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Antiviral and immunomodulator effect of *Arathai Kudineer Chooranam*–A review

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Abstract
In communicable diseases, Siddha formulations are found to act in two ways – one is directly acting against the causative organisms of the disease and another one is to prepare the body's immune system to maintain the invaders. Ancient times, man could survive through lot of diseases and outbreaks with their own traditional medicine's knowledge. An entire world has threatened by COVID -19 pandemic and it appeared in Wuhan capital of Hubei Province, China on December 2019. The WHO declared this mysterious pneumonia like disease as Corona virus Disease - 2019 caused by coronavirus family – SARS-CoV-2 has affecting humans by zoonotic transmission. The symptom onset is fever, fatigue, dry cough, myalgia and dyspnea and it spreads through the nasal discharges and salivary droplets. In Children and young adults, are mildly affected whereas in aged people with co-morbidities like diabetes, hypertension, cardiovascular diseases may develop severe illness, even death may also occur. In pharmacological aspects of Siddha medicines are always being a potential source for the production of new drugs and enhances the effect of antiviral drugs, which will probably decreasing cost effect and improving the quality of treatment and providing better outcomes. *Arathai Kudineer Chooranam* is one of such medicines generally used for treating respiratory and digestive complaints of *kapha* imbalance, cough with sputum, fever, headache, joint pain and swelling. *Arathai Kudineer Chooranam* is available in market in a coarse powdered form. It consists of totally 12 active ingredients in equal parts apart from *Sitrarathai* (*Alpinia officinarum*) which is the chief ingredient of this formulation, after the medicine is named. The aim of this review article is to bring out the ethnopharmacological aspects of the drug *Arathai Kudineer Chooranam* in pandemic scenario.

Keywords: *Arathai Kudineer Chooranam*, COVID – 19, Siddha medicine, Antiviral, Immunomodulator

Introduction
India is the native place of several traditional practices, like Siddha and Ayurvedha. In South India Siddha medicine is the traditional medicine especially in Tamil people. It was flourished by Tamil people with the knowledge of traditional medicine in the native of rich biodiversity region in Western Ghats. The heritage of medical knowledge was established by Siddhars. Siddha formulations are based on 3 *kuttram.* The fundamental physio-pathological humours which are derived from the combination of 5 basic elements of *panchabootham* theory. Since olden days, mankind survived through several diseases and outbreaks with their own traditional medicines. The Siddha System of medicines are entangled with spiritual and culture of the ancient Tamil civilization that was already existed in Indian peninsula, predating more recorded history. Siddha medicine gives the remedy of many ailments, but to reach globally the scientific studies are very important to prove the quality, safety and efficacy of the drug. A retrospective study enlisted different kind of Siddha medicines for viral diseases like Chicken pox, Mumps, Measles Influenza etc. Siddha medicines are more effective as a prophylaxis and also to treat various viral diseases without any side effects since a long time [1].
Recently the world is threatened by COVID-19 pandemic and is caused by the coronavirus family – SARS-CoV-2. Coronaviruses (CoVs) mostly affecting the human beings through zoonotic transmission. The common onset of symptoms is fever (99%), fatigue (70%), dry cough (60%), body pain (44%) and dyspnea [2]. Less common symptoms are headache, nausea, diarrhoea and vomiting. In severe cases presents with the symptoms like breathlessness, dizziness, anorexia, pain in pharynx and abdomen.[3] In addition, aged patients having co-morbidities such as diabetes, hypertension, cardio and cerebrovascular disease are more prone to have a serious adverse effect. So, there is an essential and also immediate need to boost the overall immunity an ingest the medicines which possess antiviral and are mucolytic in nature.

Arathai Kudineer Chooranam (AKC) is one such medicines generally used for digestive complaints of *kapha* imbalance, cough with sputum, headache, fever with painful joints and swelling.[4] The word "*Kudineer*" denotes an aqueous solution whereas the various parts of the plant like roots, barks, leaves, flowers and fruits (fresh or dried) are mixed with certain quantity of water and boiled well to condense a particular ratio as per the indication and requirement.

