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Review Article

PHARMCOLOGICAL POTENTIAL OF *GUDUCHYADI KWATHAM* IN COMBATING COVID-19

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ABSTRACT

Guduchyadi kwatham is a renowned Ayurvedic formulation used by Ayurvedic physicians all over India against influenza attacks and viral diseases. It is indicated for *Pitta* and *Kapha* aggravated conditions, *Jwaram* (Fever) and diseases of gastrointestinal system in classical Ayurvedic literature. Indications and pharmacological activities of the ingredients in respiratory diseases and *Rakta* (Blood) vitiated conditions suggest the use of this formulation in viral diseases that mainly involve respiratory system. In order to assess the pharmacological potential, Ayurvedic literature of the formulation and the pharmacological evaluations conducted with the part used and phytoconstituents of individual drugs were collected. Informations about the pathogenesis and symptomatology of COVID-19 were gathered from the recent research publications which were available online. Common symptoms of Coronavirus disease 2019 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are fever, cough, sputum production, fatigue, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia. When the disease progresses clinical conditions like Pneumonia, RNAaemia, acute respiratory distress syndrome, etc that lead to may develop death. Significantly increased level of leukocytes, pro-inflammatory cytokines and chemokines in plasma are seen during pathogenesis. The manifestation of systemic inflammatory response along with respiratory symptoms reveals that the main *Doshas* involved in this viral infection are *Pitta* and *Kapha*. The formulation possesses *Pittakapha samana* action and the ingredients are beneficial in diseases of *Pranavahasrotas*, *Annavahasrotas*, *Rasavahasrotas* and *Raktavahasrotas*. Pharmacological screening of drugs demonstrated anti-inflammatory, antipyretic, antiviral, antibacterial, anti allergic, antioxidant and immunomodulatory effects. Ayurvedic literature and findings of various phytochemical and pharmacological researches validate the use of *Guduchyadi kwatham in* the prevention and mitigation of this viral disease.

KEYWORDS: *Guduchyadi kwatham*, COVID-19, Viral infection, Respiratory symptoms.

INTRODUCTION

Guduchyadi kwatham is an Ayurvedic formulation prepared out of the drugs mentioned in *Guduchyadi ganam* described in one of the important classical Ayurvedic text *Ashtangahridayam* in the section *Sutrasthanam* 15th Chapter.[1] *Guduchyadi ganam* is also cited in the text *Ashtangasamgraham* in the same section.[2] It is a renowned pharmaceutical preparation suggested by Ayurvedic physicians of Kerala against manifestation of viral diseases. Classical indications in literature advise the use of this medicine in *Pitta* and *Kapha* aggravated conditions, *Jwaram* (Fever) and diseases of gastrointestinal system.[1,2] Indications of the ingredients suggest the use in diseases of respiratory system and *Rakta* (Blood) vitiated conditions. *Guduchyadi kwatham* is extensively used in influenza attack and various hepatic viral infections by Ayurvedic practitioners all over India. It has also been used in different stage of HIV, Dengue fever and H1N1 infection. Various pharmacological and biological activities reported by the drugs supports the use of this formulation in viral diseases that affect respiratory system.

MATERIALS AND METHODS

Relevant sections of *Samhitas* and *Nighantus* were referred to collect the Ayurvedic literature relating to the formulation and ingredients of *Guduchyadi kwatham*. Pharmacological evaluations conducted with the part used and phytoconstituents of individual drugs were collected from the research articles available online mainly through PubMed search engine. Important phytoconstituents that were screened for pharmacological actions were

selected after comprehensive evaluation of the available literature.

Pipeline pharmacological activites considered were Anti viral, Anti-Dengue, Anti-HIV, Anti-Malarial, Anti-inflammatory, Antipyretic, Analgesic, Anti-bacterial, Anti-tubercular, Anti-allergic, Antioxidant and Immunomodulatory. Gastroprotective, Hepato-protective and Cardio-protective activites of the drugs were evaluated to assess the benefit of the drugs in organ specific pathologies. Diseases such as Diabetes, Hyperlipidaemia, Cancer, Anxiety and Depression were considered to get the advantage in comorbid conditions. In vitro, in vivo and clinical studies conducted with aqueous extract were opted for correlation with dosage form i.e., *Kwatham* of the medicine. If such studies were not available results of various extracts were selected.

