

# COVID-19 in Siddha Medicine: A Review

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## ABSTRACT

“Severe acute respiratory syndrome coronavirus-2” is responsible for the COVID-19. It was identified in China in December 2019 and it was “declared as a pandemic” disease by “the World Health Organization” in “March 2020”. This review article is an attempt to give an insight into the management of COVID-19 in the Siddha medicine aspect to potential treatment strategies in herbal and herbomineral formulations for the recently recognized “SARS-CoV-2” L strain.

**Keywords:** “COVID-19”; Herbal, Herbomineral formulations, SARS CoV-2, Siddha medicine.

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## INTRODUCTION

In 1960, coronaviruses belong to Coronaviridae family, where wrapped “positive sense single-stranded ribonucleic acid (RNA) viruses”.<sup>1</sup> Corona is derived from Latin, it signifies “Crown” or “Halo”, which is a unique “appearance under two-dimensional transmission electron microscopy” and it would seem that club-molded spike peplomers covering their surfaces.<sup>2</sup> Within the Coronaviridae subfamily, the  $\alpha$  and  $\beta$  coronaviruses are transmissible to people.  $\beta$  coronavirus strains are begun “from the bat species (*Rousettus leschenaultii*)”.<sup>3-5</sup> The  $\beta$  coronavirus strains are MERS-CoV, SARS-CoV, and SARS-CoV-2. SARS-CoV-2 is responsible for the COVID-19<sup>6</sup> and it was distinguished “in Wuhan, China in December 2019”, it was announced as a pandemic by WHO in March 2020.<sup>7,8</sup> COVID-19 clinical manifestations range from the mild cold-like symptoms to serious respiratory distress leads to cause death.<sup>9</sup> Globally, 4,088,848 people have been diagnosed with COVID-19 until 12 May 2020.<sup>10</sup> The researchers revealed that COVID-19 exist in two forms, S and L forms. COVID-19 S strains to be less virulent and less adoptable than L strains to the human receptor and their gene mutations cause the variation in filling (i.e., L form is mutated).<sup>11</sup> “It is caused by a rapidly spreading virus which works by injecting its genome into other’s gene and multiplies. Hence, it depends on other organisms for its development and therefore makes it challenging to eradicate the disease-causing agent and it” is becoming an important topic for research among the drug developers, the researchers, and the scientists.<sup>12</sup>

Traditional medicine is playing a key role in meeting global healthcare needs. Siddha is a unique system of medicine, which is originated from Tamil Nadu and has its origin in the Tamil language. Literally, the word “Siddha” means “established truth”.<sup>13</sup> Siddha medicine is claimed to alleviate the root cause of the disease by maintaining the equilibrium among vatham, pitham, and kapam. There are many Siddha formulations, such as kudineer, mattirai, chooranam, parpam, chendurum, karuppu, and mezhugu.<sup>14</sup> The aim of the current review is to explore some of the herbal and herbomineral formulations used to prevent or treat COVID-19.

## SIDDHA FORMULATIONS

The Siddha drugs selected for the management of COVID-19 depends on its pharmacological action, mentioned in published articles in journals and book references which may help the health

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professionals and researchers for the patient care. The herbal formulations and its documented pharmacological activity are shown in Table 1.<sup>15-29</sup>

## Adathodai Manapagu

This preparation is based on the *Adhatoda vasica* (AV) leaf juice. *Adhatoda vasica* belongs to the Acanthaceae family. The plants consist of “quinazoline alkaloids (vasicine, 7-hydroxy vasicine, vasicinolone, 3-deoxy vasicine, vasicol, vasicoline, vasicolinone, triterpenes, anisotine), betaine, steroids carbohydrate, and alkanes. In the flowers, triterpenes (a-amirine) and flavonoids (apigenin, astragalin, kaempferol, quercetin, vitexin) have been” found.<sup>30</sup> The crude extract of *Justicia adhatoda* acts against the influenza virus by hemagglutination (HA) decrease. In two unique layouts of simultaneous and posttreatment, assay shows antiviral activity in the non-cytotoxic range. Methanolic extract of AV revealed a 100% rebate “in HA in the simultaneous and posttreatment at the concentration of 10 mg/mL. The aqueous extract of *J. adhatoda* at 10 and 5 mg/mL concentrations shows reduced HA to 33% and 16.67%, respectively, in the simultaneous assay. These results showed that aqueous and methanolic extracts of *J. adhatoda* have strong antiviral activity that can inhibit viral attachment and/or viral replication, and may be used for viral” prevention.<sup>11</sup> The compound vasicine shows the excellent antiviral property in Dock assay.<sup>30</sup>

## Kabasura Kudineer

The Siddha classical formulation kabasura kudineer chooranam consists of 15 ingredients of herbs (*Zingiber officinale*, *Piper longum*,

