REVIEW ARTICLE

Test, Track, and Treat Ameliorative Strategy to Contain Severe Acute Respiratory Syndrome Coronavirus 2: An Indian Perspective

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Abstract

Ever since in January 2020, the WHO declared an international public health emergency, emerged as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease-19) pandemic which has devastated human race with its human-to-human transmission, mutation, and mortality with complex pathogenicity mechanism. Earlier theories postulated it to have emerged from "Wet Market," Huanan Seafood Wholesale Market in Wuhan city of Hubei Province in China. Based on initial speculations, this pandemic was suggested to be of enzootic origin, considerably bats and pangolins as connecting link between human-animal transmissions, which were later refuted. Time bound and effective Test, Track, and Treat policy initiatives taken by Indian Government proved to be a benchmark in controlling the pandemic, up to certain extent. Molecular diagnostics have witnessed a scaled up trend in terms of reverse transcription polymerase chain reaction and Rapid Antigen Tests to detect the contagion in oro-pharyngeal and naso-pharyngeal swabs. It is imperative that frequent mutations in SARS-CoV-2 lead to development of new serotypes making screening for novel therapeutics or repurposing of drugs cumbersome. With an effort to consummate existing clinico-pharamaceutical gaps to curb SARS-CoV-2, ardent remains the fact that plants have been considered as medicinal power houses. Green therapeutics are formulation of active phyto components when administered, enhance the bio-availability through different drug delivery systems. Exploration of medicinal plants for their bio-active ingredients to develop immune-boosters as an antiviral prophylactic tool against SARS-CoV-2 remains a preferred choice among health-care practitioners, pharmacologists, and life sciences fraternity at large. In addition, indigenous vaccines have been granted approval for Emergency Use Authorization which would help lower the rates of transmission and mortality by significant numbers in times to come.

Key words: Test, track, and treat, green therapeutics, molecular diagnostics, severe acute respiratory syndrome coronavirus 2, vaccines

INTRODUCTION TO SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2): EMERGENCE AS A GLOBAL PANDEMIC

Viruses are specific obligate intracellular parasites possessing either DNA or RNA genome with or without an enveloped protein (capsid). They are devoid of *de novo* metabolic machinery hence they depend on hosts for their replication. Respiratory viruses have been known to cause both upper and lower airway disorders. Transmission is attained by droplet nuclei, exchange of body fluids, contact spread, and blood-sucking insects.[1] One such group of respiratory viruses is Coronaviruses (CoVs), encompassing 39 species fall under the broad realm of Riboviria which constitute all RNA viruses and viroids that replicate by means of *RNA Dependent RNA*

