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A review on medicinal plant adhatodai– therapetic choice for the management of COVID 19

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Abstract
COVID-19 is the highest newly revealed coronavirus infectious disease and leads to pandemic all over the world. Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).
The clinical scale of COVID-19 varies from mild illness with non-specific signs and symptoms of acute respiratory disease to extreme respiratory pneumonia and other complication. It can transmit from animal to human in the form of contact, Droplets or aerosols. Airborne transmission Surface transmission and fecal-oral. COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. Adhatoda is a notable regular bush in siddha system of medicine which has a helpful impacts, especially in respiratory problems. This study investigates the probability of *Justiciaadhatoda* (Adhatodavasica Nees) in the expectation and the beam of indications related with COVID-19.

Keywords: medicinal plant adhatodai, coronavirus (CoV) infectious

Introduction
Corona infection illness 19 (COVID-19) episode is a current pandemic that causes intense Respiratory disorder with massive mortality around the world. Corona viruses is a single stranded, enveloped, positive sense RNA viruses which belong to family Coronaviridae [1], Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV) [2]. SARS-CoV-2 is a novel severe acute respiratory syndrome coronavirus2. It was first isolated from three people with pneumonia connected to the cluster of acute respiratory illness cases in Wuhan [3]. All structural features of the novel SARS-CoV-2 virus particle occur in related coronaviruses in nature. SARS-CoV-2 is closely related to the original SARS-CoV. It is thought to have an animal (zoonotic) origin [4, 5]. Genetic analysis has revealed that the coronavirus genetically clusters with the genus Betacorona virus, in subgenus Sarbeco virus (lineage B) together with two bat-derived strains It is 96% identical at the whole genome level to other bat coronavirus samples (Bat Cov RaTG13) [6, 7] The structural proteins of SARS-CoV-2 include membrane glycoprotein (M), envelope protein (E), nucleocapsid protein (N), and the spike protein (S). The M protein of SARS-CoV-2 is about 98% similar to the M protein of bat SARS-CoV, maintains around 98% homology with pangolin SARS-CoV, and has 90% homology with the M protein of SARS-CoV; whereas, the similarity is only around 38% with the M protein of MERS-CoV. The structure of the M protein resembles the sugar transporter [8]. The chief clinical components of COVID-19 are the Presence of respiratory indications, with serious cardiovascular and renal inconveniences in certain patients [9]. Symptoms of COVID-19 are variable, ranging from mild symptoms to severe illness [10]. Common symptoms include headache, loss of smell and taste, nasal congestion and runny nose, cough, muscle pain, sore throat, fever, diarrhea and breathing difficulties [11]. Three common clusters of symptoms have been identified: one respiratory symptom cluster with cough, sputum, shortness of breath and fever; a musculoskeletal symptom cluster with muscle and joint pain, headache and fatigue; a cluster of digestive symptoms with abdominal pain, vomiting and diarrhea [12]. In people without prior ear, nose, and throat disorders, loss of taste combined with loss of smell is associated with COVID-19 [12]. In siddha system various type of medicinal plants are described for the treatment of such type of pandemic disease among them *Adhatodai* which has been used in the treatment of different respiratory system related diseases, we reviewed various researches on *Adhatodai* and its use in the management of respiratory system related diseases, viral diseases and other diseases in various journals and Siddha classical texts It has various action like anti-viral, anti-bacterial, anti-pyretic, antispasmodic, anti-inflammatory, diuretic hepatoprotective, cardioprotective, antitubercular antioxidant and expectorant activities [13]. We have preferred *Adhatodai* for the management of *COVID 19.*This review explores the potency of *Justicia Adhatoda* and shares its consequence in the management of *COVID19* related symptoms

Plant Description and Classification
Adhatodai is a famous evergreen shrub of 4-8 feet in height with many Long opposite branches. Leaves are 3-8 inches in length and Lance-shaped, opposite, and estipulate. Stem is herbaceous Flowers are spikes, small irregular Zygomorphic, bisexual, and hypogenous. The flowers are either white or purple in colour. It has four seeded fruits

with Capsule Its trade name Vasaka is based on Sanskritname. Inflorescences in axillary spicate cymes, densely flowered; peduncles short; bractbroadly ovate, foliaceous [14].

[Kingdom: Plantae; Order: Lamiales; Family: Acanthaceae; Genus: Adhatoda; Species: Vasica; Common name: Adhatoda, Vasaka, Vasa; English Name: Malabar nut; Nepali Name: Asuro, Botanical Name-Justiciaadhatoda Linn [15].

Literature View of Adhatodai

Adhathodaipannamaiyamarukkumvathamuthar
Kodakodisurathinkothozhikkum-nadina
Miguththezhunthasanthipathinmoontrumvilakkum
Agaththunoipokkummari

Fig 1

Adhatoda, medicinal plant native to Asia, widely used in traditional medicine. The plant's native range is the Indian subcontinent, Laos and Myanmar. Various parts of this plant have been used to treat of several ailments as herbal remedy such as, cold, cough, whooping cough, chronic bronchitis, fever, jaundice, asthma, sedative, expectorant, diarrhoea and dysentery [15].