**Table 1:** Some of the Siddha medicine used for the management of COVID-19

S. no	Siddha drugs	Pharmacological activity	Ref.
1	Adathodai manapagu <sup>15,16</sup>	Antipyretic activity, anti-inflammatory activity, antioxidant activity, antiviral activity, and hepatoprotective activity	17
2	Kabasura kudineer <sup>15,16</sup>	Antipyretic activity, expectorant, antispasmodic, anti-asthmatic activity, antiviral activity, immunomodulatory activity, hepatoprotective activity, and antioxidant activity	18
3	Thontha sura kudineer <sup>19</sup>	Antiviral activity, anti-inflammatory activity, anti-asthmatic activity, hepatoprotective activity, and immunomodulatory activity	20–24
4	Vajra kandi chenduram <sup>25</sup>	Antipyretic activity, anti-inflammatory activity, antioxidant activity, and immunomodulatory agent	26
5	Visha sura kudineer <sup>15,27</sup>	Antiviral activity, antipyretic activity, anti-asthmatic activity, anti-inflammatory activity, antioxidant activity, hepatoprotective activity, and immunostimulant activity	28
6	Nilavembu kudineer <sup>15,16</sup>	Anti-inflammatory activity, antipyretic activity, hepatoprotective activity, immunostimulant property, antiviral activity, antioxidant activity, neuroprotective activity, and immunomodulatory activity	29

*Syzygium aromaticum*, *Tragia involucrata*, *Anacyclus pyrethrum*, *Hygrophila auriculata*, *Terminalia chebula*, *AV*, *Coleus amboinicus*, *Saussurea lappa*, *Tinospora cordifolia*, *Clerodendrum serratum*, *Andrographis paniculata*, *Sida acuta*, and *Cyperus rotundus*". The mechanism of action of the phytochemicals present in the kabasura kudineer Siddha formulation attracting/binding multiple amino acids at different sites of viral proteins which corroborated with the well-known antimalarial drug, artemisinin.<sup>18</sup> This showed the synergistic activity of phytochemicals not only against the viral proteins but also modulate the immune system for fighting against viral replication. The active molecules of the respective medicinal plants, *Trichosanthes cucumerina*, *T. cordifolia*, *H. auriculata*, *A. pyrethrum*, *A. paniculata*, *AV*, *S. lappa*, *C. serratum*, *S. aromaticum*, and *Z. officinale*, might inhibit the viral pathogenesis at various levels spanning from prevention to cure. It revealed that the functionally significant formulations against corona viral protein showed a more efficient inhibitory effect against viral replication.<sup>18</sup>

### Thontha Sura Kudineer

Thontha sura kudineer chooranam consists of 10 ingredients of herbs (*Z. officinale*, *AV*, *A. paniculata*, *T. cordifolia*, *Elettaria cardamomum*, *Solanum xanthocarpum*, *T. cucumerina*, *Tephrosia purpurea*, *Mollugo*

*cerviana*, and *Vitis vinifera*) was studied for antiviral activity by in silico docking analysis.<sup>22</sup> The phytochemicals in thontha sura kudineer had promising activity against the viral spike glycoprotein which prevents the spike proteins binding with host cell receptor.<sup>21</sup>

### Nilavembu Kudineer (NVK)

"Nilavembu kudineer is a polyherbal formulation with *A. paniculata* as the main ingredient that controls all types of fever related to body pain. Other components include *Vetiveria zizanioides*, *V. zizanioides*, *Santalum album*, *T. cucumerina*, *C. rotundus*, *Zingiber officinale*, *Piper nigrum*, and *M. cerviana*.<sup>20</sup> All these plants are utilized traditionally in the treatment of pyretic, "inflammation, arthralgia, arthritis, gastric ulcer, jaundice, and general debility conditions". Nilavembu kudineer extensively controls fever through its managing consequences effects on temperature, inflammation control, body pain, and it also acts in a way to improve immunity.<sup>17</sup> All the components in this formulation have the bioactive molecules that show excellent activity against dengue, chikungunya, herpes simplex virus (HSV), and influenza virus.<sup>29</sup>

### Vajra Kandi Chenduram

It is a herbomineral preparation broadly utilized particularly in Siddha practitioners regards the management of several acute and chronic illnesses ranging from fever to chronic inflammatory disorders and immune-mediated diseases. This formulation is made of purified lingam, veeram, pooram, and rasa sindhuram. This component shows antipyretic, anti-inflammatory, and antioxidant activity. Vajra kandi chenduram through its antipyretic and anti-inflammatory activity can be the potential to prevent the release of the inflammatory mediators and cytokine storm of COVID-19 which is a major cause for severe lung complication. Therefore, this formulation can be advised as a safe and effective supportive therapy in the absence of any specific target treatment measures. "In targeting key molecules within the inflammatory cytokine network such as interleukin-6 (IL-6) is a novel strategy for COVID-19 induced" cytokine release syndrome (CRS). "Interleukin-6 inhibitors may ameliorate severe damage to bronchial tissue caused by cytokine release in patients with serious COVID-19 infections. Several damages to bronchial tissue caused by cytokine release in patients with serious COVID-19 infections are being reported.<sup>26</sup> Several studies have indicated a "cytokine storm" with the release of IL-6, IL-1, IL-2, and IL-8 along with 'tumor necrosis factor' α (TNF α) and other inflammatory mediators".<sup>31</sup>

