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Review Article

Role Of *Guduchi (Tinospora Cordifolia)* In Covid-19– A Review

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Abstract: The cause of COVID-19 disease is the newly found corona virus which can transmit from animals to humans. The epidemic commenced in Wuhan city of China in December 2019. It manifests as pyrexia, fatigue, and cough. Symptoms like headache, running nose, congestion, sore throat, and shortness of breath are also seen in several individuals. Currently, no definite medicines are available to prevent and manage Corona disease. Prevention is the only measure to fight against Corona. Ayurveda is the best option having many preventive as well as curative measures. For disease prevention, *Rasayanachikitsa* (Rejuvenating therapy) is described in Ayurveda, which helps in boosting immunity. This review aims to focus on the immunomodulatory properties of Guduchi and its benefits in the prevention and management of COVID-19 diseases. Related literature and research articles were searched and reviewed thoroughly. Many herbal drugs having *Rasayana* properties are described in Ayurveda, which help in activating immune system. Immunity is the body's defense mechanism that protects an individual from invading microorganisms and thus prevents disorders caused by them.*Guduchi(Tinispora cordifolia)* is one of the *Rasayana*herbal drugs which can be used in COVID-19. Many research studies conducted on*Guduchi*proveditsimmunomodulatory, antioxidant, antimicrobial, antiviral, anti-inflammatory, and antipyretic properties. Hence this review is conducted to study the role of*Guduchi* in prevention and relieving symptoms of *COVID-19*. Research studies should be conducted to prove its efficacy and exact mechanism in Coronavirus disease.

Keywords- Coronavirus; COVID-19; *Guduchi;* Immunity*; Tinospora cordifolia; Vyadhikshamatwa*1.

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1. INTRODUCTION

The highly contagious "Coronavirus disease (COVID-19)" is triggered by a newly discovered Coronavirus. MERS-CoV and SARS-CoV are the types of Coronavirus causing "Severe Acute Respiratory Syndrome" (SARS) and the "Middle East Respiratory Syndrome" (MERS), correspondingly. The main symptoms of COVID-19 disease are pyrexia, fatigue, and dry cough. Some individuals also develop headaches, congestion, running nose, sore throat, and breathlessness. The symptoms may appear in 2 to 14 days. Individuals aged more than 60 years and having systemic diseases like heart disease, uncontrolled diabetes mellitus, chronic respiratory illness, and malignancy have more risk of affecting Coronavirus disease. The transmission of "COVID-19" takes place while coughing, sneezing, or touching infected surfaces. COVID-19 reduces immunity to fight against diseases. A natural defense mechanism of the body should be increased to combat it in such a pandemic crisis.[1] Cells of the immunology system produce a group of proteins called Cytokines having chemical messenger-like action. They have their action single, in combination, or in opposition with each other, but finally, cytokines aid in the regulation of the immune reaction. Cytokines have also been involved in the inflammatory process and immune mechanism. So Immune system has a defensive mechanism that protects animals from the attack of pathogens and developing malignancies.[2]Immunity and the body's defense mechanism protect an individual from various pathogens entering the body via air and water; thus, it fails to develop the disease. Immunity plays a vital role in keeping oneself healthy and free from disease.[3] Researchers have stepped up their search for an effective COVID-19 therapy and vaccination as the number of cases of novel Coronavirus grows worldwide. Numerous clinical studies are taking place worldwide, and several drugs and plants have been identified as potential COVID-19 virus treatments. Guduchi(*Tinospora cordifolia)*is one of the formulations used for Coronavirus.[4] "*Vyadhikshamatva*" (Immunity) described in the Ayurveda is the same as that of immunity. Ayurvedic system of medicine helps to treat diseases and also prevent disease.[6] *Vyadhikshamatwa*restricts the pathogenesis and resists the strength of the disease. *Chakrapani Datta* comments on *Charaka Samhita* that *Vyadhikshamatva*is*Vyadhi-balavirodhitvam* (capacity to restrain or withstand the strength (severity) of the diseases, i.e., strength to resist the progress of the disease.) and *Vyadhi-utpadakapratibandhakatva*(The resisting power of the body competent enough to prevent the occurrence and re-occurrence of the disease.[5]

