Rajeshbabu et al. | J Pure Appl Microbiol | 16(2):763-768 | June 2022
Article 7279 | https://doi.org/10.22207/JPAM.16.2.14
Published Online April 25, 2022
Print ISSN: 0973-7510; E-ISSN: 2581-690X

REVIEW ARTICLE OPEN ACCESS

Acute Respiratory Distress Syndrome due to COVID-19 in India and efficacy of Indian Siddha drugs - A Trial of Lopinavir-Ritonavir

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Abstract

Novel coronavirus pneumonia (COVID-19) is a respiratory infection caused by infecting lungs and respiratory pathways which has rapidly spread to 216 countries. It is causing serious harm to the world's entire population and a huge social burden, which can spread mainly by droplets produced during coughing and sneezing from animal to animal or human to human. There were no drugs or vaccines available as of May 2020. Though the severity and infectious behavior and mortality rate of COVID-19 led to the discovery of various vaccines and drugs that are available to control COVID-19 pandemic. India has two vaccines: Covishield and Covaxin approved by the Government of India on 2nd January 2021. Of this sudden and lethal disease, the traditional Indian siddha medicine was proficient as an alternative source, in performing differentiation with fewer side effects and better ability to prevent and control. In this article, we have comprehensively analyzed the case study and the efficacy of Indian Siddha medicine Kabasura Kudineer chooranam. Naturally occurring Indian Siddha medicinal (Kabasura Kudineer chooranam) compounds and its treatment as prevention measures so as to provide strategy and suggestions for the disease COVID-19 are discussed.

Keywords: COVID-19, Kabasura Kudineer chooranam, siddha drugs

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(Received: August 27, 2021; accepted: March 7, 2022)

Citation: Rajeshbabu P, Priadharsini K, SUM Riyaz, Dhayalan M. Acute Respiratory Distress Syndrome due to COVID-19 in India and efficacy of Indian Siddha drugs - A Trial of Lopinavir– Ritonavir. *J Pure Appl Microbiol.* 2022;16(2):763-768. doi: 10.22207/JPAM.16.2.14

INTRODUCTION

In the modern world of biotechnology, population of over one million new cases are affected from different types of coronavirus per year worldwide, the high rate of respiratory tract infections, which leads to the infection of viral pneumonia in these patients, which is ultimately, remains a big task in treatment and significantly there is a cause of increase in morbidity and mortality.[1-3] In India, it accounts for an estimated 2.5 million cases and still it is growing every 47 year. In the wake of drug and vaccine against the conventional respiratory tract infections, researchers and common man are looking for an alternative that will overcome these impacts. According to WHO statistics, the world now is facing an unpredictable and uncontrolled virus disease of COVID-19 which has infected approximately 4.44 million world's population with 15,85,286 cases recovered and 3,02,025 death cases. As on 15.05.2020, In India around 78,003 people have confirmed for COVID-19, out of this 26,235 cases are recovered, and around 2,549 patients were died, the symptoms of COVID-19 were fever, cold, cough, shortness of breath, in additional some suffered from fatigue and diarrhoea. It's still unclear how long a patient gets infected by the virus, due to asymptomatic nature.[4]

During December 2021, the number of new COVID-19 cases increased when compared with the previous cases while the number of new deaths were comparatively lower. As of 26 December, over 278 million cases and just under 5.4 million deaths have been reported globally by WHO. There have been 35,018,358 confirmed cases of COVID-19 with 482,551 deaths, reported to WHO from 3rd to 5th January, with a total of 1,476,253,454 vaccine doses administered as of 3rd January 2022, in India. The more the virus circulates, the more the virus evolves over time. However, some changes to SARS-CoV-2 led to the emergence of few variants that affect virus transmissibility, disease severity and effectiveness of vaccines. Several SARS-CoV-2 variants have been identified and some were characterized as variants of interest (VOI) or variants of concern (VOC) by WHO.

As per the Indian theory of subsistence declared by Christal Quintasket (1936-1988), if all life on earth has an intention, every single plant present has a curing effect on each disease. Indeed, India has a potentially huge natural resource to treat various infectious diseases. Natural plants or plant parts have been used in traditional siddha and ayurvedic systems of Indian medicine, which constitutes the main source for present pharmaceutical products. Due to its non-toxicity, this type of traditional medicinal practices are used as an essential alternative therapeutic treatment to cure and treat any diseases including cardiac and respiratory tract infections.[9]