### Visha Sura Kudineer

Visha sura kudineer (VSK) is a polyherbal formulation from Siddha literature "Kaaviya Sura Nool". The components were *Azadirachta indica*, *Indigofera tinctoria*, *Z. officinale*, *Hemidesmus indicus*, *Aristolochia bracteata*, *V. zizanioides*, *Glycyrrhiza glabra*, *E. cardamomum*, and *Santalum album*. Each of the component shows antiviral activity against wide range of viruses. "Aqueous leaf extract of *A. indica* offers antiviral activity against vaccinia virus, chikungunya measles virus, dengue virus type-2, and HSV" type-1, it also has immune stimulant, anticomplement activity.<sup>32</sup> *Indigofera tinctoria* shows an inhibitory effect of HIV-1 (III B) and HIV-2.<sup>33</sup> "*Zingiber officinale* has antiviral activity against the human respiratory syncytial virus in human respiratory tract cell lines". *Hemidesmus indicus* antiviral activity was studied against the Ranikhet virus. "A component of licorice root glycyrrhizic acid has antiviral activity by inhibiting the growth and cytopathic effect of several DNA and RNA viruses, such as vaccinia, HSV-1, Newcastle



disease, and vesicular stomatitis viruses". It also shows antiviral activity against flaviviruses, such as dengue, Japanese encephalitis, Yellow fever, mammalian tick-borne encephalitis, influenza, and hepatitis A, B, C viruses.<sup>34</sup> Sandalwood oil, the essential oil of *Santalum album* L., indicated antiviral activity against HSV-1 and HSV-2.<sup>33</sup>

## MANAGEMENT

Isolation is the best measure for the containment of COVID-19. No particular antiviral treatment or "vaccine is currently available."<sup>35</sup> Hence, the treatment of COVID-19 combines with symptomatic care and oxygen therapy. Patients with mild infections lack early supportive management". However, in Siddha, this infection is adequately "treated by a specific course of treatment that is termed as a regimen. The regimen that is utilized during the initial days of infection in the treatment" includes one or more formulations, such as adathodai manapagu, kabasura kudineer, thontha sura kudineer, vajra kandi chenduram, VSK, and NVK. The dynamic active biomolecules in the abovementioned formulations strongly act against a wide range of viruses out of six formulations AV is common in four formulations, so the treatment regimen should be with a combination of adathodai manapagu.

"However, the efficacy of corticosteroids, commonly used anti-inflammatory agent, to treat COVID-19-induced CRS is controversial. There is an urgent need for novel therapies to treat COVID-19-induced CRS. The British Pharmacological Society has reacted to concerns that the use of non-steroidal anti-inflammatory drugs (NSAIDs) could exacerbate symptoms of the novel coronavirus infection, COVID-19. The World Health Organization on March 18, 2020, released a statement, that it "is aware of concerns on the use of ibuprofen for the treatment of fever for people with COVID-19".<sup>34</sup> Hence at this juncture, the use of Siddha anti-inflammatory, antipyretic, and immune-modulatory agents can provide immense support toward the management of CRS. Vajra kandi chendooram shows all this activity; hence, this can be replaced for corticosteroids. Thereby Siddha drugs can aid in the prevention of stage-I coronavirus into the next stage and can prevent the morbidity and mortality of COVID-19 patients. Hence, these drugs are safe to be administered at prescribed doses under the medical supervision of Siddha physician. Moreover, all the ingredients have been tested toxicologically and be safe in humans. Therefore, the abovementioned Siddha formulation may be considered to be of public use during this global pandemic.

## CONCLUSION

The "COVID-19 is spreading across the globe at a disturbing rate. It has caused more infections and passing as contrasted with SARS or MERS. The rapid widening of infection permits exceptional surveillance and disengagement protocols to prevent further transmission. No affirmed treatment or immunization has been developed. Current treatment techniques" are focused on indicative consideration oxygen treatment. Through this review work, all the ingredients of the Siddha formulations have been explored scientifically for its pharmacological actions, toxicity evaluation, and is safe in humans. Further preclinical studies on its antiviral actions of the Siddha formulation may be warranted to confirm our hypothesis scientifically and has been planned to be performed shortly.

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