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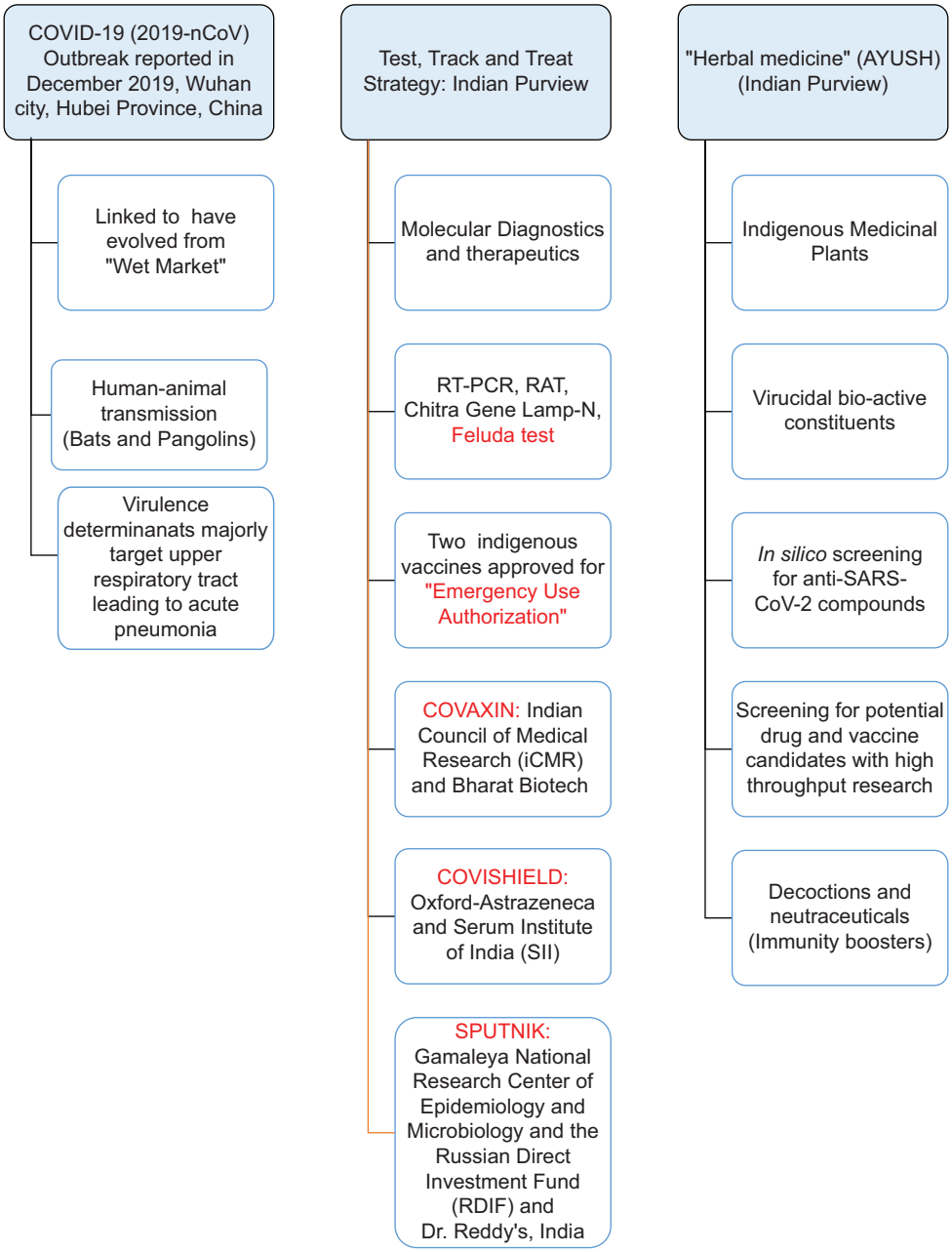
GRAPHICAL ABSTRACT



Polymerases. They belong to the family Coronaviridae, suborder Cornidovirineae, and order Nidovirales.[2] Structurally, CoVs are enveloped, positive sense, single stranded RNA (ssRNA) large viruses (genome size 26–32 kb) exhibiting their virulence in both humans and animals; mostly being confined to enzootic category.[3,4] These viruses can be categorized into four genera based on genotypic and serological properties.[5,6]

1. Alpha
2. Beta
3. Gamma
4. Delta

Until recently, seven Human CoVs (HCoVs) have been confirmed[7] [Figure 1] with SARS-CoV-2 presumably of zoonotic origin belonging to the subgenus Sarbecovirus with 96.2% shared sequence homology with bat coronavirus.[2,8,9] Despite its similarity to SARS-CoV, its transmission efficiency and diagnostic methods are rather different. The distinguishing factor is probably the nucleotide changes in the spike (S) protein and its Receptor-Binding Domain (RBD).[10-12]

The term Coronavirus disease (COVID-19) (2019-nCoV), declared as a global public health emergency was coined by the WHO on January 11, 2020.[13,14] The pathogen to blame is SARS-CoV-2 which is thought to have emerged in "Wet Market" aptly referred to as Huanan Seafood Wholesale Market in Wuhan city of Hubei Province in China in December 2019 with sufficient reported cases of human-to-human

transmission.[15-17] In addition to MERS-CoV, SARS-CoV-2 has led to onset of severe pneumonia in humans[18] with flu-like symptoms including fever, cough, and severe acute respiratory distress syndrome with fatalities reported.[19,20] Few recent reports have confirmed human-to-human transmission of SARS-CoV-2.[21] As per the recent report by BBC, 2020, infection is transmitted by droplet nuclei which is manifested by contact spread directly by mucous membranes or indirectly by hands which can cross-transmit the inoculum in nasal or oral mucosa, the most potential reservoirs for initiating viral replication. These infections are significantly contributing to morbidity and mortality by obstructing tremendous collateral economic health-care disruptions with unimaginable societal costs and a crashed economy.[22] Asymptomatic infectivity has also been reported hence suggesting self-isolation.[23] Temporary recommendations under International Health Regulations were laid down to contain the accelerating pace of COVID-19 with paucity of treatment options[24] some of the crucial being by practicing self-hygiene and social distancing in addition to early detection and isolation.[25,26]

