



A Perspective Review on *Siddha* System of Medicine in the Management of Corona Virus Disease 2019

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Abstract

Respiratory Tract Infections (RTIs) are the most common, and potentially most severe, of infections treated by health care practitioners. Lower RTIs along with influenza, are the most common cause of death by infection. The fatality risk is doubled if the person is with other morbid conditions or in extremes of age. These seasonal respiratory infections caused by viruses are of more concern as their spread is very vast than we imagine. COVID-19 (corona virus disease 2019) is such a pandemic respiratory illness caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), a strain of Corona virus. The emerging anti-microbial resistance and easy spread of respiratory pathogens has also increased the challenge for appropriate management of RTI like COVID-19. Drugs with anti-viral property and potency to prevent the comorbidity stand are the need of the hour. This review article includes information on preclinical studies and clinical studies to add a scientific validation to formulations that are commonly used in *Siddha* system of Medicine. The ingredients of the *Siddha* drugs possessing anti-viral property and immune-modulatory effect particularly against respiratory pathogens are elaborated. Evidence of anti-viral property has been made out to the light for further clinical trials.

Keywords: Antiviral Drug, Immuno-modulator, Influenza, Respiratory Tract Infection, *Siddha* Medicine, COVID-19

1. Introduction

Corona virus disease (COVID-19) is an infectious disease caused by a new virus. COVID-19 is an illness caused due to the novel Corona virus-2 (nCoV-2/2019-nCoV), known as Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2)¹. In the early December 2019, patients with pneumonia of unknown origin were first identified in the city of Wuhan of Hubei province of China². China reported first to the World Health Organization (WHO) Country Office in China on 31 December 2019³. WHO declared it as a pandemic on March 11, 2020, as it had confirmed its presence in all the continents⁴. The clinical characteristics of SARS CoV-2 infection vary from mild to severe as reported. The most common symptoms at

the onset of illness were fever, cough, myalgia and less common symptoms were sputum production, headache. More than half of the affected patients developed dyspnea and shortness of breath that demanded mechanical ventilation as the disease advanced^{5,6}. The incubation period for COVID-19 is thought to extend to 14 days, with a median time of 4–5 days from exposure to symptoms onset. A study reported that 97.5% of patients with COVID-19 who develop symptoms will do so within 11.5 days of SARS-CoV-2 infection^{7–9}. According to WHO, it is estimated that 80% of the world's population still depend mainly on traditional medicines for their health care¹⁰. Complementary and alternative medicines have been used effectively by humans over several centuries for treating various diseases and can be effectively employed

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to target the host response during influenza outbreaks¹¹. *Siddha* system of medicine is one of the traditional systems of medicines practiced particularly in southern parts of India that has an enormous collection of classical literature, and has in store several herbals, metallo-mineral, aquatic and animal products that are spectacular in the prevention and treatment of respiratory infections. As per the concept of the *Siddha* system of medicine, *SiddharTheran* has defined *Vatham (Vali)* to be responsible for the creation, *Pittam (Azhai)* for prevention and *Kabam (Sethumam / Aiyam)* for destruction¹². A Person gets infected when his immunity is challenged which could be related to the reduction of *Azhai*.

The clinical features of COVID-19 in the initial stage can be correlated with *KabaSuram* in the pathology of disease as per *Siddha* literature in “*YugiVaithiyaSinthamani800*”. The clinical characteristics mentioned are cough, chest discomfort, anorexia, dyspnoea and shortness of breath. So, it has been unanimously agreed to equate the diagnosis to ‘*Kabasuram*’¹³ in *Siddha* in its early stage and further implications proceeding to *Sanni*. *Sanniroganidhanam* of *YugiVaithiyaSinthamani* classifies *Sannirogam* into 13 types, among them *Abinyasa Sanni* can be correlated with the third stage of COVID-19. This will be also reaffirmed through Delphi or other sources of FGD¹⁴. This paper is a compilation of various research studies conducted on the efficacy of ingredients of *Siddha* formulations and herbs for the symptomatic management of SARS CoV-2 Infection through anti-viral property, Immuno-modulation and preventive aspect.