1.1 Need of Study

Understanding the pathophysiology of COVID-19 is a prerequisite for determining Ayurvedic prevention and treatment techniques. With an understanding of Ayurveda's epistemology, bridging the gap between Ayurveda and evidence-based medicine is possible.[6]

1.2 Infectious disease in Ayurveda

Description regarding disease-causing microorganisms and infectious diseases was described in the literature of Ayurveda. Acharya *Sushruta*named*Aupsargika* (Infectious) and *Sankramak* (Contagious) *rogas*. The communicable illnesses are mentioned while describing Janapadodhwamsa *vyadhi, Jwara, Krimi, Visha*and *Ritucharya*. Most infectious diseases manifest the commencement of fever as a main symptom. The *Krimi* indicates the bacteria, viruses, fungi or parasites, helminth, or microbes. *AshtangHridaya*, it is stated that these pathogens are invisible by the naked eye, but their characteristic manifestations can experience their presence.[7] *Ritucharya* is the seasonal regime that one has to follow as per changes in ritu[8]diseases mainly can be caused due to seasonal changes in the environment, like excess cold, heat, and moisture hamper health by compromising the immune system and making it prone to cause infections, mainly affecting the respiratory tract.[9] The *Rasayana* therapy is one of the branches of *Ashtanga* Ayurveda involving Immunity and immunomodulation. According to Ayurveda, *Rasayana* helps in strengthening *Oja*(Vital essence of the body) and *Bala* (Strength) and thus increases *Vyadhikshamatva*.[10]

1.3 Correlation of Epidemiology and Janapadodhwamsa in COVID

After entering the respiratory passage in epidemics, infectious pathogens cause manifestations like fever, coryza, breathlessness, rhinitis, headache, and loss of smell. These manifestations described by Acharya Sushruta are similar to that of epidemics such as COVID-19. Infectious diseases are spread by direct bodily contact, through inhalation, sharing food substances, living and sitting together, and sharing clothes and things like garlands, described in Sushruta Samhita as aupasargika roga.[11]

1.4 Etiological factor (Hetu) of COVID

The pathogen of COVID-19-causing disease is *Agantuj hetu*(exogenous factor), but nearly 80 percent of subjects who suffered from COVID-19 have no apparent symptoms. Therefore, it can be better understood by the term *VyanjakaHetu* (causative factors acting at the time of disease production). At the same time, *Utpadaka*re*Hetu* is causative factors, mainly dietary and behavioral, leading to the aggravation and vitiation of *Dosha*. The imbalance of doshas is the main cause of disease stated in Ayurveda. *Therefore, UtpadakaHetu* is important and related to the prognosis of COVID-19 associated with co-morbidities. It can be studied by original retrospectively conducted studies of dead or seriously ill patients of COVID-19, which can confirm the role of dietary and behavioral lifestyle factors such as *UtpadakaHetu* in the worse prognosis of COVID-19.[12.]

Table no 1 -Symptoms (*Linga*)of COVID

Sr. No.	Symptoms	Ayurvedic Name	Strotas
1.	Fever	*Jawar*	PranavahaStrotas
2.	Dry Cough	*VatajKasa*	RasavahaStrotas
3.	Loss of taste	*Aruchi*	AnnavahaStrotas
4.	Loss of Smell	Anosmia	PranvahaStrotas
5.	Breathlessness	*Shwasa*	PranvahaStrotas
6.	Sore Throat	*kanthavrodha*	PranvahaStrotas

6.	Headache	*Shirshool*	RaktavahaStrotas
7.	Diarrhoea	*Atisaar*	PurishvahaStrotas
8.	Arthralgia	*Angamarda*	AsthivahaStrotas

Thus there are a variety of symptoms showing involvement (mentioned in table no 1) of *Pranavaha*, *Rasavaha*, *Raktavaha*, and Purishvaha strotras. These varied Symptoms indicate involvement of multiple systems in COVID-19.