METHODS

To collate this review, a comprehensive search encompassing different databases such as (LitCovid) PubMed were used to search articles till January 21, 2021, with keywords such as novel coronavirus, SARS-CoV-2, potent drug inhibitors against SARS-CoV-2 RNA, enzootic, phyto-chemicals, and Traditional Chinese Medicine (TCM) Systems in addition to databases such as World Health Organization, Centre for Disease Control and Prevention[27-29] [7,30] independently screened, reviewed, and elaborated an extensive review consisting of morphology, patho-physiology of SARS-CoV-2. Imperative is the fact, that both the research groups highlighted the significance of phyto-chemicals being considered as potential anti-SARS-CoV-2 compounds through virtual screening procedures. Importance of Indian medicinal plants is reported as per Ayurveda, Yoga, Unani, Siddha, and Homeopathy (AYUSH).[31] Bioefficacy of 25 Indian Medicinal plants for their anti-HCoV properties (27 articles) has been examined.[7] *In silico* screening procedures were adopted to validate *in vivo* anti-SARS-CoV-2 properties in 115 phyto-constituents derived from 26 Chinese Traditional herbs among 125 potential candidates as screened in TCM Systems Pharmacology database TCMSP, The Encyclopedia of TCM and SymMap.[30,32-34] Other resources which we considered for this review are The Lancet (four articles).

Patho-physiology of SARS-CoV-2

The SARS-CoV-2 is a part of largest RNA virus family with its genome ranging from 27 to 32 kilobases in size (~125 nm