2. *Siddha* System of Medicine in the Management of SARS COV-2 Infection

The line of treatment will begin with balancing the derangement of three humors such as *Vatham*, *Pithamand Kabam*. It includes internal and external *Siddha* medicines, Yoga and pranayama is indicated to maintain the physical and mental well-being. Proper diet (*Pathiyam*) also plays a significant role to enhance innate immunity and nutritional requirement. In COVID-19, the novel Corona Virus is symptomatically managed by the medical system. The WHO interim guidance ver.1.2, suggests mainly two ways of clinical management for SARI (Severe Acute Respiratory Infection) in COVID-19¹⁵.

1. Symptomatic management
2. Infection Prevention and Control (IPC)

In SARS CoV-2 infection, there is an initial increase in body temperature, cough and throat pain, which might subside if there is a good amount of immunity

which is when *Azhai Thathu* comes into action. If not, it escalates to a phase of *Aiyathodam* which is mentioned as “*Thanamulla sethumanthan ilagilveppu*”. If not treated at this stage it slowly moves to the Stage of *Sanni*¹².

This review article includes information on preclinical studies and clinical studies to add a scientific validation to formulations, herbs that are commonly used in *Siddha* system of Medicine. The drugs are selected from Classical *Siddha* literatures based on their indication for ailments like flu like infections, fever, cough, bronchial asthma, pulmonary tuberculosis, and other respiratory infections. The ingredients of the drugs possessing anti-viral property and immune-modulatory effects are also elaborated in Table 1.

On the emergence of COVID-19, guidelines for *Siddha* Clinical Management of COVID-19 were framed and published by the Central Council for Research in *Siddha*. The herbs, the internal medicines for prevention of infection prescribed in the guidelines were selected and the scientific evidence validating their antiviral property has been tabulated below in Tables 2 & 3 respectively.

3. Discussion

Anti-viral are the class of medicines that do not destroy or deactivate the microbes but by arrest the viral replication cycle at various stages. Either they prevent the attachment to host cell or prevent penetration, inhibit neuraminidase activity, or reverse transcriptase enzyme necessary for viral replication. Thus, they decrease the viral load and make it easier for our innate immune mechanisms to neutralize the virus. Moreover, since viruses are intracellular parasite it is difficult to find an antiviral drug without harming the host cells. Lack of effective therapeutics for most of viral diseases, emergence of antiviral drug resistance, high cost are the challenges in the treatment of viral infections and of some antiviral therapies necessitate finding new effective antiviral compounds. In order to circumvent the above said challenges it is the need of the hour to identify and develop new antiviral products. From the results it is evident that the selected medicines have the ingredients that constitute the anti-viral property.

Andrograpis paniculata the key ingredient of *Nilavembu kudineeris* loaded with antiviral and antimicrobial properties^{17–26,125–127}. The other ingredients like *Plectranthus amboinicus*^{128,129}, Sandal wood^{130,131}, *Cyperus rotundus*^{132,133} are effective against *Klebsiella pneumoniae*. *Kaba sura kudineer* medicine having potent anti-viral herbs such as *Tragia involucrata* and *Terminalia chebula* which acts against Influenza virus¹³⁴ and also effective against Swine flu²⁷. Vasa leaves (*Justicia adhatoda*) the