1.5 *Pathophysiology of COVID according to Ayurveda*

It is a pathology of *Agantu Jwara*(exogenous) showing vitiation of *RasavahaStrotas*, with *Pranavaha* and *RaktavahaStrotas*. It causes loss of strength and reduced immune power. Various coagulation disorders seen in COVID indicate vitiation of *RaktavahaStrotas.* InAyurveda, many herbal drugs are described as having *Rasayana* properties, such as "*Ashwagandha* (Withania somnifera), *Gulvel (Tinospora cordifolia), Amla (Emblica officinalis),* and *Hirata (Terminalia chebula).*13 Many research studies conducted on *Guduchi* proved its immunomodulatory, anti-inflammatory, antioxidant, antimicrobial, antiviral, and antipyretic properties in many research studies.

1.6 Habit & habitat of Guduchi (Tinospora cordifolia Willd) -

A big smooth deciduous climbing vine known as *Tinospora cordifolia* is found in Sri Lanka, China, India, and Burma (Fig. 1). The plant mainly grows in Australia and Africa's tropical regions. However, it occurs throughout the country from the Kumaon Mountains in the north to Kanyakumari, India's southernmost tip. The botanical identity of Guduchi is correlated to *Tinospora cordifolia* (Willd.) Miers (Family: Menispermaceae) by the Ayurvedic Pharmacopoeia of India (API). It is a substantial, deciduous, climbing shrub that spreads widely and has several long, twining branches. Branches produce copious long, filiform, pale brown, fleshy aerial roots hanging down like strings. Stems are greenish, smooth with thin greyish papery peeling, and with many small roundish protuberances called lenticels. Simple, alternate, exstipulate leaves have long petioles that can reach a length of 15 cm. These petioles are roundish and pulvinate at the base and apex, with the basal being longer and twisted halfway around. Because of its heart-shaped leaves and reddish fruit, it is known as Heart Leaved Moonseed (Fig.3). The raw drug "occurs as pieces of varying thickness (0.6-5 cm diameter), young stems are green with smooth surfaces and swelling at nodes, whereas older ones show a light brown surface marked with warty protuberances due to circular lenticels; transversely smoothened surface shows a radial structure with conspicuous medullary rays traversing porous tissues and tastes bitter," according to API (2001) [14] (Fig. 2).

1.7 Table no. 2 Bionomial classification of Tinospora cardifolia

Table no. 2 Bionomial classification of Tinospora cardifolia	
Kingdom	Plantae
Subkingdom	Tracheophytes
Super division	Spermatophyta
Division	Magnoliophyta

Subdivision	Angiosperms
Class	Magnoliophyta
Subclass	Polypeptalae
Order	Ranunculales
Family	Menispermaceae
Genus	Tinospora
Species	**Cordifolia**
Binomial name	**T.cordifolia**

1.8 Table 3: Different parts of Tinospora cordifolia and required dosage

Table 3: Different parts of Tinospora cordifolia and required dosage

Plant part	Requirement dosage
Tinospora cordifolia Stem powder	1-3 g
Tinospora cordifolia stem juice	**1-5 ml**
Tinospora cordifolia stem extract	125-500 mg
Tinospora cordifolia stem water	50-100 ml
Tinospora cordifolia sativa	250-1000 mg
Tinospora cordifolia leaves juice	2.5-10 ml
Tinospora cordifolia leaves powder	1-3 g

1.9 Morphology of Tinospora cordifolia –

Figure no. 4 Showing Morphology of Tinospora cordifolia

1.10 *SARS-CoV-2 and the immune system*:

Four structural proteins make up SARS-CoV-2: Spike (S), Envelop (E), Membrane (M), and Nucleocapsid (N). The first three proteins comprise the viral envelope, while the nucleocapsid (N) protein packages the RNA genome. Coronavirus requires a host in the form of a living cell for replication. Specifically, SARS-CoV-2 damages immunological homeostasis and immune regulatory mechanisms.[15] There are two stages to the immunological response to SARS-CoV-2 infection

Defense phase

When SARS-CoV-2 is inhaled aerosolized, it reaches the lungs and infects target cells that express ACE2, such as alveolar type 2 cells. During this stage, cells that secrete antibodies, helper T-cells, activated CD4, and CD8 T-cells that bind to SARSCoV-2 are produced. Interferon (IFN) type I is essential for the innate immune response against viral infection because it regulates viral replication. Angiotensin-converting enzyme 2 (ACE2), the cell receptor shared by SARS-CoV and SARSCoV-2 upon human entrance, is used by MERS-CoV, whereas dipeptidyl peptidase and amino peptidase N are used by SARS-CoV.[16]

Damage phase

Because of cytokine release syndrome (CRS), often known as a "cytokine storm," it is characterized by elevated levels of tumor necrosis factor (TNF)-alpha4, interleukin 2 (IL-2), and interleukin 7. Acute respiratory distress syndrome (ARDS), respiratory failure, and mortality are all potential outcomes of cytokine release syndrome (CRS), which harms the heart, kidney, and lung tissues. The pathophysiology of SARS-CoV-2 infection may be significantly influenced by cytokine storm and lymphopenia. TH1/TH2 cytokine levels establish immune homeostasis as a human illness progression and restoration marker. The immune system's hormonal messengers, or cytokines, are further divided into Th1 and Th2 subtypes that change with age. In addition to the immune system, the

nervous system is a powerful system affected by COVID-19 and develops neurological symptoms, such as headache, altered level of awareness, and paresthesia.[17]

1.11 A Possible approach to the prevention and management of COVID-19 through Ayurveda

One of the greatest Rasayanas is Guduchi, or "Amrita," which means regenerating dead cells and has immuno-modulatory properties that boost innate immunity against COVID-19 infections. Tinosporin, a diterpenoid, has potent antiviral properties, especially when used to treat viral infections, including retroviruses.[18] T. cordifolia aqueous extracts have impacted the cytokine generation and activation of immunological effector cells.[19] Guduchi is a powerful pato-protective and is useful in preventing liver damage. It increases the level of vitamin Cand and thus serves as an antioxidant.[20] Immunomodulatory protein in the guduchistem enhances the number of macrophages and their phagocytic activity.[21]As a preventive and prophylactic medication for COVID-19, Sanshamani Vati (also known as Guduchi ghana vati), which contains an aqueous extract of T. cordifolia, might be recommended as 500 mg twice daily for 15 days with warm water. [22]

1.12 Ongoing clinical trials in Ayurveda for COVID-19-

The AYUSH Ministry and the Council of Scientific and Industrial Research (CSIR) have begun collaborative work on four Ayush formulations to validate Ayurvedic formulations against COVID-19. These compositions include AYUSH-64, Guduchi + Pippali, Yashtimadhu (Mulethi), and Ashwagandha, shown in table no. 4. A comparative research between Ashwagandha and Hydroxychloroquine is being developed for a high-risk population.

Table no.4 Showing Ongoing clinical trials in Ayurveda for COVID-19-

Drug	Ingredients	Dose	Indication
Tab. AYUSH -64	Saptaparna stem bark (*Alstonia scholaris* (L.) R. Br.), Katuki roots (*Picrorhiza kurroa* Royle ex Benth.), Chirayata whole plant (*Swertia chirata* Buch.-Ham. ex Wall.) and Kuberaksha seed (*Caesalpinia crista* L.) 2[3]	2 tablets twice a day.	Respiratory infections
Agastya Haritaki churna	Haritaki (**Terminalia chebula** Retz.), Dashamoola,Pippali (**Piper longum L.) etc.** 2[4]	5 grams twice a day with warm water.	Respiratory infections
Anuthaila (oil)	Anutaila consists of 27 ingredients like Sesame oil, Vidanga (*Embelia ribes* Burm. f), Ajadugdha (goat milk) etc. 2[5]	2 drops in each nostril daily morning.	Respiratory infections