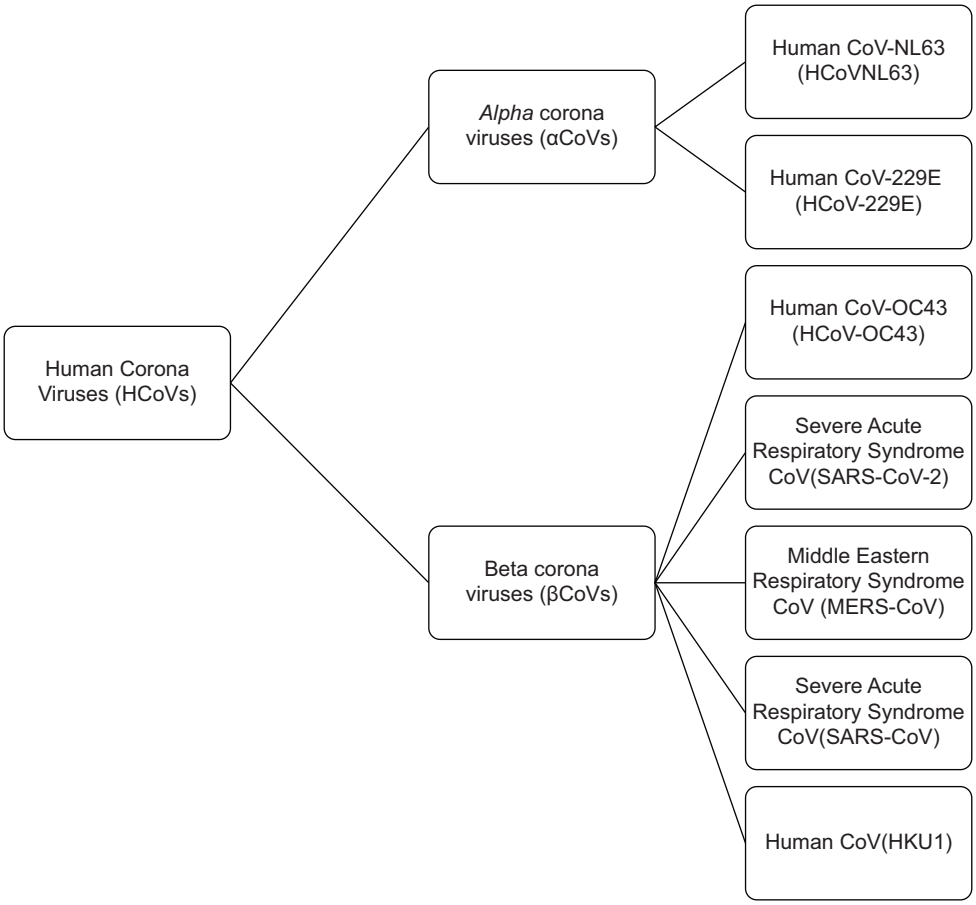


Figure 1: Different types of Human Coronaviruses

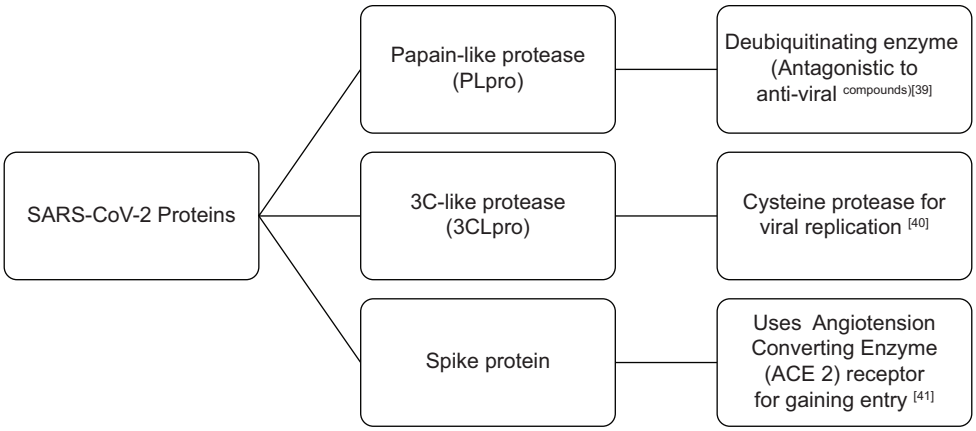


Figure 2: Types of SARS-CoV-2 proteins[39-41]

or 0.125 μm). It is a single stranded enveloped RNA virus which possesses a positive-sense RNA genome also known as (+ssRNA) with a 5′-capstructure and 3′-poly-A tail.[35] Morphologically, the virus possesses four proteins which impart both structural and functional integrity to the pathogen.

1. (E) The envelope protein
2. (M) The membrane protein
3. (S) The spike protein
4. (N) The nucleo capsid protein.

Among these, N and S proteins are responsible for structural stability and adhesion of virus to host cell, respectively, by virtue of large ectodomain, single-pass transmembrane anchor, and a short intracellular tail.[36,37] Furthermore, ectodomain has two subunits, the S1 receptor-binding subunit and S2 the membrane fusion subunit arranged in a clove-trimeric or crown structure which has purportedly given CoVs is name (corona = crown).[38] Apart from these proteins, CoVs encode other proteins like [Figure 2].

- Papain-like protease (PLpro)
- 3C-like protease (3CLpro)

SARS-CoV-2 is found to possess structural and functional homology with its predecessor SARS-CoV, contrary is the fact that its rate of transmission and infection has witnessed an accelerated trend. It is believed that both SARS-CoV and SARS-CoV-2 possess similar kind of receptors such as RBD present in C-terminal of S1 region of S protein and Receptor Binding Motif in their viral genome.[42,43] Notably, a gain of functional mutation encompassing an absent 8a, longer 8b, and shorter 8c fragments and contagious Nsp 2 and 3 proteins has been reported.[44-46] Morphological modification of furin like cleavage site in S protein is also reported which is known to exhibit increased virulence.[11] Genomic analysis revealed that SARS-CoV-2 shares 70% similarity with SARS-CoV.[47-49]

