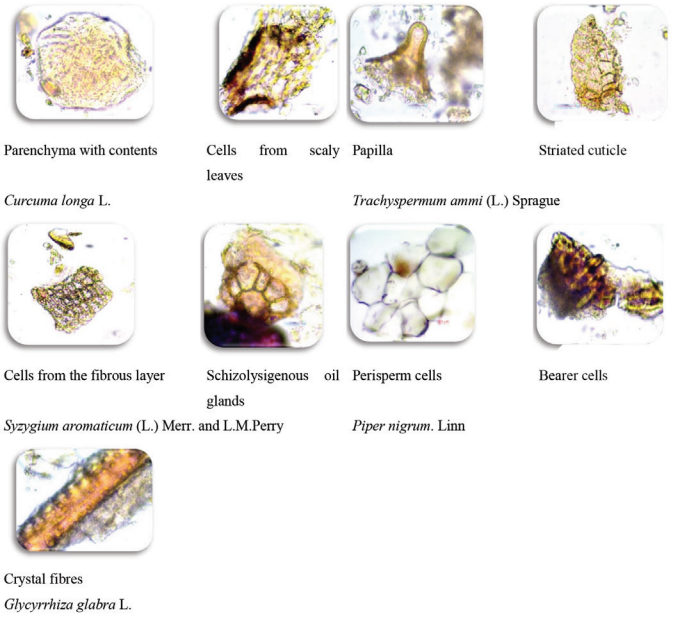

Figure 2: Powder microscopy characters of the ingredients of KK formulation.* **Z. officinale* is used only in the fresh form, hence powder microscopy not performed

Table 2: Physicochemical parameters of KK.

Parameters	Results (Mean ± SD)
Total solid (%)	2.9 ± 0.21
Specific gravity	10.40 ± 0.42
Colour	Dark brown
Odour	Aromatic
Taste	Bitter, pungent

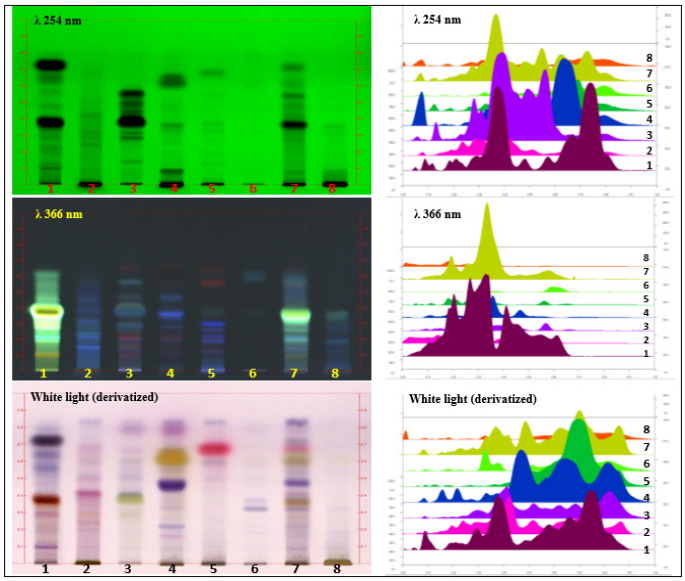

Figure 3: TLC photodocumentation and HPTLC 3D chromatogram of KEG, KK and ingredients. Track 1-*C. longa*, Track 2-*G. glabra*, Track 3-*P. nigrum*, Track 4-*S. aromaticum*, Track 5-*T. ammi*, Track 6-*Z. officinale*, Track 7- KEG, Track 8- KK.

Table 3: Physicochemical parameters of KEG.

Parameters	Results (Mean ± SD)
Loss on Drying (105°C) (%)	10.40 ± 0.42
Total Ash (%)	6.51 ± 0.06
Acid Insoluble Ash (%)	0.37 ± 0.04
Water Soluble Extractive (%)	21.13 ± 0.04
Alcohol Soluble Extractive (%)	15.82 ± 0.25
pH (10% solution)	5.32

At long wavelength of 366 nm, corresponding to the ingredient *C. longa*, *G. glabra*, *P. nigrum, S. aromaticum, T. ammi*, *Z. officinale,* there was observation of 9, 7, 8, 8, 9, and 3 spots respectively. The R_f values of KEG were recorded at 0.09 (yellow), 0.15 (blue), 0.18 (blue), 0.20 (green), 0.26 (green), 0.33 (fluorescent green), 0.37 (green), 0.46 (blue), 0.55 (green), 0.58 (blue) and 0.64 (red). The R_f values of KK were recorded at 0.15 (blue), 0.20, 0.33 and 0.37 (green).