Ingredients of *Guduchyadi Kwatham*

1. *Guduchi- Tinospora cordifolia* (Willd.) Miers ex Hook.f. & Thoms.
2. *Padmaka- Caesalpinia sappan* Linn./ Prunus cerasoides D.Don
3. *Aristha- Azadirachta indica*. A. Juss
4. *Dhanyaka- Coriandrum sativum* Linn
5. *Raktachandana- Pterocarpus santalinus* Linn. f

Indications of *Guduchyadi Kwatham*

Guduchyadi kwatham is indicated in the following conditions or diseases.[1,2]

1. As a *Deepana* drug - With Appetizer action
2. *Pithakaphajaroga* – Diseases due to *Pitta* and *Kapha Dosa* vitiation.
3. *Jwara* - Fever
4. *Chardi*- Vomitting
5. *Daham*- Burning sensation
6. *Trishna*- Thirst

Drugs with Botanical Source and Parts Used

Table 1: Botanical name of drugs with Family and Parts used in *Guduchyadi kwatham*

Drugs	Botanical name	Family	Part used
Guduchi	*Tinospora cordifolia* (Willd.) Miers ex Hook.f. & Thoms.	Menispermaceae	Stem
Padmaka	*Prunus cerasoides* D. Don (Ayurvedic Pharmacopoeia of India)/ *Caesalpinia sappan* Linn. (used in Kerala)	Rosaceae Caesalpiniaceae	Heartwood
Arishta	*Azadirachta indica* A. Juss	Meliaceae	Stem bark
Dhanyaka	*Coriandrum sativum* Linn	Umbelliferae	Fruit
Raktachandana	*Pterocarpus santalinus* Linn. f	Fabaceae	Heartwood

Method of Preparation

Take 12gm of each drug, wash well and dry. Then crush the raw drugs well. Put the entire material in 1.5 litres of water taken in an earthern pot and boil in low flame till it reduces to 180ml. Then filter and use as gently warm *Kwatham*.

Dose

90ml *Kwatham* morning and evening one hour before food or as prescribed by the physician.

Pharmacological Properties (*Rasadi Gunas*) of the Drugs

Pharmacological properties of the drugs described in Ayurvedic classics reveal that most of the drugs are *Kashaya* (astringent) and *Tikta* (bitter) predominat in *Rasa* (taste) and *Laghu* (light) in *Guna* (quality). *Veerya* (potency) of the drugs varies as *Ushna* (hot) or Seetha (cold) and *Vipaka* (post-digestive taste) as *Madhuram* (sweet) or *Katu* (acrid).[1]

Table 2: Ayurvedic Pharmacological properties of drugs in *Guduchyadi kwatham*

Drug	*Rasam* (Taste)	*Gunam* (Quality)	*Veeryam* (Potency)	*Vipakam* (Post-digestive taste)
Guduchi	*Kashayam, Tiktam, Katu, Madhuram*	*Laghu*	*Ushnam*	*Madhuram*
Padmaka	*Kashayam, Tiktam*	*Laghu*	*Seetam*	
Arista	*Tikta, Katu*	*Laghu*	*Seetam*	*Katu*
Dhanyaka	*Kashayam, Tiktam, Madhuram*	*Snigdham, Laghu*	*Ushnam*	*Madhuram*
Raktachandana	*Tiktam, Madhuram*	*Guru*	*Seetam*	*Katu*

Note: *Madhuram*– Sweeet; *Tiktam*– Bitter; *Katu*– Acrid; *Kashayam*- Astringent

Pharmacological Actions (*Karmam*) of the Drugs

A. Actions on Body constituents (*Dosha* (Bio-regulatory principle), *Dhatu* (Structure) and *Malam* (Excretory product)

Drugs in *Guduchyadi kwatham* are useful in *Ekadoshaja* (that involves one *Dosha*), *Dwidoshaja* (that involve two *Doshas*) and *Tridoshaja* (that involve three *Doshas*) vitiated conditions. *Guduchi, Padmaka* and *Raktachandana* are advised for *Dosha* vitiation associated with *Rakta* (Blood). *Raktachandana* increases semen and possess powerful blood purifying activity. *Guduchi* has fat diminishing action. *Dhanyaka* increases urine, obstructs faeces and helps in removing foul smell of body.[3]