Case studies of COVID-19 in India

Even though 80% of the Indian population had mild illness, more than a quarter of those hospitalized were with a transience of 47%, whereas those with Acute Respiratory Distress Syndrome (ARDS) had a transience of 51.7%. It was clear that several other countries were not been able to constrict COVID-19 spread, due to unavailability of exposure of the near beginning extensive testing, first and foremost due to the scientist who are all involved in testing are at risk with respect to frequent exposure to virus infected individual samples without proper personal protective equipment (PPE), secondly health officials are worsening to trace all contacts of infected patients, due to nosocomial spread of the infection, in some overcrowded settings.[5] With respect to this, there is a serious anxiety regarding a lack of ICU beds and ventilators, skilled medical staff, sufficient PPE and ever-changing recommendations about health groups and supportive care, at a time when no ultimate therapy for COVID-19 is accessible. All of these factor serve as a huge intricacy to Pulmonary and Critical Care Medicine (PCCM) clinicians, and we require to have a plan for meeting these challenge, cause to this circumstances, is some significant essential facts about COVID-19 are still life form strong-minded, most prominently the transience rate, which as high as 4-7%, the rates vary extensively by age and sternness of illness.[6] Predictors of transience have incorporated older age, elevated D-dimer on admission and superior degree of initial organ dysfunction. However, the designed transience rate is also a manifestation of the degree of extensive diagnostic testing, since many contaminated individuals have negligible symptoms and may not be habitually evaluated,

as a serious concern, the Indian government need to do some serious initial screening efforts for example in South Korea, efforts have been complete to do wide inhabitants testing, and when a more precise number of infected persons is integrated, the overall transience rate may be less than 1%. Conversely, this makes COVID-19 more tedious than seasonal virus, which has a 0.1% transience rate, which may reproduce not only the natural history of the virus, but also the constructive collision of immunization and antiviral prescription.[7] In comparison to other corona viruses such as MERS and SARS, which have much higher transience rates, estimated to be 40% and 10% respectively COVID-19 does current unique challenge as we study about its moderately long asymptomatic, but contagious incubation period (7-21 days) during which community spread may occur, and the protracted detaching of virus after symptom resolution (an additional 21-28 days).

In a series of cases with specialized exposure and indication onset, the middle incubation period was 14-21 days, but it was not until 21 days that 97.5% of patients had symptoms and 82% of patients had no symptoms. In investigational studies, SARS-CoV-2 can remain viable in aerosols for hours and on surfaces for days, construction aerosol and environmental spread extremely possible.[8] These findings have implications not only for community propagation of illness by it seems that well and asymptomatic patients, but also for the protection of PCCM provider and their staff as they assess and treat these patients early and later in the course of infection.

To contain the infection, it is essential to make a precise and early diagnosis. In India, during the early pandemic period where there was absence of tests, it was an ordeal to prevent the infection spreading from person to person in the community because of an initial lack of knowledge and surveillance. To address these issues, our health welfare team used thermal body scanners to identify the body temperature of an individual and manage the suspected COVID-19 infectants. Later on, diagnostic testings included nucleic acid detection in a variety of samples (noropharyngeal and asopharyngeal swabs), lower respiratory tract (bronchoalveolar lavage and sputum), urine and blood. In this case, disease control occurred with a amalgamation of widespread testing, contact tracing, use of negative pressure isolation rooms for infected patients, and social distancing to reduce disease spread.

Effect of Lopinavir-Ritonavir against COVID-19

The disease COVID-19 had alarmed globally to create a significant focus on the healthcare industry to rectify the transmission of the virus and overcome the outbreak of pandemic situation at the earliest to save millions of lives. Lopinavir-Ritonavir has been one among the developed antivirals that has been used to treat Human Immunodeficiency Virus (HIV) initially and later the same drug combination was used to treat Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS).[9] The addition of Lopinavir-ritonavir along with the standard treatment protocol was incorporated to study the efficacy of drugs to reduce the mortality rate. The trial of Lopinavir-Ritonavir drug combination was established by WHO before the findings of appropriate vaccines against COVID-19. Based on the available evidence, the efficacy of Lopinavir-Ritonavir was less effective against COVID-19 but by adding Lopinavir-Ritonavir to the standard therapy could bring better clinical benefits.[10] demonstrated that considering Lopinavir-Ritonavir in addition to ribavirin and interferon-β confers clinical benefits and this method can still be maintained.

Efficacy of Indian Siddha medicinal system

With over the modern era in the technology world over one million novel cases per year global, respiratory tract infections remain a tricky disease to treat and the considerable cause of morbidity and transience. In India, it accounts for an estimated 2.5 million cases and still it is growing every year. In the wake of toxic and resistance by the conventional respiratory tract infections, researchers and common man are looking for an alternative that will overcome these impacts.[11] The main idea to use medicinal plant extract is to avoid the extensive use of synthetic anti-inflammatory non-toxic chemicals. Recently, increased risk of respiratory tract infections with strategies using foods and medicinal herbs has been regarded as one of the most visible fields for treating respiratory tract infections. A growing dependence on the use of medicinal vegetation in the mechanized societies has been traced to the