Table 1. Siddha Formulations used in the management of SARS CoV-2 Infection

Siddha Formulations and their indications	Composition	Therapeutic effects	Ref.
Nilavembu Kudineer (NVK) Indication: Suram (Fever) ¹⁶ .	<i>Andrographis paniculata</i> , <i>Vetiveria zezonides</i> , <i>Plectranthus amboinicus</i> , <i>Santalum album</i> , <i>Cyperus rotandus</i> , <i>Piper nigrum</i> , <i>Zingiber officinale</i> , <i>Trichosanthes cucumerina</i>	Stimulates interferon synthesis leading to immunomodulation. Ethanol extract of NVK inhibits inflammation in higher level carrageen-induced paw edema NVK has antipyretic, anti-inflammatory, and analgesic activity. Analgesic and inflammatory properties, reduced COVID-19 associated myalgia and malaise symptoms through inhibiting ACE2± Inhibitor, which repels the route of entry of Corona virus. Andrographolide exerts its antiviral effects through inhibiting the dysregulation of signal transduction pathways necessary for viral replication and HIV-1 induced T cell cytopathicity.	17-26
Kabasura Kudineer Indication: Kapa Suram (Fever) ¹⁶ .	<i>Zingiber officinale</i> , <i>Piper nigrum</i> , <i>Syzygium aromaticum</i> , <i>Tragacanth volucrata</i> , <i>Anacardium occidentale</i> , <i>Terminalia chebula</i> , <i>Adathoda vasica</i> , <i>Costus speciosus</i> , <i>Tinospora cordifolia</i> , <i>Clerodendrum serratum</i> , <i>Andrographis paniculata</i> , <i>Caesalpinhia parea</i> , <i>Cyperus rotandus</i>	In Siddha system, it used for all types of fever and immune enhancement Kaba Sura Kudineer also neutralize or normalize the 3 humors mentioned in Siddha. Has anti-inflammatory, antipyretic activity. Benzeneopropanol, 4-hydroxy-a-methyl, 2-furancarboxaldehyde, and 5-(hydroxymethyl) are the predominant components which have significant immunomodulator and anti-inflammatory action that potentiates the therapeutic effects are also present in Kaba Sura Kudineer.	27,28
Adathodai manapagu Indication: <i>Kapathikam</i> , <i>Irumal</i> , <i>Suram</i> , <i>vayitrunoi</i> (deranged Kapham, cough, fever, digestive problem) ¹⁶ .	<i>Adathoda vasica</i>	Leaf is reported to possess expectorant, bronchodilator, antitussive, anti-tubercular, enhancer of platelet count, anti-inflammatory, anti-microbial, anti-viral, anti-helminthic, hepatoprotective activities and also effective against viral diseases including severe acute respiratory syndrome (SARS). Aqueous and methanolic extracts of <i>Adhatoda vasica</i> has marked Hemagglutination(HA) reduction. Extract has been proven to possess strong anti-influenza virus activity.	29-32
Ammaiyar koonthal Kudineer (AAK) Indication: <i>Vishakaichal</i> , <i>Veekam</i> (Fever due to toximeia, anasarca) ³³ .	<i>Cuscuta reflexa</i> , <i>Hemidesmus indicus</i> , <i>Allium cepa</i> , <i>Acorus calamus</i> , <i>Emblia officinalis</i> , <i>Terminalia chebula</i> , <i>Citrus aurantium</i> , <i>Citrus limon</i> , <i>Evolvulus alsinoides</i> , <i>Trichosanthes tricuspidata</i> , <i>Phyllanthus niruri</i> , <i>Sida acuta</i> , <i>Diospyros montana</i> , <i>Lagenaria siceraria</i> , <i>Cucurbita pepo</i> , <i>Asarum europaeum</i> , <i>Asystasia gangetica</i>	Anti-viral, anti-bacterial, anti-pyretic, anti-inflammatory, anti-HIV activity. Neutralizing virus Inhibit CD4/gp120 from the virus interaction. Anti-HSV-2, anti-proliferative. In Silico analysis of AAK explore the 16 active compounds has a high binding affinity with COVID-19 protease, it may suggest a possibility to protease inhibitor mechanism.	34