Table 3: Pharmacological actions of drugs in *Dosha*, *Dhatu* and *Malam*

I. Action on *Doshas*			
1	*Guduchi*	**Pacifying actions**	
		Ekadoshajam	*Pitta visoshanam* (diminish *Pitta*)
		Dwidoshajam	*Kaphavatakhnam* (eliminate *Kapha* and *Vata*) *Vatapittanut* (remove *Vata* and *Pitta*) *Rakta vata prasamanam* (pacify *Rakta* and *Vata*)
		Tridoshajam	*Tridosha haram* (destroy *Vata*, *Pitta* and *Kapha*)
2	*Padmaka*	**Pacifying actions**	
		Ekadoshajam	*Vatanut* (remove *Vata*)
		Dwidoshajam	*Pittakaphaharam* (destroy *Pitta* and *Kapha*) *Raktapittakhnam* (eliminate *Rakta* and *Pitta*)
		Tridoshajam	*Sleshmaasrapittanut* (remove *Kapha*, *Rakta* and *Pitta*)
		Aggravating actions	
		Ekadoshajam	*Vatalam* (increases *Vata*)
3	*Arishta*	**Pacifying actions**	
		Ekadoshajam	*Kaphasaanti* (soothes *Kapha*) *Pittadosahjit* (wins *Pitta*) *Balasabhid* (breaks *Kapha*)
		Tridoshajam	*Sleshmaasrapittanut* (remove *Kapha*, *Rakta* and *Pitta*)
4	*Dhanyaka*	**Pacifying actions**	
		Ekadoshajam	*Pittanasanam* (eradicate *Pitta*) *Kaphaharam* (destroy *Kapha*)
		Tridoshajam	*Tridoshanut* (remove *Vata, Pitta* and *Kapha*)
5	*Raktachandana*	**Pacifying actions**	
		Dwidoshajam	*Asrapittahrit* (destroy *Rakta* and *Pitta*) *Pittakaphajit* (win *Pitta* and *Kapha*)
II. Action on *Dhatus*			
1	*Guduchi*	*Medo vishoshanam* (diminish *Medas* - Fat)	
5	*Raktachandana*	*Visheshat raktasudhikrit* (especially purifies Blood) *Sukralam* (increases *Sukra* - Semen)	
III. Action on *Malas*			
4	*Dhanyaka*	*Mootralam* (increases urine) *Dourgandhyanasanam* (eradicate foul smell) *Badhavidkam* (obstructs feces)	

B. Actions on Metabolic functions (*Agni* and *Amam*)

Guduchi, *Arishta* and *Dhanyaka* possess action on *Agni* and increases digestive fire. *Guduchi* and *Dhanyaka* helps in the digestion of *Amam* also ie, the vitiated *Rasa* formed during digestion.[3]

Table 4: Pharmacological actions of drugs in *Agni* and *Amam*

I. Action on *Agni* (Digestive fire)		
1	*Guduchi*	*Agnideepani* (increases digestive fire)
3	*Arishta*	*Agnikrit* (produces digestive fire)
4	*Dhanyaka*	*Deepanam* (increases digestive fire)
II. Action on *Amam*		
1	*Guduchi*	*Ama haram* (destroy *Ama* - vitiated *Rasa* formed during digestion)
4	*Dhanyaka*	*Pachanam* (digests *Ama*)

C. Actions on Sense organs and Mental faculties (*Indriyam* and *Budhi*)

Drug, *Dhanyaka* is good for enhancing the taste of food. More over *Dhanyaka* and *Raktachandana* are beneficial for improving the functions of eyes and vision. *Guduchi* helps in improving the mental power.[3]

Table 5: Pharmacological actions of drugs in *Indriyam* and *Budhi*

I. Action on *Indriyam* (Sense organs)		
4	*Dhanyaka*	*Rochanam* (produces Taste) *Chakshusyam* (beneficial for vision)
5	*Raktachandana*	*Netrahitam* (favorable for eyes) *Chakshusyam* (beneficial for vision)
II. Action on *Budhi* (Intellect)		
1	*Guduchi*	*Medhyam* (improves mental power)