Post derivatization, under white light, corresponding to the ingredient *C. longa*, *G. glabra*, *P. nigrum, S. aromaticum, T. ammi*, *Z. officinale,* there were observation of 9, 9, 8, 9, 7, and 7 spots respectively. The R_f values of KEG was recorded at 0.09, 0.18, 0.23 (blue), 0.28 (brown), 0.32 (blue), 0.36 (brown), 0.42 (pink), 0.49, 0.55 (blue), 0.62 (green), 0.67 (pink), 0.72 and 0.84 (blue). The R_f values of KK were recorded at 0.09, 0.18 (blue), 0.28 (yellow), 0.31 (blue) and 0.62 (yellow).

Densitometric scan of the samples *C. longa*, *G. glabra*, *P. nigrum*, *S. aromaticum*, *Z. officinale*, KEG and KK revealed 11, 10, 9, 9, 7, 5, 10 and 9 number of peaks respectively under short UV (λ_{254} nm). Under long UV (λ_{366} nm) samples *C. longa*, *G. glabra*, *P. nigrum*, *S. aromaticum*, *Z. officinale*, KEG and Kirāmpu kutinīr showed 8, 6, 9, 6, 9, 1, 7 and 3 number of peaks respectively. The post derivatized plate possessed 11, 10, 10, 9, 8, 8, 11 and 8 number of peaks for *P. nigrum, S. aromaticum, Z. officinale*, KEG and KK respectively under white light scanning.

Table 4: R_f values and color of spots in different conditions.

C. longa		*G. glabra*		*P. nigrum*		*S. aromaticum*		*T. ammi*		*Z. officinale*		KEG extract		KK decoction	
R_f	Color	R_f	Color	R_f	Color	R_f	Color	R_f	Color	R_f	Color	R_f	Color	R_f	Color
UV 254 nm															
0.11	Green	0.24	Green	0.07	Green	0.09	Green	0.13	Green	0.63	Green	0.07	Green	0.11	Green
0.13	Green	0.29	Green	0.14	Green	0.25	Green	0.19	Green			0.11	green	0.19	Green
0.20	Green	0.32	Green	0.29	Green	0.29	Green	0.27	Green			0.14	Green	0.26	Green
0.23	Green	0.42	Green	0.32	Green	0.33	Green	0.33	Green			0.19	Green	0.31	Green
0.31	Green	0.67	Green	0.39	Green	0.37	Green	0.37	Green			0.23	Green	0.37	Green
0.38	Green			0.45	Green	0.48	Green	0.55	Green			0.28	Green		
0.48	Green			0.50	Green	0.63	Green	0.69	Green			0.31	Green		
0.57	Green			0.56	Green							0.37	Green		
0.66	Green											0.42	Green		
0.73	Green											0.49	Green		
												0.55	Green		
												0.62	Green		
												0.72	Green		
UV 366 nm															
0.09	Yellow	0.15	Blue	0.10	Red	0.12	Blue	0.06	Blue	0.37	Green	0.09	Yellow	0.15	Blue
0.19	Green	0.21	Blue	0.17	Blue	0.21	Red	0.09	Blue	0.59	Blue	0.15	Blue	0.20	Green
0.22	F.Blue	0.25	Blue	0.21	Red	0.24	Red	0.13	Blue	0.63	Blue	0.18	Blue	0.33	Green
0.28	F. green	0.32	Blue	0.29	Blue	0.28	Blue	0.19	Blue			0.20	Green	0.37	green
0.30	F. green	0.39	Blue	0.38	Blue	0.34	Blue	0.23	Blue			0.26	Green		
0.38	Green	0.46	Blue	0.47	Blue	0.36	Blue	0.26	Blue			0.33	F.Green		
0.47	Green	0.57	Green	0.56	Blue	0.46	Blue	0.38	Green			0.37	Green		
0.54	Green			0.65	Red	0.56	Red	0.56	Red			0.46	Blue		
0.62	green					0.66	Red	0.64	Red			0.55	Green		
												0.58	Blue		
												0.64	Red		
White light (derivatized)															
0.10	Violet	0.10	Pink	0.10	Blue	0.10	Blue	0.09	Blue	0.10	Blue	0.09	Blue	0.09	Blue
0.18	Violet	0.19	Pink	0.28	Green	0.16	Pink	0.36	Blue	0.18	Blue	0.18	Blue	0.18	Blue
0.29	Brown	0.24	Pink	0.38	Green	0.22	blue	0.45	Blue	0.32	Blue	0.23	Blue	0.28	Yellow
0.38	Violet	0.29	Yellow	0.41	Blue	0.33	Blue	0.50	Blue	0.38	Blue	0.28	Brown	0.31	Blue
0.47	Violet	0.41	Pink	0.51	Pink	0.47	Blue	0.60	Blue	0.50	Blue	0.32	Blue	0.62	Yellow
0.56	Violet	0.51	Pink	0.60	Pink	0.55	Pink	0.68	Pink	0.62	Brown	0.36	Brown		
0.64	Violet	0.51	Pink	0.67	Pink	0.63	Yellow	0.84	Blue	0.79	Blue	0.42	Pink		
0.72	Violet	0.69	Pink	0.79	Pink	0.79	Pink					0.49	Blue		
0.80	Violet	0.84	Blue			0.84	Blue					0.55	Blue		
												0.62	Green		
												0.67	Pink		
												0.72	Blue		
												0.84	Blue		