1.13 Symptomatic treatment from Ayurveda

AYUSH has neither asserted an effective Coronavirus treatment nor a specific medication to combat COVID-19. For symptoms like coryza and fever, some traditional formulations like Sudarshan Ghana vati and Sanshamani vati are used as safer symptomatic measures. AYUSH indicated some Ayurvedic medications for treating COVID-19-like sickness described in Table 3.

2 Aim and Objective-

This study focuses on the role of *Guduchi*(*Tinospora cordifolia)* in preventing and relieving Coronavirus disease(COVID-19) symptoms.

3 METHODOLOGY

Information was collected from Ayurveda and Modern medicine literature, the internet, and related available research studies from PubMed, Scopus, and Google scholar.

4. OBSERVATIONS AND RESULTS

In Ayurveda following properties of Guduchi(*Tinospora cordifolia)* are described.[26] Properties of *Tinosporacordifolia(Guduchi)*are shown in table 2. The Pharmacodynamics action and indications of *Tinosporacordifolia(Guduchi) are* shown in the Table No. 3.[27]

Table 5 - Properties of *Tinospora cordifolia (Guduchi)*

Rasa	*Guna*	*Virya*	*Vipak*	*Prabhav*
Tikta, Katu	*Laghu, Guru, Snighdha*	*Ushna*	*Madhur*	*Vishaghna*

Table ~~3~~ 6-Action –Pharmacodynamics and indications of *Tinospora cordifolia (Guduchi)*

Action - Pharmacodynamics	Indications
Rasayana, Sangrahi, Balya, Agnidipana, Tridoshshamaka	Kasa, Jwara, Krimi, Shwas, Hridroga
Sangrahi, Vatakaphashamaka, Deepana	Malabaddhata
Tridoshahar, Vishaghna, Jwaranashaka-krimighna	All types of Jwar
Tridoshahar, Balvadhaka	Kasa, Laghujwara
Tridoshashamaka, Rasayana, Grahi	Jwar, Daha
Grahi, Balya, deepana	Jwara, Kamala, Kushtha
Rasayana, Hriddhya, Tridoshahar, Balvardhaka, Aayusthapana	Jwara, Pandu, Chhardi, Daha, Trishna, Bhrama, Prameha, Kasa, Hikka

4.1 Importance of Tinospora cordifolia in Traditional Indian System-

Since the beginning of human civilization, medicines made from plants have been used to maintain health and treat illness.[28] Tinospora cordifolia has long been a component of Indian traditional medicine. The tribal population uses this because each component has important health advantages. It has been recognized by various names, Giloy, Guduchi Amrita, and Shindilkodi in the local dialect. Giloy translates to "Amrita," the source of immortality. It is regarded as a medicine that can increase body resistance capacity. Its chemical components prevent and fight against viral attacks. It is designated "Rasayana" in Ayurveda due to its therapeutic potential. Guduchi is listed in the traditional Ayurvedic scriptures as a component of several formulations and is recommended for general fatigue, fever, dyspepsia, and urinary disorders. Its stem primarily treats thirst and fever, prevents vomiting, is helpful for skin conditions, and treats jaundice. Its juice also treats an enlarged spleen, diabetes, and discharges from the vaginal area.[29]

4.2 Tinosporacordifolia(Guduchi)

Guduchi of the family Menispermaceae is an Ayurvedic drug used for Rasayan Chikitsa. Rasayan (rejuvenation) is one of the eight branches described in Ayurveda and is widely used in all age groups. Rasayana drugs stimulate the immune system and thus help in disease prevention. Guduchi is a large spreading, deciduous, climbing shrub. It has antioxidant, anti-inflammatory, antiarthritic, anti-stress, antimalarial, hepato protective, antiallergic, antidiabetic, and immunomodulatory properties. It is an important drug used in preparations like Satva, Ghrita, Tail, Swaras, etc. Also, as important ingredients in many formulations. It is commonly used for Jwara, Shwetapradara, Mandagani, Prameha, Daurbalya, Kamla, etc. *Guduchi* has Ras Tikta, VeeryaUshna and Vipaka Madhura. It is the best drug in availability, economy, and administration.[30]