<p>Thippili rasayanam Indication: Kaasam, kshyam, Irumal, Iraippu, sethumam 96. (Pulmonary Tuberculosis, Cough, Bronchial asthma, All kind of Kapha diseases)¹⁶.</p>	<p><i>Piper longum, Piper nigrum, Cuminum cyminum, Nigella sativa, Carum copticum, Syzygium aromaticum, Alpinia galanga, Hyocymus niger, Three myrobalans, Taxus baccata, Plumbago zeylanica, Eletria cardamom</i></p>	<p>Methanolic extract of cumin seeds has inhibitory effect on HSV-1. The essential oil of <i>Carum copticum</i> has anti-viral activity. It also has a relatively Bronchodilator effect on asthmatic airways which was comparable with the effect of theophylline. Ten piperamides isolated from black pepper has been tested against various viral showed effective inhibition of Coxsackie virus type B3 and moderate activity against Human Rhino Virus.</p>	35-45
<p>Swasakudori Mathirai Indication: Suvasam, Irumal, Kaasam (Asthma, cough and other respiratory disorders)¹⁶.</p>	<p><i>Calotropis flower, Piper nigrum</i></p>	<p>Calotropis flower and pepper is widely employed in respiratory diseases as it has antispasmodic activity. The glycoside isolated from the latex of <i>Calotropis gigantea</i> showed inhibitory effect against human influenza viruses also in both subtypes A and B while had no effect on avian influenza viruses.</p>	46,47
<p>Thalishathy Chooranam Indication: Sethumam⁹⁶, Kamalai, Irumal, Thondaikattu, Kshyam, Atthisuram. (Kaba diseases 96, Jaundice, Cough, Throat infection, Pulmonary tuberculosis)¹⁶.</p>	<p><i>Taxus bucata, Syzygium aromaticum, Eletria cardamom, Zingiber officinale(dried), Ferula asafetida, Embilica ribes, Costus speciosus, Piper longum, Cuminum cyminum, Myrsticafragarns, Terminalia bellarica, Terminalia chebula, Nardostachys grandiflora, Anethum gravelons, Phyllanthus emblica, Piper nigrum, Mesua fera, Michalia champak buds, Corriandrum sativum seeds, Rhus succedanea, Carum copticum,</i></p>	<p>Phytochemical screening of <i>T. baccata</i> showed the presence of lignans, flavonoids, sugar derivatives, etc. It acts on lipoxygenase (LOX) enzymes that are potential targets for the treatment of bronchial asthma, inflammation, cancer and autoimmune diseases. The alcoholic extract of the leaves of <i>T. baccata</i> possesses significant anti-asthmatic activity and has beneficial effect in asthma by causing broncho relaxation and decreasing bronchial hyper reactivity. Lignans are known to possess various biological activities including antiviral, antibacterial, antioxidant, anticancer, spasmolytic and anti-inflammatory effects. Flavonoids are known to possess various biological activities including antibacterial, antifungal, spasmolytic, antiviral, anticancer and anti-inflammatory effects.</p>	48-54
<p>RAN therapy Indication: HIV infection</p>	<p><i>Rasa Gandhi Mezhugu (RGM), Amukkara Chooranam, Nellikailehyam⁵⁵</i></p>	<p>Reduced viral load, improve CD4 and CD8 cells counts, controls symptoms and increase body weight. <i>Withania somnifera</i> had shown antiretroviral activity against HIV infection and human respiratory syncytial virus. Has anti-herpes simplex virus type 1 (HSV-1) activity. Anti-inflammatory and neuro protective features and immunomodulatory activity during the post-pyretic phase of CHIKV in an animal model.</p>	56-59

