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Review Article

ROLE OF AYURVEDIC ANTICOAGULANT AND ANTIOXIDANT TREATMENT IN COVID 19

Amrut.S. Salunke[1], Adarsh Ramkalap Sharma[2]*, Sonali Sunil Tadasarkar[2]

*[1]H.O.D & Associate Professor, [2]Final year P.G. Scholar, Dept. of Shalakyatantra, R.A.Podar Medical (Ayu) College and M.A.Podar Hospital, Worli, Mumbai, India.

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ABSTRACT

Corona virus disease is caused by severe acute respiratory syndrome Corona virus 2 [SARS-CoV-2] infections attacking multisystem of the human body at a time, of which respiratory system, immune system and circulatory system are most affected. The complications of the disease arise or it becomes more pronounced, after the cytokinine storm phase becomes established leading to hypercoagulative state affecting the circulatory and respiratory system. In *Ayurveda*, there is a holistic approach in treating the disease and the body as a whole. Drugs such as *Haridra, Tulasi, Guduchi, Yashtimadhu, Twak, Triphala, Lavang, Maricha, Pippali etc* and few *Visha Dravyas* like *Langali, Dravanti* etc can be used a single drug or a group of drugs with their phytochemical properties and active principles leading to delay and prevention of hyper coagulable states thereby preventing the cascade of complications caused by COVID, additionally having anti-inflammatory and immune-modulatory effect. Scientific research on these drugs may reveal a new approach for management and prevention of COVID related complications and can be a subject of future research interest.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by (SARS-CoV-2) severe acute respiratory syndrome infection mainly targeting the immune system of the body. In December 2019, its outbreak occurred in Wuhan city, Hubei province, China which further got spread worldwide.[1]

AIM

To review research which has already been conducted and currently carried out on different herbal plants for their anticoagulant property which might have a possible application in the prevention and treatment of Covid-19 and related complications.

OBJECTIVES

- To study patho-physiology of Covid-19 in both Ayurvedic and modern aspects.
- To quantify the use of Ayurvedic anticoagulant drugs with antioxidant property and its role in breaking patho-physiology of Covid-19 and its adjunct use for treating with post COVID complications and effects.

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MATERIALS AND METHODS

- The published literature about COVID 19.
- Ayurvedic *Nighantus,* standard textbooks and their commentaries.
- Scholarly articles written and published on various internet platforms related to COVID 19 and its Ayurvedic treatment were reviewed.

Patho-physiology of Covid-19 According to Modern and Ayurvedic Aspects

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) causes COVID-19, a respiratory pandemic. It has 96.2 percentage structural similarity with bat corona virus and 79.5 percent similarity with severe acute respiratory syndrome corona virus.[2] Corona viruses have a single-stranded RNA genome covered by an enveloped structure. Size ranges from 26.2 to 31.7 kilo bases and 50 to 200 nanometers in diameter which is largest for any RNA viruses. SARS-CoV-2 spike protein directly binds with the host cell surface ACE2 receptor facilitating virus entry and replication.[3] SARS-CoV-2 uses ACE2 as a cellular entry receptor and compared to SARS-COV has 10 to 20 times more affinity leading to increase chances of human to human transmission.[4]

Types of COVID variants found in India: UK variant [B.1.617], South Africa variant [B.1.351], Brazil variant [P1 variant]. Among all the mutant COVID-19

variants in India, of all double mutated virus B.1.617 is becoming the most prevalent according to genome sequencing data submitted by Indian scientists to a global database. The B.1.617 variant contains mutations from two separate virus variants- E484 and L452R.

SARS-CoV-2 mainly alters immune regulatory mechanism and damage immune homeostasis,[5] the immune response of this infection occurs in two phases:

Defense Phase

When aerolised uptake of SARS-CoV-2 enters in lungs leads to infection of ACE2 expressing target cells such as alveolar type 2 cell. This generates antibody secreting cells, helper T-cells, activated CD4, CD8, T cells that bind to this virus. The innate immune response against viral infection relies on the interferon type 1 and controls replication of the virus. SARS-COV and SARS-COV-2 share the same cell receptor in the human entry as angiotensin converting enzyme 2 but MERS-COV uses another specific receptor di-peptidyl peptidase and amino peptidase N. [6]

Damage Phase

It leads to the uncontrolled release of cytokines that causes cytokine storm or cytokine release syndrome (CRS) characterized by increased interleukin 2, interleukin 7, interferon- gamma, tumor necrosis factor etc. CRS damages the tissues of lungs, kidney and heart likely leading to severe complications like ARDS, respiratory failure and even death. Cytokine storm and lymphopaenia may have a significant role in the pathogenesis of COVID infection. [7]

Cytokines are further divided into TH1 and TH2 and they are the hormonal messengers responsible for immune response.