Phyto chemicals and pharmacological action

The main phytochemical component found in Adhatodavasica Nees is a bitter quinazoline alkaloid called vasicine which is present in the leaves, roots and flowers. Besides vasicine, the leaves contain several alkaloids such as Vasicinone, Vasicinol, Adhatodine, Adhatonine, Adhvasinone, Anisotinand Hydroxypeganine, betaine, steroids and alkanes [16].

The leaves of Adhatodavasica contains many secondary metabolites and phytochemicals such as, vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone, vasicol, vasicoline, vasicolinone and adhatodine [17, 18] responsible for its biological properties [19, 20]. However, some reportsare available towards the antibacterial potentiality focused on Adhatoda. vasica extracts, but more research is required to assess its antibacterial efficacy [21, 22].

Phytochemical analysis of the leaves extracts (ethanol, acetone, ethyl acetate and petroleum ether) of Adhatodai have been analyzed for the presence of phytochemicals. It can be observed that the extracts of *adhatodai* leaves, contain phytochemicals (such as, alkaloids, flavonoids, terpenoids, tannins and saponins. Therefore, tannins and saponins were observed in ethanol and petroleum ether extracts only [23].

Pharmacological actions of *Adhatoda* are anti-viral, anti-bacterial, anti-pyretic, antispasmodic, anti-inflammatory, diuretic, hepatoprotective, Cardioprotective, Anti tubercular, antioxidant and expectorant activities [24].

Covid-19- Pathogenisis and Pathophysiology

COVID-19 can disturb the upper respiratory tract (sinuses, nose, and throat) and the lower respiratory tract (windpipe and lungs) [25]. The lungs are the organs most affected by COVID-19 because the virus accesses host cells via the receptor for the enzyme angiotensin-converting enzyme 2 (ACE2), which is most plentiful on the surface of type II alveolar cells of the lungs [26].The virus uses a special surface glycoprotein called a "spike" to connect to the ACE2 receptor and enter the host cell [27].

COVID 19-Immunity

The immune response by humans to CoV-2 virus occurs as a combination of the cell-mediated immunity and Humoral Immunity leads to antibody production [28] just as with most other infections [29]. B cells act together with T cells and begin splitting before selection into the plasma cell, partly on the basis of their affinity for antigen [30].

Immunomodulation

Immunomodulation is the process that alters the immune system of the host resulting in either immuno stimulation or immunosuppression thus regulating or normalizing it. Hence, immunomodulators are referred to as the biological response modifiers, which can improve the host defense mechanism against diseases by a striking balance between controlling and effector cells. Immuno stimulators are suggested to enhance the immune response against infectious diseases, tumors, primary or secondary immune deficiency, and alterations in antibody transfer [31].

Immunomodulatory Effect of Adhatodai

The phytochemical analysis show that phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids and reducing sugars were found in the leaves of *Justicia Adhatoda*, But the pharmacologically most studied chemical component in J. adhatoda is a bitter quinazoline alkaloid, vasicine which is present in the leaves, roots and flowers(32). It has been expected that the primary boats of Dengue viral proliferation are monocytes. The activated dengue infected monocytes accelerate the cytokines and chemokines such as TNFαand interleukins and cause apoptosis. These factors are identified to assign the integrity of vascular endothelial cell layer due to the loss of barrier function leading to vascular leakage which is the hallmark of severe dengue infection [33]. Other study on the plant Justicia adhatoda has shown immunostimulatory activity by potentiating humoral as well as cellular immunity [34]. A recent study carried out to access the Binding energy with protease and Binding energy with replicase of COVID-19 virus using COVID-19 Docking Server were compared with hydroxychloroquine, 4-Methyl-2-propylquinoline, Pemirolast, vasicoline, anisotine, ethambutol of these, two more compounds vasicoline and anisotine which are alkaloids obtained from Justicia adhatoda leaves. The results of the docking study revealvasicoline and anisotine are higher efficacy compared with other drugs for COVID-19 [35].

Therapeutic Deed of Justicia Adhatoda

Anti-Viralproperty

One animal study indicates that aqueous and methanol extract of *Justicia adhatoda* has potent anti-viral agents against herpes simplex viruses [36]. In one more study Chavan *et al*. has proposed that aqueous and methanolic extracts of *Justicia Adhatoda* have strong anti-influenza virus activity that can inhibit viral attachment and viral replication. It was possibly by blockage of viral attachment through inhibition of viral HA protein, by blocking the viral absorption to cells, by synergistically binding to the free virus particles or by blocking the sialic acid receptors to prevent virus entry into the cells and by inhibiting the replication of influenza virus [37].