Table 2. Siddha herbs used for the treatment of SARS CoV-2 Infection

Herbs in Siddha System of Medicine	Therapeutic effects	Ref
<p>Inji: (<i>Zingiber officinale</i>) Irumal, Thondai pun, Kuralkammal, Iraippu (Cough, Throat infection, Hoarseness of voice, Bronchial asthma)³³.</p>	<p>Has antiviral, analgesic, and antipyretic properties. Aqueous extract of fresh ginger was found to have antiviral activity against human respiratory syncytial virus on HEp2 and A549 cell line and anti-rhinoviral effect.</p>	60–62
<p>Thulasi: (<i>Ocimum sanctum</i>) Iyyam, Irumal, Kapasuramsuram, (fever, cough)³³.</p>	<p>It gives excellent results for cough caused due to <i>kabam</i>, allergic bronchitis, asthma, and eosinophilia. The ethanol extract of <i>Ocimum sanctum</i> (EEOs) has antiviral activity against the H1N1 pdm virus demonstrated through in-vitro inhibition assay in Madindarby canine kidney cells (MDCK). The crude extract and terpenoid isolated from the leaves of <i>O. sanctum</i> has shown promising antiviral properties against H9N2 virus.</p>	63–65
<p>Milaku: (<i>Piper nigrum</i>) Kulirsuram, Irumal, Kamalai, Seriyamai (fever with rigor, cough, Jaundice, Indigestion)³³.</p>	<p>Piperine the major phytochemical of black pepper is described to have antiviral property. Studies had suggested that aqueous and ethanol extracts from plants used are potential sources of antiviral, antitumor and antimicrobial agents. It is also found to have bioavailability-enhancing properties of other drugs. Ten piperamides isolated from black pepper has been tested against various viral strains which showed effective inhibition of Coxsackie virus type B3 and moderate activity against Human Rhino Virus.</p>	44, 66–68
<p>Karunjeerakam: (<i>Nigella sativa</i>) Sirangu, Irumal, Suram (Scabies, Cough, fever)³³.</p>	<p>Thymoquinone (TQ) is one of the most active constituents and has different beneficial properties. Focus on antimicrobial effects, different extracts of <i>N. sativa</i> as well as TQ, have a broad antimicrobial spectrum including Gram-negative, Gram-positive bacteria, viruses, parasites, Schistosoma and fungi. Oil of <i>Nigella sativa</i> was administered continuously for 3 months a dose of (450 mg three times daily) in patient with hepatitis C virus (HCV) infection who were not eligible for IFN-α therapy that significantly improved HCV viral load.</p>	42, 43, 69
<p>Keezhanelli: (<i>Phyllanthus niruri</i>) Suram, Kamalai, Perumbadu (Fever, Jaundice, menorrhagia)³³.</p>	<p>Febrifuge, antiviral. The whole plant inhibits hepatitis B virus DNA polymerase, the enzyme needed for the hepatitis virus to reproduce. The phytochemicals nirtetralin and niranthin has potent antiHBV activity. A novel lignin found in <i>P. niruri</i>, nirtetralin B and its two stereoisomers, nirtetralin and nirtetralin A. Nirtetralin significantly had a dose-dependent inhibitory effect on the in-vitro titres of HBV antigens. Aqueous extracts of <i>P. niruri</i> containing repandusinic acid, have been shown to exert a significant inhibitory effect on HIV-1 reverse transcriptase (HIV-1-RT). Repandusinic acid competitively inhibits the template primer during the process of reverse transcription. The alkaloid extract of <i>P. niruri</i> has an inhibitory effect on HIV-1 replication and dose-dependent cytoprotectivity against HIV infection. Niruriside inhibits REV/RRE binding during the movement of viral RNA from the cell nucleus to the cytoplasm, the Phyllanthus extract affected the early phases of viral infection such as the viral attachment and entry.</p>	58 70–77