4.3 Phytoactive compounds of Tinosporacordifolia(Guduchi)

Tinosporacordifolia(Guduchi) constitute different classes of phytoactive compounds they are shown in Table no.4 [31-33]

Table 7 4- Phytoactive compounds of Tinosporacordifolia(Guduchi)

SN	Class	Chemical constituents	Activity	Plant Part
1	Alkaloids	Berberine, Magnoflorine, CholinePalmatin. Tembetarine, Tinosporine, Isocolumbin, and Aporphine alkaloids	Anti- Viral infection, Immunomodulatory, Anti Cancer	Stem and Root
2	Diterpenoid Lactones	Furanolactone,Tinosporon, Tinosporides, Columbin	Anti- Viral, Anti-microbial, Anti-inflammatory, Anti- Hypertensive	Whole plant
3	Sesquiterpenoid	Tinocordifolin	Anti- Septic	Steam

4.4 Immunomodulator Activity of Tinospora cordifolia- Rasayan effect of Guduchi

Rasayan drugs are beneficial that help in the rejuvenation of the body. Rasayan therapy helps to increase intellectual ability and physical and mental strength, maintenance of lives, and aids in disease avoidance. Using Rasayana, one can attain longevity, memory, intelligence, freedom from illness, youthfulness, complexion, optimum body strength, decency, and brightness. Rasayan helps produce excellent quality dhatu (bodily tissues) in the body. Guduchi is an Ayurvedic drug that is used for Rasayan Chikitsa.[34] Various research studies showed that the Guduchihas Rasayan effect increases the life span of Drosophila melanogaster, which confirms the action of Rasayan. An increase in the life span of the F-1 generation of Drosophila indicates that the Rasayan effect of GuduchiChurna also exists in the subsequent generation.[35] This implies that a specific dose of GuduchiChurna (about 0.25 g/100 ml of diet) produces optimum life enhancement. The doses above that have no effect on longevity, which could be attributed to GuduchiChurna's absorption limit. The significant antioxidant qualities of GuduchiChurna can be attributed to the flies' increased longevity. Tinospora cordifolia has long been studied for its potential to modulate the immune system. For this, different compounds are separated from it, and their potential immunomodulatory effects are researched. Due to the presence of arabinogalactan, an aqueous extract from the plant's stem has demonstrated the ability to elicit immunological activity. This plant has potentially immunomodulatory chemicals N-formylannonain, magnolorine, hydroxymustakone, cordifolioside A, N-methyl-2-pyrrolidone, and tinocordiside. The alcoholic and aqueous extracts of T. cordifolia have been studied for their immunomodulatory action [36] and are thought to be advantageous to the immune system.

4.5 Antioxidant properties of Tinospora Cordifolia

Tinospora cordifolia has been shown to have antioxidant properties in numerous research. When given orally to rats, methanol extracts from the stem of Tinospora cordifolia contain anti-oxidant properties that improve catalase activity and erythrocyte membrane lipid peroxide.[37]. Tinospora cordifolia and other herbal medications was used to create the herbomineral formulation "Pepticare," which underwent an in vivo investigation to demonstrate its antioxidant and antiulcer properties. [38]

4.6 Antipyretic effect of Guduchi

Guduchi is effective in the management of Jwara (fever).In classical texts, GuduchiSwarasa and Guduchi Kalka are indicated for the treatment of fever. Significant antipyretic efficacy is demonstrated by the Tinospora cordifolia "Guduchi ghrita" formulation in albino rats.[40] In a different investigation, the T. cordifolia extract showed a significant antipyretic effect in the Pyrexes test brought on by brewer's yeast. [41] Tinospora cordifolia was the subject of a few clinical research, which revealed its Jwaraghna (Anti-pyretic) function.[42]