Out of 32 types of internal medicines, *surasam* (extract), *saaru* (juice), *kudineer* (decoction), *manapagu* (syrup), *thylam* (oil), *dhiraavagam* (distillate) which are liquid form but they are varying in densities. Some other names in Siddha to denotes decoction like *marunthu neer, unneer, kiyaazham, vaai kuditthidum punal*. This article aims to bring out the ethnopharmacological aspects of the drug *Arathai Kudineer Chooranam*.

Siddha Concepts: [5]

Pandemic (*Kollai Noi / Ottu Noi):*

The word pandemic is called as *Kollai noi* in Siddha aspect. It means the disease spreads quickly and affect a wider population ratio in a province or country or whole continent. It occurs during weather changes, from February to May.

According to Siddha, an infectious disease is known as *Ottu noi*, caused by microbes. Few pandemic or infectious diseases are small pox (*Ammai Noi*) and Cholera (*Oozhi Noi*) etc.,

Mode of Transmission (*Ottunoi*):

- An infected person excretions such as respiratory droplets, sputum, urine and stools may spread this disease.
- The disease (*Ottunoi*) spreads through an infected person or an object handled by them.

Ex. Small pox (*Ammai Noi*), Cholera (*OozhiNoi*)

Siddha Management in Pandemic:

There are 4 steps in Siddha management.[6]

a. Notification

When a person is identified by an infectious disease, Neem leaves and turmeric are tied in front of the house which means to notify that 'Someone is infected in the house'. In COVID - 19 pandemic scenario, people who are in home quarantine are identified by a notice sticks in front of home, in olden days it was identified by neem and turmeric.

b. Isolation

For preventing purpose, an infected person is isolated in a separate room and disinfected with turmeric water and blockade by turmeric dipped cloth. Curcumin acts as an antiviral, antimicrobial and antibacterial.[7] An infected person and their family members won't go to other's houses and don't share their things with others.

c. Quarantine

Quarantine is an effective way to prevent the non-infected person. It is the best way to separate and restrict the people movement who are exposed or prolonged exposure of infectious disease.[8] It was already practiced in small pox.

- An infected person is isolated in a separate room and lay down in a clean cloth and spreads by neem leaves. Every day the cloth and neem leaves should be changed. Neem possesses an antiseptic, antiviral properties against different viruses such as Coxsackie B virus, variola, polio, mumps, measles, influenza etc.,[9]
- When an outbreak occurs, the others (visitors) are not allowed to go outside and come inside the town.

d. Disinfection

Neem leaves, turmeric water and Cow dung are used as a disinfectant. The house floor and streets are wiped by the cow dung. Garlic peel, turmeric powder, Carom seeds and Loban (*Styrax benzoin* and *Boswellia species*) are fumigated for reducing air borne bacterial and viral disinfection. Cow dung has an antiseptic and anti - thermal activities [10].

Arathai Kudineer Chooranam (AKC)

Composition and Preparation Method

Arathai kudineer chooranam is available in the market in a coarse powdered form. It consists of totally 12 active herbal ingredients in equal parts. *Sitrarathai (Alpinia officinarum)* is the main ingredient of this formulation. Other ingredients of *AKC* include *Sitramutti (Sida cordifolia), Thanneervittan kizhangu (Asparagus racemosus), Peipudal (Trichosanthes cucumerina), Parpadagam (Mollugo cerviana), Koraikizhangu (Cyperus rotundus), Chandanam (Santalum album) Chukku (Zingiber officinale), Milagu (Piper nigrum), Aamanakku ver (Ricinus communis), Aadathodai ver (Justicia adhatoda), Kaanjori ver (Tragia involucrate)*. All the ingredients are purified as per traditional purification methods, dried in shadow and ground into coarse powder form. The above said ingredients are permissible for medicinal preparations as per schedule E (1) of the Drug and Cosmetic Act 1940. *AKC* is manufactured by GMP certified companies in Siddha by following SOP and other guidelines are

notified in Drug and Cosmetic Act 1940. The quality of the medicine is assessed by the Pharmaceutical Laboratories of Indian Medicine prescribed parameters.