Common clinical features of COVID19 includes fever (99%), dry cough (60%), myalgia (44%), fatigue (70%) and breathlessness still in advanced stages may cause (acute respiratory distress syndrome) ARDS, kidney failure and even death. [8]

A new variant symptom includes abdominal pain, diarrhea, unexplained headache, conjunctivitis or pink eyes, extreme headache or acute pain above eyelids and confusion of the brain – brain fog.

Ideal laboratory confirmation of a suspected case includes nasopharyngeal and oro-pharyngeal swab. Nasopharyngeal swabs become the preferred swab as it is better tolerated, safe to operate.[9] At present confirmation of COVID -19 cases is based on RT-PCR [real time reverse transcriptase polymerase chain reaction] by confirmation by nucleic acid sequencing.[10]

Patho-physiology of Covid-19 According to Ayurveda

It is evident that Covid-19 is known to trigger inflammatory pathways and subsequent cytokine storm leading to multiple organs dysfunction (MOD) and failure. Viral infections are always being considered as manifestation of *Pitta Dosha* vitiation in Ayurveda's paradigm. *Pitta Dosha* is characterized by properties heat, sharpness, pungency and liquid form in normal state.

Hypothetically, like Herpes Zoster and Chickenpox if it is believed that SARS-CoV-2 is also creating an imbalance in *Pitta Dosha* and allowing body heat to exacerbate causing damage to tissues then the clinical picture fits into this pathology.

Aggravated heat from vitiated *Pitta* leads to triggering of inflammatory pathways which may be causing initial symptoms of Covid-19 such as dryness initially leading to weakness, malaise, body ache and fever. *Pitta* vitiation possibly results in the disruption of the immune-regulatory molecules skewed towards the unregulated trigger of pro-inflammatory cytokines facilitating more cytokine release and viraemia resulting in cytokine storm leading to MODS.

Aggravation of *Pitta* allowing dryness and raised temperature to manifest aggravated heat has a strong potential to attract the moisture from the healthy tissues causing excess accumulation of water content, accumulated water allows *Kapha* to increase due to homologous nature.[11]

DISCUSSION

Drug/ *Dravya*	**Properties**	**Additional properties**
Haridra	*Rasa: Tikta, Katu Guna: Ruksha, Laghu Veerya: Ushna Vipaka: Katu*	*Raktaprasadan, Raktavardhak, Kaphaghna, Jwaraghna, Peenasa Aruchi-nashan*[12]
Twak	*Rasa: Tikta, Katu, Madhur Guna: Ruksha, Laghu, Tikshna Veerya: Ushna Vipaka: Katu*	*Kaphavatashamak, Yakshmanashak, Aruchi-nashan, Peenasa Kasajit*[13]
Yashtimadhu	*Rasa: Madhur Guna: Guru, Snigdha Veerya: Sheeta Vipaka: Madhur*	*Kshayapaha,* Contains Glycosides*:* liquiritin, isoliquiritin.[14]
Tulasi	*Rasa: Tikta, Katu Guna: Ruksha, Laghu*	*Hridya, Raktashodhak, Deepan, Pachan, Anuloman, Kasashwasahar, Kshayanashak,*