4.7 Anti-Inflammatory Activity of Tinospora Cordifolia

T. cordifolia alcohol extract exhibits anti-inflammatory properties in acute and subacute inflammation models.[43] A study used a water extract from T. cordifolia stems found on Azadirachta indica plants. In this investigation, the extract significantly reduced the acute inflammatory response from intraperitoneal and oral carrageenin administration. A model of arthritis caused by an adjuvant showed significant inhibition.[44] The formalin-induced arthritis model and cotton pellet granuloma showed significant anti-inflammatory action when this plant's aqueous extract was used.[45]

5. DISCUSSION

Bacteria, viruses, parasites, or fungi are pathogens causing infectious diseases. These microorganisms enter the human body and cause disease when the immune system fails to fight against them. According to Ayurveda imbalance of *Doshas*(biological energy) and *Agnimandya* (reduction in digestive fire) leads to the production of *Ama* (endotoxins).This results in *strotorodha* (obstruction of microchannels), causing depletion of nutrition to *Dhatus(*bodily tissues*),* which causes *Dhatushithilata(*tissue degradation). Diminished and poor quality *Dhatus* results in vikruti (impairment). *Rasayana* acts on *Dosha*, *Agni*, *Strotas*, and *Rasadidhatu*. It helps in maintaining the equilibrium of *Doshas*, correction of *Agni*, *and Amapachana*(detoxification of toxins), remove the obstruction of *strotas,* and enable *Dhatuposhana*(nutrition of bodily tissue).*Dhatuposhana*helps in increasing bala (strength) and thereby*Vyadhikshamata* (immune power). *Rasayana*can be used in healthy individuals for a prophylactic purpose and in treating illness in ill persons. *Tinosporacordifolia(Guduchi)*has been known for its *Rasayana*property from ancient times. Research studies can confirm the immunomodulatory property of T.cordifolia. In one preclinical in vivo study, its extracts cause the cytokine IL-6 to be upregulated, which causes B cell differentiation. In an experimental rat model, active compounds from aqueous extracts of T. cordifolia, like alkaloids, steroids, phenolics, polysaccharides, di-terpenoid lactones, glycosides, and sesquiterpenoid, have been reported for their cytotoxic action.[46] Tinospora cordifolia extract has also shown an immunomodulatory effect in patients with HIV disease. An in vivo study was conducted in CCl 4 induced rats evaluated for immunomodulatory and Hepatoprotective properties of Tinospora cordifolia. [47] *Tinospora cordifolia (Guduchi)* is an herbal drug used to prevent and manage many diseases. Different parts of *Tinospora cordifolia (Guduchi)* are used in traditional systems of medicine. It contains many Chemical constituents that benefit the body in maintaining good health. The most important biological properties proved by the above-collected research are anti-oxidant, anti-inflammatory, antipyretic, hepatoprotective, immunomodulatory, antimicrobial, antiviral, and antineoplastic activities. Researchers have found that *Tinospora cordifolia* contains various phytochemicals like tannins, alkaloids, cardiac glycosides, saponins, triterpenoids, phytosterols, and polyphenols which have proved to be of great medicinal value, which may be helpful in COVID.Phytochemicals of *Tinospora*hashave been reported to have immunomodulation and cytotoxic effects. As a result, they're often used to boost macrophage phagocytosis and the formation of reactive oxygen species (ROS) in humans. Malve H, More D, and More A. conducted a study to evaluate the immunomodulatory effects of two formulations, Tinospora cordifolia (Tc) and Phyllanthus emblica (Pe) with and without a coating of Ocimum sanctum (Os) and found that Tc alone exerted a better degree of protection as compared to Tc + Pe and Tc + Pe + Os. Thus, this experimental study validated the immunomodulatory role of Tc.