D. Action on Organs and Body (*Sthanam*, *Avayavam* and *Sarva Sareeram*)

Padmaka is a drug that protects the foetus specifically. *Arishta* and *Raktachandana* help in healing ulcers. *Guduchi* and *Dhanyaka* are reported as beneficial for the health of heart. All the drugs except *Raktachandana* dries up the unwanted fluid produced in the body. *Guduchi* and *Raktachandana* promotes the strength of the body and *Padmaka* and *Raktachandana* improves vigor and sexual desire. *Guduchi* is supportive to life. *Raktachandana* possess *Rakshokhna* property ie, protects from disease manifestation.

Table 6: Pharmacological actions of drugs in *Sthanam*, *Avayavam* and *Sarva Sareeram*

I. Action on *Sthanam* (Site)		
2	*Padmaka*	*Garbha Samsthapanam* (sustains pregnancy specifically) *Garbha Sthairyakaram* (gives stability to pregnancy)
3	*Arishta*	*Vranavisodhanam* (cleanse wound specifically) *Sophapakakaram* (inflames odoema)
5	*Raktachandana*	*Vranyam* (beneficial for healing ulcer)
II. Action on *Avayavam* (Organ)		
1	*Guduchi*	*Hridyam* (beneficial to Heart)
3	*Arishta*	*Ahridyam* (not beneficial to Heart)
4	*Dhanyaka*	*Hridyam* (beneficial to Heart)
III. Action on *Sarva Sareeram* (Whole body)		
1	*Guduchi*	*Samgrahi* (dries up fluid specifically) *Balyam* (produces strength) *Ayushyam* (beneficial to life) *Rasayanam* (prevents old age and disease manifestation)
2	*Padmaka*	*Grahi* (dries up fluid)

		Vrishyam (improves vigor and sexual desire)
3	*Arishta*	*Grahi* (dries up fluid)
4	*Dhanyaka*	*Grahi* (dries up fluid) *Avrishyam* (not improves vigor and sexual desire)
5	*Raktachandana*	*Rakshokhnam* (protects from disease manifestation) *Balyam* (produces strength) *Vrishyam* (improves vigor and sexual desire)

Therapeutic Indications of Drugs

The drugs of *Guduchyadi kwatham* are useful in the diseases of *Pranavahasrotas* (Respiratory system), *Udakavahasrotas* (Channels of fluid), *Annavahasrotas* (Gastrointestinal system), *Rasavahasrotas* (Plasma and Lymphatic system), *Raktavahasrotas* (Blood and Cardiovascular system), *Mamsavahasrotas* (Muscular tissue) and *Medovahasrotas* (Adipose tissue), disorders due to extremely vitiated *Pitta*, toxic conditions and agony due to the disease. *Raktachandana* is specified for its use against microorganisms. All the above drugs are also indicated for the diseases due to exogenous pathogens.[3]

Indications of respiratory diseases include cough and dyspnoea. Important clinical features of gastrointestinal system comprise of vomiting, loss of taste, nausea and *Amam* or vitiated *Rasa* formed during digestion due to lack of digestive fire.

Table 7: Therapeutic indications of drugs in *Guduchyadi kwatham*

Disease/Condition	*Guduchi*	*Padmaka*	*Arishta*	*Dhanyaka*	*Rakta Chandana*
I. *Nija vikaras* (Endogenous diseases)					
a. *Doshic* condition					
Pittadosham (Disorders due to vitiated *Pitta*)	-	-	Y	-	-
Sudaruna pittakopam (Disorders due to extremely vitiated *Pitta*)	-	-	-	-	Y
b. Diseases of *Pranavahasrotas*					
Kasam (Cough)	Y	-	Y	Y	-
Kaphapittakasam (Cough due to *Kapha* and *Pitta* predominance)	-	-	-	-	Y
Swasam (Dyspnoea)	-	-	Y	Y	-
c. *Udkavahasrotas*					
Trid (Thirst)	Y	Y	Y	Y	Y
Daham (Burning sensation)	Y	Y	Y	Y	-
d. *Annavahasrotas*					
Chardhi (Vomiting)	Y	Y	Y	Y	Y
Aruchi (Loss of taste)	-	-	Y	-	-
Hrillasam (Nausea)	-	-	Y	-	-
Amam (Vitiated *Rasa* formed during digestion)	-	-	Y	-	-
e. *Rasavahasrotas*					
Jwaram (Fever)	Y	Y	Y	Y	Y
Sramam (Fatigue)	-	-	Y	-	-
Swayadhu (Odoema)	-	-	Y	-	-
Kaphasopham (Odoema due to *Kapha* aggravation)	-	-	Y	-	-