Both TLC photo documentation and densitometric scan revealed that the KEG comprises of the said ingredients. It also divulges that KEG and KK are of same bands and same pattern.

DISCUSSION

The ingredients of KEG have been individually studied in various studies and the therapeutic effects are promising. In herbal medicine, *S. aromaticum* is used in many forms such as *curnam* (fine powders) or *kutinīr* (decoctions) and is added up in numerous drug formulations indicated for fevers or phlegmatic illnesses affecting the respiratory system.[16] Cloves are frequently used in herbal teas that are effective respiratory aids and to control cough. Steam inhalation with cloves and other spices proves effective in the symptomatic management of cough, cold and sinusitis.[17] Traditional Siddha practitioners advocates the use of chewing betel leaf with clove and black pepper. Plain cloves are chewed for its effectiveness in controlling sore throat, hoarseness of voice and pharyngitis.[17] *T. ammi* on the other hand possessed broncho-dilatory effect due to the presence of carvacrol,[17] showed improvised effects in asthmatic patients when compared to theophylline.[18] In a *in silico* study, carvacrol was selected to estimate its binding nature with SARC-CoV-2 main protease. The study shown its efficacy in inhibiting protease and thus halting viral replication rate.[19] Evidence has been documented of curcumin's (active ingredient of *C. longa*) direct antiviral activity against several enveloped viruses including SARS-CoV.[20,21] The death of COVID-19 patients is mainly caused due to respiratory failure and multiorgan failure which is the by effect of hyperactivated immune response called 'cytokine storm'.[22,23] Many *in vitro* and *in vivo* studies had showed that curcumin inhibits the production and release of pro-inflammatory cytokines such as IL-1, IL-6, IL-8, TNF-α.[24-27] Studies on virus-induced pneumonia have highlighted the potential usage of curcumin in the improvement of lung index and survival rate.[24,26] *P. nigrum* is used as a dried fruit or decorticated fruits as *curnam*, *kutinīr* and *theeneer* (distillate) and is added up in numerous drug formulations, indicated for fevers or phlegmatic illnesses affecting the respiratory system.[28] In a study that involved piperine, a histopathological section of the nasal mucosa showed that piperine attenuated inflammation, redness, and disruption of alveoli and bronchiole.[29] 6-gingerol, an active ingredient in *Z. officinale* proves anti-viral efficiency against SARS CoV-2 by showing the highest binding affinity and interaction with multiple targets of COVID-19 including Viral proteases, RNA binding protein and Spike protein.[30] A docking study[31] presented the inhibitory action of curcumin, dimethoxy curcumin from *Curcuma longa*, gingerol and zingerol from *Zingiber officinale* against COVID 19 protease. *Z. officinale* was reported to inhibit plaque development caused by human respiratory syncytial virus (HRSV) in respiratory tract cell lines. it was also active in hindering viral attachment and internalization.[31] Glycyrrhizin, an active ingredient in *G. glabra* blocks SARS-CoV-2 replication mainly via a mechanism by inhibiting SARS-CoV-2 main protease (Mpro) which is necessary for viral replication.[32] In spite of the aforesaid evidences of efficacy of KK ingredients individually, the formulation consisting of all these ingredients together has to be studied further and will definitely be in the interest of the researchers because of its therapeutic effectiveness and growing popularity which further makes its standardization necessary.

CONCLUSION

The pharmacognostic profiling of ingredients of *kirāmpu kutinīr*, physiochemical evaluation and HPTLC analysis were performed as a part of standardization of this popular formulation. Findings of the study is helpful in standardization of polyherbal Siddha formulation *kirāmpu kutinīr*, which will promote global acceptance of the formulation and reputation of the Siddha system. Further, biological studies on the lines of its usefulness in combating viral infections including COVID-19 will help to translate this traditional knowledge into validated clinical formulation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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