<p>Athimadhuram: (<i>Glycyrrhiza glabra</i>) Irumal, kamalai (Cough, Jaundice)³³.</p>	<p>Antiviral properties against HSV, Rotavirus, HPV, SARS, Flavivirus, Human immunodeficiency virus, Vaccinia virus, Poliovirus (type 1), Vesicular stomatitis virus, IAV, SARS-related Corona virus, human respiratory syncytial virus, and Arboviruses.</p>	78–94
<p>Vellaipoondu : (<i>Allium sativum</i>) Irumal, Iraippu, Neeretram (Cough, Bronchial asthma, Sinusitis)³³.</p>	<p>Antiviral, antiprotozoal, disinfectant. Prevent blood clotting and increases the rate of clot dissolution. Garlic extract has been shown to have antiviral activity against influenza B and herpes simplex type 1 virus in cell culture, and influenza virus strain AO/RR8 in infected mice if the garlic extract was administered 15 days before inoculation with the virus. Studies have determined the antiviral activity of garlic and a new commercially available garlic product, garlicin, against seven different animal viruses in two cell lines: herpes simplex virus type 1 and 2 (HSV-1 and -2), vaccinia virus, and vesicular stomatitis virus in vero cells; parainfluenza type 3 (Para-3), poliovirus type 1, and human rhinovirus type 2 in HeLA cells.</p>	60, 95–98
<p>Citramutti: (<i>Sidacordifolia</i>) Athi suram, Kunmam (A type of fever, gastritis)³³.</p>	<p>Bronchodilator. <i>Sida cordifolia</i> showed promising antiviral activity against DNA (HSV I & II, HSV TK- and Adenovirus type VIII) and RNA (Poliovirus type-I and Influenza virus type A (H1N1)).</p>	99, 100
<p>Seenthil: (<i>Tinospora cordifolia</i>) Pithasuram, kabapini (Fever, kaba disease) ³³.</p>	<p><i>Tinospora cordifolia</i> has shown anti-HIV potential by 3 different mechanisms (interference with the gp120 / CD4 interaction, inhibition of HIV-reverse transcriptase and probable inhibition of HIV-protease enzyme). Anti-HIV activity could be an added advantage along with the immunomodulatory effect of these plants to fight Acquired Immunodeficiency Syndrome (AIDS). Extracts, only petroleum ether and ethanol (successive) extracts of <i>T.cordifolia</i> significantly inhibited gp120/CD4 interaction by binding to gp120 and by competitive inhibition and by binding to immobilized CD4. The virus suspensions of HSV1 & HSV2 were incubated with test compounds of concentration 100µg/ml and 50µg/ml of <i>T.cordifolia</i> extract and it was observed that at a test concentration level of 100µg/ml and 50µg/ml the percentage protection offered is approximately 61.43% and 23.22% respectively.</p>	101 – 104
<p>Manjal: (<i>Curcuma longa</i>) Thalaivali, Neeretram, mookuneerpaithal (Headache, Sinusitis, Rhinitis)³³.</p>	<p>Curcumin an alkaloid of turmeric inhibits the HIV-1 integrase protein, indicating that integrase inhibition may contribute to the anti-HIV activity of curcumin¹³⁴. Curcuminoid has inhibitory activities on influenza A neuraminidase and could be used as supplementary materials for battle of influenza virus as neuraminidase inhibitors of influenza A¹³⁵ curcumin might be beneficial for the treatment of an influenza virus infection by inhibiting haemagglutinin (HA) protein¹³⁶. The study of different bioconjugates of curcumin, against variety of viruses including parainfluenza virus type 3 (PIV-3), feline infectious peritonitis virus (FIPV), vesicular stomatitis virus (VSV), herpes simplex virus (HSV), flock house virus (FHV), and respiratory syncytial virus (RSV) assessed by MTT test showed the potent antiviral activity of curcumin and its bioconjugates. Curcumin was found to be an inhibitor of HIV-1 and HIV-2 protease with IC50 of 100 µM and 250 µM, respectively. The curcumin boron complexes exhibited noteworthy inhibition reduced to the IC50 value of 6 µM with time-dependent activity. The elevated affinity of Curcumin showed the anti-influenza activity against influenza viruses PR8, H1N1, and H6N1. In H1N1 and also H6N1 subtypes, the inhibition of haemagglutinin interaction reflected the direct effect of curcumin on infectivity of viral particles and this has proved by time of drug addiction experiment. Additionally, unlike amantadine, viruses developed no resistance to curcumin¹³⁷. These results proved the significant potential of curcumin for inhibition of influenza. In vitro study of curcumin and its derivatives, namely, gallium-curcumin and Cu-curcumin, exhibited remarkable antiviral activity against herpes simplex virus type 1 (HSV-1) in cell culture.</p>	105–110