The preparation method of decoction: 25 grams of *Arathai kudineer chooranam* powder is taken and boiled with 500 ml of water till the decoction is concentrated up to 125 ml then filtered. The dose level of *AKC* for adults (above 12 years) is 30-60 ml, twice daily. It is rendered in the dosage of 20 ml bid for 3-5 years and 30 ml bid for 5-12 years. As per Siddha guidelines shelf life for the decoction is only 3 hours [11].

Fig 1

Table 1: *Arathai kudineer chooranam* – Pharmacognostic Aspect

S. No	Tamil Name	Botanical name / Family	Part used	Phytochemical constituents	Traditional uses
1.	*Sitrarathai*	*Alpinia officinarum* Hance./*Zingiberaceae*	Rhizome	kaempferide, galangin and alpinin.[12]	It is used for Phlegm, bronchitis, heart disease, dropsy, dental disease, *kapha* disease due to *pittha*, *vatha* diseases, eczema, flatulence, head disorders, chills, cough and many types of fever and induces appetite.[13]
2.	*Sitramutti*	*Sida cordifolia*L./Malvaceae	Whole plant	sidasterone A, sidasterone B [14]	It is used for Tuberculosis and *Pittha* diseases. It Promotes an eye sight. Root decoction is administered for TB and cures thirsty fever.[13]
3.	*Thanneervittan kizhangu*	*Asparagus racemosus* Willd / Liliaceae	Root tuber	Asparagine, Shatavarin sarasapogenin, saponin arginine, tyrosine, flavonoids (kaempferol,	It is mainly given for Diabetes, chronic fever, genitourinary tract disorders, leucorrhoea and excess heat. [13]

				quercetin, and rutin) [15]	
4.	*Peipudal*	*Trichosanthes cucumerina* L./Cucurbitaceae	Whole plant	bryonolic acid, cucurbitacin B, cucurbitacin E, isocucurbitacin B [16]	It is given in fever due to *pittha* and *kapha*, jaundice, pox, thirst and fatigue etc. [13]
5.	*Parpadagam*	*Mollugo cerviana* L. /Molluginaceae	Whole plant	flavonoids, tannins, saponins, triterpenoids, phenolic groups and glycosides C-glycosyl flavones specifically orientin and vitexin [17].	Siddha literature reveals that it is helpful in fever, psychic disorder, thirst, *pittha* diseases etc.,[13]
6.	*Koraikizhangu*	*Cyperus rotundus* L. / Cyperaceae	Root tuber	alkaloids, flavonoids, tannins, starch, glycosides, monoterpenes, sesquiterpenes, sitosterol, glycerol, linolenic, myristic and stearic acids [18] Polyphenols, Rotundene, Rotundenol, Rotundone, Selinatriene, Sitosterol, Stearic-acid, Sugeonol, Sugetriol [19].	This drug is used for fever with rigor, hypertension, some kind of fever, thirst, delirium, diarrhoea, mental disorder, thirst of *pittha*, ankle diseases, vomiting etc,.[13]
7.	*Sandanam*	*Santalum album* L. / Santalaceae	Heart wood	Sandalwood oil contains α- santalol, santene, α and β santalenes, α and β -santalic acid, santenol, teresantalic acid, teresantalol, isovaleraldehyde, santanone. Terpenoids, saponin, phenols and tannins.[1]	Sandal wood is helpful in fever, psychiatric diseases, itching and diseases due to vitiated *pittha*m. Paste of wood is useful in fever, headache, skin diseases and pruritis. Decoction made from sandal wood is given in fever, indigestion, palpitation. This decoction increases sweating in fever and regulates pulse rate. It is applied externally for herpes, itching and tinea. Volatile compounds isolated from *Santalum album* have been used to treat common cold, bronchitis, fever and urinary tract infections.[13]
8.	*Chukku*	*Zingiber officinale* Roscoe. / Zingiberaceae	Rhizome	Phenols, 6-shogaol, 6-gingerol, gingerdiols, 1,8 cineole, 6-gingesulphonic acid; sesquiterpenes, zingiberol, α-zingiberene, ar-curcumine, β-bisabolene, α-santalol, β-eudesmol, monoterpenes like β-phellandrene, α-pinene, β-pinene, camphene, sabinene, myrcene; glycerols gingerglycolipids A, B & C; geraniol glycosides; [15]	Useful in Indigestion, heartburn, dyspepsia, inflammations, bronchitis, asthma, vomiting and earaches, facial, head and intestinal disorder. Dried ginger is generally given for digestive diseases, asthmatic complaints, fever and phlegmatic affections, anaemia etc.,[13]
9.	*Milagu*	*Piper nigrum* L./ Piperaceae	Fruit	piperine, pipercide, feruperine, piperonal, guaiacol, n-trans-feruloylpiperidine; phenole like 1,8 cineole,	It is given in fever with chill, anaemia, phlegm, diarrhea, gastric ulcer, flatulence, dyspepsia, psychiatric disorder, haemorrhoids, fatigue, anal