f. *Raktavaha srotas*					
Raktadosham (Disorders due to vitiated blood)	Y	-	Y	-	Y
Raktodrakam (Bleeding through small vessels)	-	-	-	-	Y
Hridayavidaham (Burning sensation in Heart)	-	-	Y	-	-
Pandu (Anaemia)	Y	-	-	Y	-
Kamila (Jaundice)	Y	-	-	-	-
Vatasram (Rhematoid arthritis)	Y	-	-	-	-
Raktavatam (Disorder due to aggravated *Rakta* and *Vata*)	Y	-	-	-	-
Raktapittam (Haemoptysis)	-	Y	-	-	-
Kushtam (Skin diseases)	Y	Y	Y	-	-
Kandu (Pruritis)	Y	-	Y	-	-
Visarpam (Erysipelas)	Y	Y	-	-	-
Visphotam (Blister)	-	Y	-	-	-
Sajwarabranti (Delirium)	-	-	-	-	Y
Bhramam (Vertigo)	Y	Y	-	-	-
Moham (Loss of consciouness)	-	Y	-	-	-
g. *Mamsavahasrotas*					
Vranam (Ulcer)	-	Y	Y	-	Y
Arsas (Piles)	-	-	-	Y	-
Raktarsas (Bleeding piles)	Y	-	-	-	-
h. *Medovahasrotas*					
Medas (Obesity)	Y	-	-	-	-
Meham (Diabetes)	Y	-	Y	-	-
i. Toxic condition					
Visham (Toxins)	-	Y	-	-	Y
Bahuvisham (severe toxicity)	-	-	Y	-	-
Pittavisham (Toxicity associated with vitiated *Pitta*)	-	-	Y	-	-
j. Condition of patient					
Arti (Pain due to illness)	Y	-	-	-	-
II. *Agantuka vikaras* (Exogenous diseases)					
Krimi (Macroscopic Pathogens like worms)	Y	Y	-	Y	-
Jantu (Small animals like insects, spider, etc)	-	-	-	-	Y
Bhootam (Micro organisms)		-	-	-	Y

Pharmacological Evaluation of Drugs

Research studies of various extracts and phytoconstituents were used to evaluate the pharmacological activites of the drugs in *Guduchyadi kwatham* as mentioned in the table below. Clinical pharmacological approach and in vivo and in vitro experimental pharmacological methods were adopted to demonstrate the pharmacological activites.

Table 8: Extracts/Phytoconstituents that demonstrated Pharmacological activities of drugs in *Guduchyadi kwatham*

Pharmacological activities	**Stem of *Tinospora cordifolia***	***Heartwood of Prunus cerasoides/ #Heartwood of *Caesalpinia sappan* Linn**	**Stembark of *Azadirachta indica***	**Fruits of *Coriandrum sativum***	**Heartwood of *Pterocarpus santalinus***
Antiviral		#In vitro study- brazilein, brazilin, protosappanin A, 3-deoxysappanchalcone, sappanchalcone and rhamnetin [16]	In vitro study -Extract [29]		
Anti-dengue			In silico study - Triterpenoid constituents [30]		
Anti-HIV	Clinical study – Extract[4]				
Antimalarial			In vivo study- Tablet suspension [31]		
Anti-inflammatory	In vivo study- Aqueous extract [5]	#In vitro study - Brazilin [17]	In vitro study - Nimbidin [32]	In vivo study- Aqueous and ethanolic extracts [39]	In vivo study- Methanolic extract [51]
Antipyretic	In vivo study- Aqueous extract [5]			In vivo study- Extract [40]	In vivo study- Aqueous extract [52]
Analgesic		#In vivo study- Ethanol extract [18]	In vivo study- Fresh juice [33]	In vivo study- Aqueous extract [41]	In vivo study- Methanolic extract [51]
Antibacterial	In vitro study - Ethanol extract [6]	*In vitro study - Ethanolic extract [19] #In vitro studies - Chloroform, n-butanol, methanol and aqueous extracts [20]	In vitro study - Ethanol extract [34]	In vitro study - Ethanolic extract [42]	In vitro study - Methanolic extract [53]
Antitubercular		#In vitro study - 3-deoxysappanchalcone from ethyl acetate solvent [21]			
Anti-allergic	Clinical study – Extract [7]	#In vivo study - Dichloromethane			