	Veerya: Ushna Vipaka:Katu *Prabhav : Bhutaghni*	*Jwaraghna, Sheetaprashaman*[15] Antioxidant properties: Improves humoral and cellular immunity[16,46]
Lavang	*Rasa: Tikta, Katu* *Guna: Laghu, Snigdha* *Veerya: Sheeta Vipaka: Katu*	*Aampachak, Jwaraghna, Ruchikar, Kasa Shwasa Hikka Kshayanashak.*[17]
Marich	*Ras: Katu. Guna: Laghu, Tikshna* *Veerya: Ushna. Vipaka: Katu*	*Swedajanan, Kapha nissaarak, Kaphaghna, Vishamjwaranashak*[18]
Naagkeshar	*Rasa: Kashay, Tikta* *Guna: Ruksha,Laghu* *Veerya: Ushna, Vipaka: Katu*	*Kaphapittashamak, Uttejak, Hridya, Shonitasthapak, Jwaraghna*[19]

Drug/*Dravya*	**Properties**	**Additional properties**
Langali	*Rasa: Tikta, Katu* *Guna: Laghu, Tikshna* *Veerya: Ushna Vipaka: Katu*	*Shleshmajit, Raktashodhak, Vishamjwaranashak*[20] Latex have anticoagulant and anti-fibrinogenolytic property[21]
Dravanti	*Rasa: Katu* *Guna: Ruksha, Guru, Tikshna* *Veerya: Ushna Vipaka: Katu*	*Sarvangashothahar, Rechak*[22] Latex when diluted delays clotting time or hampers clot formation[23]
Kumbhi	*Rasa: Katu Guna: Ruksha* *Veerya: Ushna Vipaka: Katu*	Anticoagulant properties[24]
Guduchi	*Rasa: Katu, Tikta, Kashay* *Guna: Laghu, Veerya:Ushna* *Vipaka: Katu*	*Rasayan, Balya, Agnideepan, Tridoshashamak, Daha Prameha Kasa Panduhar*[25]
Pippali	*Rasa: Katu Guna: Snigdha, Laghu* *Veerya: Anushna Vipaka: Madhur*	*Rasayani, Rechani, Agnivardhak, Vrishya, Medhya, Jeernajwarahar, Medakaphanashan* with honey[26]
Sunthi	*Rasa: Katu Guna: Laghu* *Veerya: Ushna Vipaka: Madhur*	*Vibandhabhedini, Kasahar, Hrudayaamayhar*[27]
Vantrapushi	*Rasa: Tikta, Katu* *Guna: Ruksha, Laghu, Tikshna* *Veerya: Ushna Vipaka: Katu*	*Sara, Tivrarechini, Pittaraktashodhan*[28]
Sadapushpa	*Rasa: Kashay, Tikta Guna: Ruksha, Laghu* *Veerya: Ushna Vipaka: Katu*	*Vatakaphashamak, Hridya, Raktabharadhikyanashini*[29]

Properties of *Triphala*

1. Hypercholesteremic effect
2. Anti-inflammatory effect
3. Gastrointestinal effect
4. Stress reducing effect
5. Anti obesogenic effect
6. Antidiabetic effect
7. Anti-neoplastic effect
8. Anti-immunosenescence effect
9. Immuno-modulating effect
10. Analgesic effect
11. Bronchodilator effect
12. Increases red blood cells and hemoglobin production.[30]

***Haridra* (*Curcuma longa*)**

Potential benefits of alkaloids derived from turmeric have shown strong potentially inhibitory effects on the neuraminidases from two influenza viral strains.[31] It also possesses anti-viral properties by boosting the immune system.[32] It even holds skin improving and memory enhancing properties[33]. It also works as natural anti-inflammatory drug along with other herbs.[34] Turmeric also possesses anti-inflammatory and immune modulatory properties.[35]

Guduchi

Guduchi (*Tinospora cordifolia* (Willd.) Miers) One of the best *Rasayana dravya* also known as "*Amrita*" have immuno-modulatory property and

enhances innate immunity against infections. Tinosporin, diterpenoid as active principles have anti-viral properties, can be used for the treatment of retroviruses[36]. Aqueous extracts of *T. cordifolia* influences the cytokinine production and enhances activation of immune cells[37]. It is a potent hepato-protective drug hence effective in preventing hepatotoxicity. It enhances vitamin C level thereby acting as an antioxidant[38]. Stem bark has immunomodulatory activity leading to increased phagocytic activity and macrophages[39].