				n-trans-feruloyltyramine, piperoleine B[15]	disorder, cough, stroke, indigestion, jaundice etc., [13]
10.	*Aamanakku*	*Ricinus communis* L. / Euphorbiaceae	Root	Ricinusterrylbenzoate, Ricipiperanyl ester, Erandone, Ricipentatriacontanol, isoquercetin, (Ricinitin). [20]	It induces diarrhea and controls aggravated *vatha* humour. [13]
11.	*Adhatodai*	*Justicia adhatoda* L. / Acanthaceae	Root	Quinazoline, vasicine, 7-hydroxyvasicine, vasicinolone,3-deoxyvasicine,vasicol, vasicoline, vasicolinone, triterpenes, anisotine, betaine[21]	It controls the vitiated vata and *kapha* humour. It cures many kinds of fever, delirium, abdominal disorder, hypertension, cough, tuberculosis, vomiting, hiccough, pricking pain, hydrocele. It improves the voice of singers.[13]
12.	*Kanjori*	*Tragia involucrate* L./ Euphorbiaceae	Root	Terpenoids, flavones, quinones, iridin, dihexosyl quercetin, quercetin-3-O-rutinoside, stigmasterol, quercetin, rutin [22]	Siddha literature reveals that usage of root of *Tragia involucrata*L. for group of fever due to three humours, flatulence, cough, sinusitis, dyspepsia, bronchitis, and fever due to phlegmatic affection. [13]

Table 2: $describes the Ingredients of AKC with the taste of each drug, its Five Element perspective, parts used and actions of the drug.[13]

S.No	Name of the ingredient	Taste	Pancha bootham combination	Part used	Actions
1.	*Alpinia officinarum* Hance. *(Sitrarathai)*	Pungent	Air+Fire	Rhizome	Expectorant Febrifuge Stomachic
2.	*Sida cordifolia* L. *(Sitramutti)*	Astringent	Earth+Air	Whole plant	Emollient
3.	*Asparagus racemosus* Willd. *(Thanneervittan kizhangu)*	Sweet	Earth+water	Root tuber	Nutritive Demulcent Galactogogue Aphrodisiac Antispasmodic
4.	*Trichosanthes cucumerina* L.*(Peipudal)*	Bitter	Air+Space	Whole plant	Anthelmintic Antiperiodi Purgative Tonic
5.	*Mollugo cerviana* L. *(Parpadagam)*	Bitter	Air+Space	Whole plant	Laxative Stomachic Antispasmodic Febrifuge Diaphoretic
6.	*Cyperus rotundus* L. *(Koraikizhangu)*	Astringent	Earth+Air	Root tuber	Astringent Stimulant Tonic Diuretic Diaphoretic Demulcent Emmenagogue Vermifuge
7.	*Santalum album* L. *(Santhanam)*	Bitter, Mild astringent	Air + Space Earth + Air	Heart wood	Cooling Diaphoretic Diuretic Expectorant
8.	*Zingiber officinale* Roscoe. *(Chukku)*	Pungent	Air+Fire	Rhizome	Stimulant Stomachic Carminative
9.	*Piper nigrum* L. *(Milagu)*	Bitter Pungent	Air+Space Air+Fire	Fruit	Acrid Carminative Antiperiodic Rubefacient Stimulant Resolvent Anti*vatha* Antidote
10.	*Ricinus communis*L. *(Aamanakku)*	Bitter	Air+Space	Root	Anti*vatha*
11.	*Juticia adhatoda*L. *(Aadathodai)*	Bitter	Air+Space	Root	Antispasmodic Expectorant Germicide Diuretic
12.	*Tragia involucrata*L.*(Kaanjori)*	Bitter	Air+Space	Root	Diaphoretic