		extract [22]			
Antioxidant	In vitro study- Hydro-ethanolic extract [8]	#In vitro study- Ethanol extract, protosappanin A, and protosappanin B [23] , Brazelien [24]	In vitro study- Ethanol extract [35]	In vitro study - Aqueous extract [43]	In vitro study – Methanolic extract [51]
Immuno-modulatory	In vitro study- Aqueous extract [9]				
Gastroprotective			In vivo study- Extract [36]	In vivo study- Fruits [44]	In vivo study- Alcoholic extract [54]
Hepatoprotective	Clinical study- extract [10]	#In vivo study - methanol and aqueous extracts [25]	In vivo – Nimbolide [37]		
Cardioprotective	In vivo study - alcoholic extract [11]			In vivo study - hydro-methanolic extract [45]	
Antidiabetic	In vivo study - Aqueous and alcoholic extracts [12]	#In vivo study- Ethanol extract [26]		In vivo study- Aqueous extract. [46]	In vivo study- Aqueous extract [55]
Hypolipidemic	In vivo study - aqueous and alcoholic extract [13]	#In vivo study - Hydroalcoholic extract [27]		In vivo study – seeds [47]	
Anti cancerous	In vitro study in HeLa cells - methanol, aqueous and methylene chloride [14] In vitro B16F-10 melanoma cells - polysaccharide fraction [15]	#In vitro study in human cervix HeLa adenocarcinoma, human lung A549 adenocarcinoma, murine colon 26-L5 carcinoma, murine Lewis lung carcinoma (LLC) and murine B16-BL6 melanoma cells- Methanol, methanol-water (1:1) and water extract [28]	In vitro study in human hepatocarcinoma (HepG2) cells - Nimbolide [38]	In vivo study in colon cancer in rats – seeds [48]	In vitro study in cancer cell lines - Pterostilbene [56]
Anxiolytic				In vivo study - aqueous extract [49]	
Antidepressant				In vivo study- Diethyl ether extract [50]	

Benefits of *Guduchyadi Kwatham* in Coronavirus Disease (Covid-19) and its Pharmcodynamics

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV- 2 has been categorised as a HG3 organism like SARS-related and MERS-related corona viruses. Other viruses within HG3 include rabies, poliovirus, dengue virus, hepatitis virus B, C, D and E, and HIV 1 and 2. [57-59]

The virus spreads from person to person through direct or indirect contact, droplet spray or aerosol. Hence COVID-19 is being thought as an airborne disease. The virus enters the body mainly through respiratory route, the disease starts manifesting with the symptoms of upper respiratory tract infection. The incubation period ranges from 2 to 14 days after exposure. It is reported that in some case incubation period extends upto 28 days.

Clinical spectrum of COVID-19 ranges from asymptomatic patients to septic shock and multi organ dysfunction. The most common symptoms at onset of COVID-19 illness are fever, cough, sputum production, fatigue, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia. When the disease advances, clinical conditions like pneumonia, RNAaemia, acute respiratory distress syndrome, acute cardiac injury, and incidence of ground-glass opacities that lead to death may develop.[60-63]

Based on the severity, the disease is classified into mild, moderate, severe, and critical. Patients with mild illness may present with symptoms of an upper respiratory tract viral infection that includes dry cough, mild fever, nasal congestion, sore throat, headache, muscle pain, and malaise. Dyspnoea is absent in such cases. The majority of COVID-19 cases are mild in severity. Patients with mild disease can quickly deteriorate into severe or critical cases. Patients with moderate illness present with respiratory symptoms of cough, shortness of breath, and tachypnea. Patients with severe disease present with severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, or septic shock. Patients with preexisting comorbidities like diabetes, respiratory disease, cardiovascular disease, hypertension, and oncological complications have a higher case fatality rate.[64,65]