Table 1. Ingredients of *Kabasura kudineer* chooranam

No.	Tamil Name	Botanical Name	Part used	Quantity
1.	Ilavangam	*Syzygium aromaticum* (L.)Merr & L.M. Perry	Flower bud	1 part
2.	Chukku	*Zingiber officinale* Rose	Rhizome	1 part
3.	Milaku	*Piper longum* L.	Fruit	1 part
4.	Sirukanchoriver	*Tragiain volucrata* L.	Root	1 part
5.	Akkirakaramver	*Anacyclus pyrethrum* (L.) Link	Root	1 part
6.	Mulliver	*Hygrophila auriculate* (Schumach)	Root	1 part
7.	Kadukkai	*Terminalia chebula* Retz.	Pericarp	1 part
8.	Adhatoda	*Justicia adhatoda* L.	Leaf	1 part
9.	Karpuravalli	*Plectranthus amboinicus* (Lour)	Leaf	1 part
10.	Koshtam	*Saussurea costus* (Falc.) Lipsch	Root	1 part
11.	Seenthil	*Tinospora cordifolia* (Thunb.) Miers.	Stem	1 part
12.	Siruthekku	*Clerodendron serratum* (L.). Moon	Root	1 part
13.	Nilavembu	*Andrographis paniculata* Burm.f. Nees	Whole plant	1 part
14.	Vattathiruppiver	*Cissam pelospareira* L.	Root	1 part
15.	Koraikizhangu	*Cyperus rotundus* L.	Rhizome	1 part

taking out and development of several drugs.[12] One of the novel strategies for the collection of medicinal plants for anti-inflammatory drug discovery is to look for ethno medical claims for the treatment of certain anti-inflammatory, immune-stimulant related specific diseases like, infectious diseases, immune disorders, viral diseases and parasitic diseases. Quite a few plant species have been recognized to restrain and display new, valuable medicinal anti-inflammatory, immuno-stimulant via bio-active compounds through the natural tribe sources or therapeutic properties against virus and bacterial disease.

Siddha formulation Kabasura Kudineer was popularized during the COVID-19 pandemic to enhance the body immunity that helped in preventing the infection in the individuals. Despite several ongoing researches in biomedical sciences, traditional medicines were also used for clinical treatments in reducing virus transmission and preventing the disease. The results proved that the viral load significantly declined in the group treated with Kabasura Kudineer than the control group.[12] Siddha preparations have been classified into different categories of medicinal forms as 32 internal and 32 external and chooranam is one among the internal medicinal forms. Kabasura Kudineer, is a combination of different ground medicinal plant parts that are made into decoction and consumed. A consistency of herbal formulations and ingredients [Table 1 and Table 2][13] is required in order to evaluate the superiority of drugs present in the chooranam.[14]

Table 2. Preliminary phytochemical studies of *Kabasura kudineer* chooranam

No.	Phytochemicals	Observation
1.	Terpenoid	+ve
2.	Phenol	+ve
3.	Steroid	+ve
4.	Flavonoid	+ve
5.	Alkaloid	+ve
6.	Tannin	+ve
7.	Glycosides	+ve
8.	Quinones	+ve
9.	Acids	+ve
10.	Coumarin	+ve
11.	Sugars	+ve
12.	Saponins	+ve

In this paper an attempt was made to evaluate a Siddha medicine, Kabasura Kudineer formulation by analytical methods and chromatographic studies. Kabasura Kudineer chooranam consists of coarse powders of plant parts, source of drug components which is used for the decoction preparation. Decoctions should be prepared whenever required and consumed immediately. The prepared decoction cannot be stored for long period, as several molds might contaminate the water-based decoction. Kabasura kudineer chooranam is commonly used in Siddha in treating cold, cough, fever, respiratory diseases

and also as a prophylactic at the time of viral epidemics.[15] Apigenin, cardiofoliolide, cucurbitacin B and pyrethrin present in the herbal decoction were found to be effective in preventing SARS-CoV-2 binding and replication.[16] In addition, phytochemicals found in the decoction such as flavonoids, lactones, alkaloids, polysaccharides, diterpenoids and glycosides have been identified as immunomodulating agents.[17,18] The alkaloids and andrographolide present in nilavembu has been documented to have potential cytotoxicity, modulate the innate immune response and regulate the antibodies production.[19]

CONCLUSION

This study will further enrich our classical Siddha medicine system towards the component one among the global herbal medicines. The outcome of this day will evidence the preclinical safety consequence of AP treatment. Further, it will prove the potential activity of our classical Siddha drugs against respiratory tract infections and cancer disease and it will explore the real molecular mechanism behind this activity. Future studies need to be done with phytochemical drugs by synthesizing a analog chemical compound and analysis of drug effects need to be studied extensively by enormous *in vitro* and *in vivo* studies passing through all clinical phase trials approved by ICMR and US-FDA, this will furthermore will enlight on repurposing the existing drugs in Siddha system of medicine to utilize them in the treatment of COVID -19 patients.

ACKNOWLEDGMENTS

The authors would like to gratefully acknowledge to Professor Dun Yang, President & CEO and Dr. Jing Zhang, VP at Anticancer Bioscience, Tianfu International Biotown, Chengdu, China.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Not applicable.

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