Yashtimadhu

Mulethi (*Glycyrrhiza glabra* L.) Major photo component reported in *Yashtimadhu* is glycyrrhizin which is a promising candidate in inhibiting replication of the SARS- associated virus[40]. It also improves the resistance against the herpes simplex virus type 1 (HSV-1) by Type I and II interferons (IFN) and Th2 cytokines secretion.[41] It has anti- viral activity against Human Immunodeficiency Virus (HIV), potent immunomodulator and has antioxidant activity[42].

Tulasi

Tulasi (*Ocimum sanctum* L.) regarded as mother medicine of nature shortens the course of all illness. *Tulasi* has anti- bacterial, anti-viral and anti-fungal activity.[43] Flavonoids present in the extracts of *Tulasi* leaves, is found to be responsible for the immunomodulatory properties by increasing the level of IL-4, natural killer cells and helper cells.[44] Essential oils like Eugenol in leaves produce anti-viral activity against different viruses e.g. polio virus type 3, herpes virus (HSV), hepatitis B virus etc.[45] Ethanolic extract of *Tulasi* plant leaves in a range of 22.5 mg/ml concentration inhibits replication of polio type 3 virus. Extracted components of *Tulasi* like linalol and ursolic acid has shown broad- spectrum antiviral activity against RNA virus and adenoviruses.[46]

Lavang

Clove (*Syzygium aromaticum*) is one of the most valuable spices used for many centuries as food preservative and medicinal purposes. It represents one of the richest sources of phenolic compounds like eugenol, eugenol acetate and gallic acid. This plant's antioxidant and antimicrobial activity is higher than many other spices, vegetables and fruits.[47]

Marich

Piper nigrum is utilized extensively due to its antioxidant, antitumor, anti-allergic, anti-inflammatory, gastrointestinal protection and antidiarrheal properties.[48]

Twak

Cinnamon is an unusual tropical plant belonging to the Lauraceae family. It has been used for hundreds of years as a flavor additive, but it has also been used in natural Eastern medicine. Cinnamon extracts are vital oils that contain biologically active compounds, such as cinnamon aldehyde, cinnamic alcohol, cinnamic acid, and cinnamate. It has antioxidant, anti-inflammatory, and antibacterial properties and is used to treat diseases such as diabetes and cardiovascular disease.[49]

Sunthi

Ginger (*Zingiber officinale*) has hypolipidemic, antiemetic and chemoprotective action. It also possesses properties like antiviral, anti-inflammatory and antiulcerogenic.[50]

***Pippali* (*Piper longum* L.)**

Pippali Rasayana, a famous Ayurvedic preparation, reported having significantly activated macrophages in an experimental study on mice. Administration of *P. longum* extract and its phytochemical piperine increased the total WBC count, Bone marrow cellularity and α-esterase positive cells in mice. [51] Immunomodulatory action of Pippali fruits (via modulation of both specific and non-specific immune response) has been reported by using macrophage migration index (MMI), haem-agglutination titre (HA) and phagocytic index (PI) in mice. The effect was more prominent at a lower dose (225mg/kg) and was marginally reduced when the dose was increased.[52]

Naagkeshar

Mesua ferrea leaves contains phenolic, alkaloid content such as ethanol, methanol, ethyl acetate and hexane extracts all having antioxidant properties. Of the 4 extracts ethanol extract showed better antioxidant property.[53]

CONCLUSION

The drugs which are discussed above, few of them being *Vishadravya* like *Langali*, *Dravanti* should be used with great care along with the remaining drugs. Since these drugs also have abortifacient properties, its dosage and use should be carefully monitored. Due to their *Rasapanchak* properties and active constituents, they can be used in animal trials to examine the effect of their anticoagulant and anti-inflammatory property on cytokinine storm so that its progression to multi organ system dysfunction and failure can be abruptly stopped and the complications of COVID 19 and its severity can be reduced and prevented. Separate and combined drug trials with various permutations and combinations can be carried to rule out the efficacy of above mentioned drugs in COVID 19 with a view to make this world, a better place for living and making it disease-free.

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***Address for correspondence**
Dr. Adarsh Ramkalap Sharma
P.G. Scholar
Dept. of Shalakyatantra
R.A.Podar Medical (AYU) College and M.A. Podar Hospital, Worli, Mumbai.
Contact: 8082229002
Email: sharmaadarsh808@gmail.com

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