During pathogenesis infected person shows higher leukocyte numbers, abnormal respiratory findings and increased levels of plasma pro-inflammatory cytokines. Significantly high blood levels of cytokines and chemokines is usually seen in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, mMCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Sometimes, in severe cases, high levels pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα may be observed.[61] Release of large amounts of pro-inflammatory cytokines called 'cytokine storm' leading to deadly uncontrolled systemic inflammatory response is seen in individuals with severe COVID-19 infection. This is the cause of ARDS and multiple organ failure in severe cases.[66] Moreover recent studies report evidence of blood clotting pattern that causes micro-clots in lungs, brain and kidney in affected patients.

Immune system is also seriously affected by the invasion of the virus. In order to survive in host cells, SARS-CoV use multiple mechanisms to avoid immune responses and that increases the virus load in the body. [67]

Since COVID-19 is an infectious one, the main symptom seen in this disease is *Jwaram* (Fever). Because of the infection in the respiratory tract, symptoms like cough, sputum production, fatigue etc can be seen associated with fever. Diseases caused by exogenous factors are named as '*Agantu*' in Ayurvedic classics. *Jwaram* or fever caused especially by microorganisms is grouped under '*Abhishanga jwara'*. It is described that *abhishanga jwara* is manifested with the vitiation of *Vatapitta doshas*.[68] On localization of the infection in *Pranavahasrotas* or respiratory tract, the symptoms of vitiated *Kapha dosha* like *Kasam* (Cough), Sputum (*Kapham*), etc manifests. While the infection advances, the virus causes organic damage of respiratory system and spreads all over the body through *Rakta* (Blood) by vitiating the same and producing the symptoms like haemoptysis, lymphopenia, RNAaemia, blood clots and acute cardiac injury.

When the symptoms and pathogenesis of COVID-19 is considered it may be assumed that the main *Doshas* involved in the development of disease are *Pitta* and *Kapha*. The involvment of *Vata dosha* can also be assumed from the symptoms manifested like dyspnoea and tachypnea in moderate and acute respiratory distress syndrome (ARDS) and septic shock in severe cases.

The formulation '*Guduchyadi kwatham'* is indicated mainly for diseases caused by vitiation of *Pitta* and *Kapha doshas*. Since the formulation pacifies *Jwara*, it is beneficial in the symptoms fever, loss of appetite and malaise caused in the onset of the disease. The drugs in the formulation together works and act as a '*Deepana*' medicine, i.e., improve the digestive power. Two of the ingredients, *Guduchi* and *Dhanyaka* digest *Amam* – i.e., vitiated '*Rasa*' formed during digestion and impede the manifestation of *Jwara*.

On analyzing the therapeutic indications of individual drugs it can be recognized that the formulation is beneficial in disorders of respiratory system, such as *Kasam* (Cough) and *Swasam* (Dyspnoea). The drugs *Guduchi*, *Arishta*, *Dhanyaka* and *Raktachandana* are indicated for *Kasam* and *Arishta* and *Dhanyakam* for *Swasam*. The predominance of the *Rasas* (Taste), *Katu* (Acrid) *Tikta* (Bitter) and *Kashaya* (Astringent) of these drugs helps to check the production of mucus in the lungs and thereby dyspnoea due to occlusion of alveoli. [69]

The medicine is very much beneficial in diseases due to vitiation of *Raktavahasrotas* due to '*Amam*'. Diseases that manifest through *Rakta* (Blood) can be controlled by the drugs *Guduchi*, *Arishta* and *Raktachandana* as they possess blood purifiying property (*Raktasudhi*) and are indicated as a remedy for diseases due to blood vitiation (*Raktadosham*). Since *Raktachandana* pacifies *Raktodrekam* (bleeding through small vessels) the formulation can be effectively used for preventing the formation of blood clots and Haemoptysis.