Anti-Bacterial property

Adhatoda has the antibacterial activity against Gram positive and Gram-negative bacteria. The extract of adhatoda revealed higher activity against different clinical pathogens like Klebsiella pneumonia, Proteus vagaries, Staphylococcus aureus, Streptococcus Pyrogens and Pseudomonas aeruginosa [37]. One study showed that leaf extract (methanolic) of Justiciaadhatoda was effective against Salmonella typhi [38]. In one study different extracts of *Justitiaadhatoda* leaves were evaluated for their antibacterial potential against Gram negative and Gram positive bacterial strains using different solvent systems *viz*. ethanol, acetone, ethyl acetate and petroleum ether

All extracts have observed antibacterial activity against Enterococcus faecalis possessing maximum zone of inhibition. The variation of the susceptibility of microorganisms towards the *Justiciaadhatoda* leaves extract recognized to the presence of several bio-active phytochemicals and their intrinsic properties that are related to the permeability to the cell surface of micro-organisms [3, 17]. Plants generally produce many secondary metabolites which represent an important source of microbicides, pesticides and many pharmaceutical drugs.

Immunomodulatory Property

The study suggested that the methanolic, diethyl ether and chloroform extracts of Adhatodaleaves have a immunomodulatory properties [39]. Another animal study suggested that Ethyl acetate extract of Adhatoda has potent hepatoprotective effect against CCl4 - induced liver damage [40].

Broncho Dilator Property

The main chemical constituent of Adhatoda, leaves is the quinazoline alkaloidknows as vasicine showed broncho dilatory activity both *in vitro* and *in vivo* study [41].In another study reveals the chemical constituents Vasicinone, deoxyvasicine, vasicinolone and vasinol have shown significantbronchodilatory effect [45]. Vasicinone is a quinazolinealkaloid. which shows broncho dilatory activity invitro but bronchoconstrictor activity *in vivo*. Vasicinone was shown to have an anti-anaphylactic action

Anti Tussive Property

Similarly, the antitussive activity of Adhatoda extract was evaluated in anaesthetized guinea pigs, rabbits and in unanesthetized guinea pigs, revealed that adhatodai have a good antitussive activity [42]. In another experimental study ethanol extracts of Glycyrrhiza glabra and Justicia *adhatoda* shows significant improvement in SO2 gas induced cough [43]. Semi-synthetic derivatives of vasicine from the herb *Justiciaadhatoda* have a pH-dependent grow thinhibitory effect on Mycobacterium tuberculosis [44]. Adhatoda are well established as the rapeutical respiratory agents. Extracts of Adhatoda's leaves and roots are useful in treating bronchitis, and other lung and bronchiole disorders, as well as common coughs and colds. A decoction of the leaves of Adhatoda has a soothing effect on irritation in the throat, and acts as an expectorant to loosen phlegm in the respiratory passages [45].

Discussion

An outbreak of pneumonia in December, 2019 in Wuhan, China, has now been determined to be caused by a novel coronavirus. Due to its severe effect in respiratory system it is named as severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2) [46]. *Adathoda* is a well-known shrub used in *Siddha* systems of medicine for various ailments like Bronchial Asthma, Rhinitis, Sinusitis, Pulmonary tuberculosis, Cough and Breathing disorders. Numerous clinical trials also proved the effectiveness of *Adathoda* in the management of various diseases like pulmonary disease, liver diseases, neurological diseases, inflammatory diseases, cardiovascular diseases, and metabolic diseases [47] *Adathoda* leaves act as an expectorant and it" sdecoction produce soothing effect on irritation in the throat [48].

The literature review proved that *Adathoda* has been widely studied for its pharmacological activities and its pharmacological property is due to the presence of chemical constituents such as vasicine, vasicinone and vasicolone [49]. These primary alkaloids are well established as a the rapeutical respiratory agents. Many Preclinical and clinical trials were demonstrated for the anti-viral and anti-bacterial activity and immunomodulatory effect of *Adathoda [50]*. From the results it was proved that *Adathoda has* antiviral action against different viruses indicating that it could be a therapeutic option for the management of COVID19 related symptoms [51]. This study results indicate that *Adathoda* plant parts can be potentially utilized in the treatment of corona virus disease and respiratory related symptoms of COVID 19

Conclusion

Justiciaadhatoda owns several biological activities proved by many experimental studies. It signifies a category of medicinal plant with very greattheoretical or traditional base as well as a strong experimental base for its use. This review provides the expediency of Adathoda plant parts in the treatment of respiratory related diseases Siddha Literatures and the Preclinical and clinical research indicate the potentiality of *Justiciaadhatoda* in the management of COVID-19We conclded that Justiciaadhatoda has varied therapeutic effects and it could be a good choice to manage and treat the covid 19 pandemic.

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