Table 3: Scientifically proven Antiviral and Immuno modulator activities of constituents of *Arathai kudineer chooranam*

S.No	Botanical name	Antiviral activity	Immunomodulator studies
1.	*Alpinia officinarum* Hance.*(Sitrarathai)*	*In vitro* and *in vivo* anti-influenza virus activity of diarylheptanoids isolated from *Alpinia officinarum Hance* [23].	Diarylheptanoid from *Alpinia officinarum Hance*. shows promising antibacterial and immune modulatory activity [38]
2.	*Sida cordifolia* L. *(Sitramutti)*	Anti-HIV agent- *In vitro* assays and ex vivo- (10E, 12Z)-9-hydroxyoctadeca-10,12-dienoic acid (20), isolated from the whole plant[24]	Immunomodulatory activity of the ethanol extract of roots of *Sida cordifolia* L. in mice.[39]
3.	*Asparagus racemosus* Willd. *(Thanneervittan kizhangu)*	Higher protective antibody against different vaccinations including more effective cell mediated immune response for protection against various bacterial, viral, and other diseases.[25]	Several workers has studied the effect of *Asparagus racemosus* Willd. root extract in augmentation of humoral and cell mediated immune response providing better protection level against infections [40] Immuno adjuvant effect - significant increase in antibody titres to *Bordetella pertussis* as against the untreated animals [41]
4.	*Trichosanthes cucumerina* L.*(Peipudal)*	Anti-HIV effect of Trichosanthen is attributed to inhibition of replication of HIV and cytotoxicity to HIV infected cells mainly macrophages and lymphocytes especially helper T cells (CD4+T Cells) [26]	Cucurbitacin E - Anti-cancer and immunomodulatory Actions [42]
5.	*Mollugo cerviana* L. *(Parpadagam)*	Vitexin – Anti viral and anti - cancer activity[27]	The plantextract showed immunostimulatory activity when peritoneal cells were stimulated *in vitro* with BCG antigen only. Detection of quercetin and triterpenoid glycosides in the ethanolic extract of this plant material is responsible for the immune system.[43]
6.	*Cyperus rotundus* L. *(Koraikizhangu)*	Useful to developing novel antiviral and immunostimulant drugs from *Cyperus rotundus* L. against WSSV [28].	Immunomodulation of aqueous extract of *Cyperus rotundus* L. against hydatid cyst infection in mice [44]
7.	*Santalum album* L. *(Santhanam)*	*In vitro* antiviral activity against Herpes simplex viruses-1 and 2 [29] β- santalol is studied against influenza virus.[30] Sandalwood oil constituents, α- and β-santalols, against HIV and other RNA viruses[31]	Immunopharmacological activity of aqueous root extract of *Santalum album* L. against Hepatitis B surface antigen (HBsAg) and Newcastle disease virus (NDV) on human peripheral blood mononuclear cells (PBMCs). [45]
8.	*Zingiber officinale* Roscoe.*(Chukku)*	Antirhinoviral Sesquiterpenes was isolated from rhizomes.[32] Anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines.[33]	The immunomodulatory effect of *Zingiber officinale* Roscoe. essential oils was reported in mice. In the study, essential oil of *Zingiber officinale* Roscoe. was administered to mice (once a day, orally, for a week) previously immunized with sheep red blood cells. *Zingiber officinale* Roscoe essential oil showed the improvement in humoral immune response in immune suppressed mice [46]
9.	*Piper nigrum* L. *(Milagu)*	The *Piper nigrum* L. in chloroform extract shows higher activity in the case of Vesicular stomatitis Indiana virus and Human para influenza viruses.[34]	Immuno-modulatory and antitumor activity of piperine was evaluated. *In vitro* immunomodulatory activity of piperine was evaluated to enhance the efficacy of rifampicin in a murine model of *Mycobacterium tuberculosis* infection.[47]
10.	*Ricinus communis*L. *(Aamanakku)*	Fruit extract showed the greatest antiviral activity when both incubated with cell culture and virus suspension- plant-derived	Peptidic component of the immuno modulatory glycoconjugate Immunoferon[48]