All drugs in the formulation are beneficial for alleivating the gastrointestinal symptoms, *Chardhi* (Emesis) and *Trid* (thirst). Drugs, *Guduchi* and *Padmaka* are stipulated for *Bhramam* (distress) and *Rakachandana* is especially for *Bhramam* associated with Fever. *Guduchi* particularly checks the agony (*Arti*) caused by the disease. *Guduchi*, *Padmaka*, *Dhanyaka* and *Raktachandana* are useful against macroscopic pathogens (*Krimi*) and *Raktachandana* in particular for micro organisams (*Bhootam*). Drugs *Padmaka*, *Arishta* and *Raktachandana* are remedies for toxic manifestations (*Visham*) and hence they can work to prevent toxemic manifestion of the disease. Property like *Hridyam* (beneficial effect on heart) and effectiveness of the drugs in *Meham* (Diabetes) helps as a remedy for comorbid states of metabolic disorders and cardiovascular system.

Pharmacological evaluation suggests that Tinospora cordifolia possess anti-HIV activity and Azadirachta indica possess anti dengue activity. Caesalpinia sappan and Azadirachta indica demonstrated antiviral activity. All the drugs in the formulation found with the potential of anti-inflammatory action and antibacterial effect against respiratory pathogens. *Tinospora cordifolia*, *Coriandrum sativum* and *Pterocarpus santalinus* possess potent antipyretic activity. Anti malarial activity of *Azadirachta indica* was also demonstrated. All the drugs are antioxidant in nature and there by checks the oxidative stress to various tissues of the body. *Tinospora cordifolia* can be seen as an effective immunomodulator in the formulation. *Tinospora cordifolia, Coriandrum sativum* and *Pterocarpus santalinus* possess anti diabetic property. Most of the drugs have gastroprotective, hepatoprotective and cardioprotective activities. All drugs demonstrated anti-cancerous activity during in vitro studies. Pharmcological actions like hypolipidemic, Anxiolytic and antidepressant are the other benefits of the drugs in this formulation.

Main action of the formulation is in vitiated *Pittakapha* condition, and symptoms of vitiated *Pranavahasrotas*, *Annavahasrotas*, *Rasavahasrotas* and *Raktavahasrotas*. This formulation is good to administer even in *Agnimandya* (poor digestive fire) condition since the formulation, ie *kwatha kalpana* (decoction) as such and the individual drugs are *Laghu* (Light) in quality. Considering the above validated effects, it can be suggested that *Guduchyadi kwatham* is a useful medicine to prevent viral diseases upto certain extent. It is also effective in protecting *Pranavahasrotas* (respiratory system) *Annavahasrotas* (Gastrointestinal system), *Udakavahasrotas* (channels of fluid), *Rasavahasrotas* (Plasma and Lymphatic system) and *Raktavahasrotas* (Blood and Cardiovascular system). It can be used as a prophylactic measure for persons in containment zone and to treat exposed and mild cases of COVID-19. This medicine may also be valuable as an addon drug with conventional treatment approach in moderate cases. The screened activities of the drugs support the use of this medicine in comorbidities like Diabetes, Gastric ulcer, Jaundice, Cardiac diseases, Hyperlipidemia, Cancer, Anxiety and Depression.

CONCLUSION

COVID-19 is an airborne disease that affects the respiratory system. Infection generates leukocytosis and high levels pro-inflammatory cytokines and chemokines in plasma. It is the 'cytokine storm' that leads to acute respiratory distress syndrome (ARDS) in severe cases. The initial step needed in the management of SARS-CoV- 2 infection is prevention of inflammatory process and alleviation of respiratory symptoms. So, unique concern is necessary to check '*Pitta dosha'* and '*Kapha dosha'* aggravation.

Guduchyadi kwatham is a well known formulation used in the treatment of diseases due to *Pitta* and *Kapha dosa* vitiation. It is indicated in *Jwaram* (Fever) and the individual drugs in the formulation, signifies the benefit in *Pranavahasotas*, *Annavahasrotas*, *Udakavahasrotas*, *Rasavahasrotas* and *Raktavahasrotas*. Demonstrated pharmacological activities like anti-inflammatory, antipyretic, antiviral, anti-bacterial, anti allergic, etc substantiate the use of this medicine in the prevention and mitigation of this viral disease.

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