[48] El Basuini MF et al. conducted a study to evaluate the effects of the dietary Guduchi (Tinospora cordifolia) on the growth performance, antioxidative capacity, immune response, and resistance of Nile tilapia against hypoxia stress and showed that dietary Guduchi could be included at 5.17-5.49 g/kg to enhance the growth performance, digestive enzyme activity, immune and antioxidative responses, and the resistance of Nile tilapia against hypoxia stress.[49] The antipyretic property of *Tinospora*aids in improving the common symptoms of infection. *Balya* and *Rasayana* properties of *Guduchi* also benefited after the infectious phase for acquiring the lost strength of the body. *Guduchi*has immunity-enhancing and antipyretic properties, so it is helpful to boost the immune power for prevention and reducing symptoms of COVID-19. In classical texts, GuduchiSwarasa and Guduchi Kalka are indicated for the treatment of fever. Ikram et al. (1987) in their study stated the antipyretic action of it in rabbits.[50], and Rao also studied and showed that extract of Guduchi in ethanol has significant antipyretic action.[51]Many studies showed that the antipyretic action of it might be due to the presence of bitter ingredients and berberine.[52] Compared to Favipiravir, Lopinavir/Ritonavir, and Remdesivir, in-silico investigations reveal a high binding efficacy versus SARS-CoV-2 sites implicated in virus adherence and reproduction.The clinical research trials were also conducted under the Ministry of AYUSH on T.cordifolia as preventive and curative in asymptomatic patients of COVID-19 without any side effects. [53] Research studies proved hepatoprotective, antibacterial, anti-inflammatory, anticarcinogenic, and antimutagenic effects of *Tinosporacordifolia(Guduchi)*.[54-56]Animal studies conducted showed that *Tinospora cordifolia* acts as an immunomodulatory.[57-58] In one randomized, double-blind, placebo-controlled trial, [the] efficacy of *Tinospora cordifolia* extract (TCE) in HIV-positive patients was evaluated. Human Immunodeficiency Virus cases showed to reduce total leucocyte count (TLC), neutrophil, and eosinophils using *Tinospora cordifolia(Guduchi)*.[59] One animal study "to assess the immunoprophylactic potential of Cytosine-guanosinedeoxynucleotide (CpG) oligodeoxynucleotides (ODN) and *Tinospora cordifolia* stem aqueous extract in the specific pathogen-free (SPF) chicks" was conducted in which chicks experimentally infected with very virulent infectious bursal disease virus. Both (CpG ODN and herbal extract) were found effective in increasing levels of the major cytokines like interleukin-2 (IL2), interleukin-4 (IL4), interleukin-1(IL1), and interferon-gamma (IFN-γ). It proved its immunoprophylactic potential. [60] Agarwal S. et.al conducted a study to assess the antimicrobial activity of different concentrations of commercially available *T. cordifolia* powder against *Streptococcus mutans*. *Tinospora* exhibited antimicrobial activity against *S. mutans*. And stated the need to be confirmed further with *in vivo* studies.[61] All these studies conducted to confirm that the Tinospora cordifolia can be used in reducing symptoms of COVID-19

6. CONCLUSION

COVID-19 is a viral disease having no effective treatment available at present. Based on properties described in the literature and proved by available research studies, it can be concluded that *Guduchi* (*Tinospora cordifolia)* has immune system enhancing, antipyretic and antimicrobial properties; hence it can be used for prevention and relieving symptoms of COVID-19. Research should be conducted to prove the exact mechanism and action of *Tinospora cordifolia (Guduchi*) on COVID-19.

7. AUTHOR CONTRIBUTION STATEMENT

Dr.Ashish Nimbhorkar collected the relevant data and designed this review. Dr.Sadhana Misar gave the required inputs and helped in preparing the manuscript. Thus both Authors discussed and prepared the final manuscript.

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9. CONFLICT OF INTEREST

Conflict of interest declared none.

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