<p>Vembu: (<i>Azadirachta indica</i>) Vayitrupuzhu, Nachusuram, Sirangu, amai pun, Kamalai (Worm infestation, fever due to toximea, Scabies, Herpes)³³</p>	<p>Neem leaves have considerable antinociceptive, emollient, antiviral, anti-inflammatory, antiseptic, antifungal, astringent, insecticidal, anthelmintic and antibacterial properties. Molecular docking study has shown that Deacetyl-3-cinnamoyl-azadirachtin in neem leaves serve as a potential inhibitor against NS3/4A protease of HCV. In vitro inhibitory potential of Neem leaves NL aq. ext. on DEN virus type-2 in C6/36 cells revealed inhibition of virus replication in a dose dependent response with 100% inhibition being observed by all concentrations. The molecular docking results showed that nimbin, desacetylnimbin and desacetylsalannin have good binding affinity with DENV NS2B-NS3pro.</p>	111–114
<p>Elumitchai: (<i>Citrus limonia</i>) Volatile oil Soolai, Kunmam, Vaanathi (pain, Gastritis, vomiting)³³</p>	<p>The antibacterial activity of crude extracts (aqueous and ethanolic) of Citrus limonium fruits against four wound isolates Staphylococcus sp, Pseudomonas sp, Escherichia coli and Klebsiella sp. showed antibacterial effect. The antimicrobial activity of different types and parts of lemon was evaluated against different microbial isolates. The aqueous extracts of peel and juice from fresh and dried citrus and sweet lemon showed various inhibitory effects against 6 Gram-positive and 8 Gram-negative bacteria and one yeast isolates, including Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus agalactiae, Pseudomonas aeruginosa, Enterobacter aerogenes, Klebsiella pneumoniae. When Citrus peel extract was added to the CoV infected cells the virus load of corona virus (CoV) decreased, had an effect on IL-8 secretion, TRP gene expression.</p>	115–118

Table 3. Siddha Medicines used for the prevention of SARS CoV-2 infection

Siddha Formulations	Composition	Therapeutic effects	Ref.
<p>Nilavembu Kudineer</p>	<p><i>Andrographis paniculata</i>, <i>Vetiveria zizanioides</i>, <i>Plectranthus amboinicus</i> <i>Santalum album</i>, <i>Cyperus rotandus</i>, <i>Piper nigrum</i>, <i>Zingiber officinale</i>, <i>Trichosanthes cucumerina</i></p>	<p><i>Nilavembu Kudineer</i> provides protection against CHIKV and DENV-2 during active infection as well can help to prevent virus infection in the cells and it mainly depends on the cellular availability of drugs for maximum protection against both the infections. The ethanol extracts of NVK exhibits antiviral property. <i>Nilavembu kudineer</i> and <i>Adathodai manapagu</i> has promising effects in treating dengue. It can be used as discreet prophylaxis in conditions of disease outbreaks.</p>	119–133
<p>Kabasura Kudineer</p>	<p><i>Zingiber officinale</i>, <i>Piper nigrum</i>, <i>Syzygium aromaticum</i>, <i>Tragia involucrata</i>, <i>Anacardium occidentale</i>, <i>Terminalia chebula</i>, <i>Adathoda vasica</i>, <i>Costus speciosus</i>, <i>Tinospora cordifolia</i>, <i>Clerodendrum serratum</i>, <i>Andrographis paniculata</i>, <i>Caesalpinhia parera</i>, <i>Cyperus rotandus</i></p>	<p><i>Kabasura Kudineer</i> promotes to increase the immunity level of the people and to neutralize or normalize the 3 humors. Aqueous extract of <i>Kabasura Kudineer</i> possesses a vital anti-pyretic effect comparable to that of paracetamol (standard drug) from 1 h to 5 h through a possible mechanism of inhibition of prostaglandin. The anti-bacterial activity of the extract was measured by observing bacterial free zones formed around the discs. The extract was found to have significant antibacterial activity. AEKCC was found to have antibacterial activity with MIC of 250 µg/ml for both gram positive and gram-negative organism. <i>Kabasura Kudineer</i> Chooranam is widely prescribed for the management and prevention of swine flu.</p>	27,134