		nanoparticles enhance antiviral activity against coxsakievirus b3 by acting on virus particles and vero cells [35]	
11.	*Juticia adhatoda* L. *(Aadathodai)*	In-vitro antiviral effectof *Justicia adhatoda* crude extracts against influenza virus byHemagglutination (HA) reduction [36]	Methanolic, chloroform and diethyl ether extracts of leaves of *Juticia adhatoda*L. were pharmacologically validated for its immunomodulatory properties in experimental animals.[49]
12.	*Tragia involucrata* L. *(Kaanjori)*	A novel series of 2-(5-alkyl-1,3,4-oxadiazol-2-yl)-3H-benzo[f]chromen-3-ones (4a-e) have been evaluated for analgesic, antibacterial and antiviral activities [37]	Antitumor effect of Hexane and Ethyl Acetate Extracts of *Tragia involucrata* [50]

Discussion and Conclusion

Siddha drugs being used these days can be divided under two groups – classical (Sasthric) and non-classical proprietary. Classical medicines, under which many of the current Siddha medicines come, are being used without any change from the original formulation since many centuries. However, the physician can use them based on his intelligence (yukthi) for various disorders other than those mentioned in the text, if he knows the *Panchabootha* combination of those drugs. The other important factor whether classical or non-classical poly herbal medicine is the synergistic activity. While most of the research activities undertaken till now are based on individual drug or its isolated components, in which the synergistic activity cannot be seen. Approaching the research on Siddha polyherbal medicines must be in the holistic approach and not on individual herb or isolated alkaloids etc. This only would justify the results of research on Siddha medicines. In this sense, the current drug of interest AKC also needs to be approached as a whole drug. Studies on individual ingredients can only be taken as supportive evidence not conclusive. Further studies can explore the full potential of AKC.

Plants have been used by several people to treat various diseases since time immemorial. Numerous studies conducted on pharmacological aspects of medicinal plants which have been accomplished, since they constitute a potential source for the production of new medicines and enhancing the effects of conventional antiviral drugs, which will probably decrease cost effect of the drug and improve quality of the treatment.

Based on this fact, it is suitable to note that the polyherbal formulation, '*Arathai Kudineer Chooranam'* one of the versatile drugs used in the Siddha medicine possesses an excellent pharmacological property as well as unreported adverse effects clinically. Hence the review highlighted the pharmacognostical, chemical constituent details of the drug and explained about the Siddha concept of herbal properties emphasize on the antiviral and immunomodulator properties of various herbs used in this formulation. So proper clinical evaluation is to be needed to prove the role, safety and effectiveness of *Arathai Kudineer Chooranam* as an Anti-viral and Immunomodulator.

Author's Contribution

The authors are thankful to this opportunity to express their sincere gratitude to,
Department of Siddha, The TN Dr. M.G.R. Medical University, Guindy, Chennai – 32, Tamil Nadu, India.

Conflict of Interest

The authors have no conflicts of interest.

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