ingredient of *Adathodai manappagu* shows antiviral property against Influenza virus²⁹⁻³². In *Ammaiyar Koonndhal Kudineer*, Chebulagic acid showed an extremely high binding affinity in inhibiting the SARS CoV2 spike protein in the native conformation and bound state with its target ACE2(Angiotensin-Converting Enzyme) receptor³⁴. The ingredients of *Thippili rasayanam* such as *cumin seeds*, *Carum copticum*, *Nigella sativa* have antiviral property. Carvacrol present in *Carum copticum* is an efficient smooth muscle relaxant³⁵⁻⁴³. So, it can be used in respiratory infections. *Thalisathi choornam* has the key ingredient *Taxus buccata* it has relaxing effect on bronchial smooth muscles and the lignans present in it have antiviral property⁴⁷⁻⁵⁵. *Swasakudorai mathirai* has pepper and flowers of *Calotropis* with the property of antiviral and antispasmodic effect^{46,66}. The major ingredient of *Amukkara chooranam*, *Withania somnifera* is effective against HSV and HIV^{56,57}. Ginger is effective against Respiratory Syncytial Virus²². *Ocimum sanctum* has antiviral activity against the H1N1 pandemic virus^{64,65}. *Piper nigrum* was found to be antiviral against Human Rhino virus, also found to have bio availability enhancing properties of other drugs^{44,136}. *Nigella sativa* has broad spectrum anti-microbial activity^{42,43}. *Phyllanthus niruri* was found to be active against HBV, HIV and Dengue viruses⁷¹⁻⁷⁷.

Glycyrrhiza glabra has specific antiviral property against the influenza virus⁷⁸⁻⁹⁴. Garlic has antiviral property against many viruses including para-influenza type 3 and Human Rhino Virus. *Sida cordifolia* was found to inhibit RNA and DNA viruses including influenza virus type-A¹⁰⁰. *Tinospora cordifolia* has anti-HIV, HSV1 and HSV 2 activity¹⁰¹⁻¹⁰⁴. Turmeric is a potent antiviral herb with the alkaloids providing efficient anti-viral activity against various viral strains including parainfluenza^{107,108}. *Azadirachtaindica* inhibits HCV and Dengue virus by destructing the enzymes responsible for viral replication¹¹¹⁻¹¹³. *Citrus limonia* has anti-bacterial activity against *Klebsiella species* and affects IL-8 secretion, TRP (T-Cell Receptor Beta locus) gene expression in Corona virus¹¹⁵⁻¹¹⁷.

4. Conclusion

From this review it is evident that the ingredients of the listed *Siddha* formulations and herbs possess potent antiviral activity, antioxidant property that could enhance the immunity. It is also proven that despite the etiological factor these medicines have the inbound capacity to fight against many respiratory infections, seasonal attacks

more specifically of viral origin including COVID-19. Also, the study suggests more literature formulations have to be identified and clinical research could be carried out to identify the molecular level pharmacodynamic targets of *Siddha* medicines to achieve clinical success in the management, prevention of viral respiratory infections and eradication of epidemic and pandemic outbreaks.

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