Diagnostic tools: Time bound accurate and precise detection of COVID-19

With an ever increasing surge in COVID-19 cases globally, screening and diagnosis of prospective population at mass scale remain a forefront task. Specificity and sensitivity of diagnostic measures must address cost effectiveness, time window, sources of contamination, volume, and number of samples which can be processed in a batch/cycle. Erratic output can be questionable with reference to precision.[50] Smart-phone surveillance has been deciphered as an alternate and cost effective diagnostic approach for early detection of COVID-19.[51] Some of the recent important tools employed for screening purposes are as follows:

- A novel, rapid, innovative, precise, specific, less time consuming, and cost effective RT-Lamp technique known as Chitra Gene LAMP-N for diagnosing N-gene of COVID-19 virus have been developed by Sree Chitra Tirunal Institute for Medical Sciences and Technology in Thiruvananthapuram, Kerela, under the Department of Science and Technology, Government of India. The test can detect two regions of the gene which nullifies genetic mutation if any Detection time is only 10 min and the sample to result time will be <2 h. At least 30 samples can be tested in a single batch in a single machine. The device presently used for detection of COVID-19 costs nearly 15 to 45 lakh (INR) whereas the new test device amounts to only 2.5 lakh (INR) and the test kit of the presently used polymerase chain reaction (PCR) kit, costs around 2, 500 INR per test, whereas the newly developed test kit costs only 1000 INR per test.[52]
- PCR based genomic detection is the most promiscuous tool for diagnosing SARS-CoV-2.[53-55]
- Centre for Disease Control and Prevention (CDC) has recommended the collection of upper respiratory Nasopharyngeal (NP) swabs for the diagnostic tests which detect N region and two unique probes for SARS-CoV-2.[29]
- Charité algorithm comprises of probes for E protein and RNA dependent RNA polymerase (RdRp). Once both are positive, the sample is again tested against specific SARS-CoV-2 RdRp.[56]
- E protein detection with RdRp.[57]
    - Imaging techniques such as chest Computed Tomography (CT) scans have been facilitated to detect lung abnormalities in this SARS-CoV-2 infection with a scope of detectable abnormalities with disease

progression and prognosis. Efficacy to diagnose asymptomatic carriers remains low with CT-scans.[58,59]

Current treatment regime

While specific vaccines and antiviral agents are the most effective methods to prevent and treat viral infection, there are not yet effective treatments that target the 2019-nCoV.[60] For a moiety to qualify as a potential drug candidate to abate SARS-CoV-2, it must exhibit neutralization efficacy aimed to prevent virus from entering host cells.[61] Host's ACE2 protein must remain unchanged to nullify the probable effects of mutation which might hinder drug development.[62] Understanding structural properties of viral receptors and its targets, viral replication, and assembly might be paramount in finding a remedy for the SARS-CoV-2 pathogenicity. Witnessing a global logarithmic spike in COVID-19 cases, there are no FDA approved drugs as yet. As a rational practice, following are the categorized drugs which are in the present use to combat COVID-19 [Figure 3].

Herbal medicine: Promiscuous approach for amelioration of COVID-19

Plants are integral to human well-being and have been explicitly considered power-houses of pharmacologically active compounds which have constituted the backbone of traditional medicine.[66] Inevitably, bio-prospecting has resulted in screening of plants and their parts for pharmacologically bio-active compounds as a practice of Complementary and Alternate Medicine. Dearth of high throughput techniques has led to minimum exploration of ethno-botanical resources.[67] Archeological evidence suggests that plants were first used by humans for medicinal purposes during the Paleolithic age, with the first written evidence dating back to the Sumerians.[68] An estimate suggests that there are 300,000 plant species of pharmacological significance across the world.[69] The WHO in 2010 has released monographs of medicinal plants which contain a list of species with recognized medicinal benefits. To ensure quality adherence of medicinal plants, certain steps established in the Pharmacopoeias must be followed, including correct identification of the plant species, analysis of the purity and confirmation of the presence, and minimum concentration of the active ingredients chemical marker(s).[70] Most importantly, selection of herbal treatment depends upon the type of herb and patient's symptoms. To generate anti-viral efficacy, sufficient information of both phyto-chemistry and viral pathogenicity needs to be elucidated.[27] In the present practice, molecular approach using DNA barcoding for species identification has gained worldwide acceptance because of its high precision.[71]

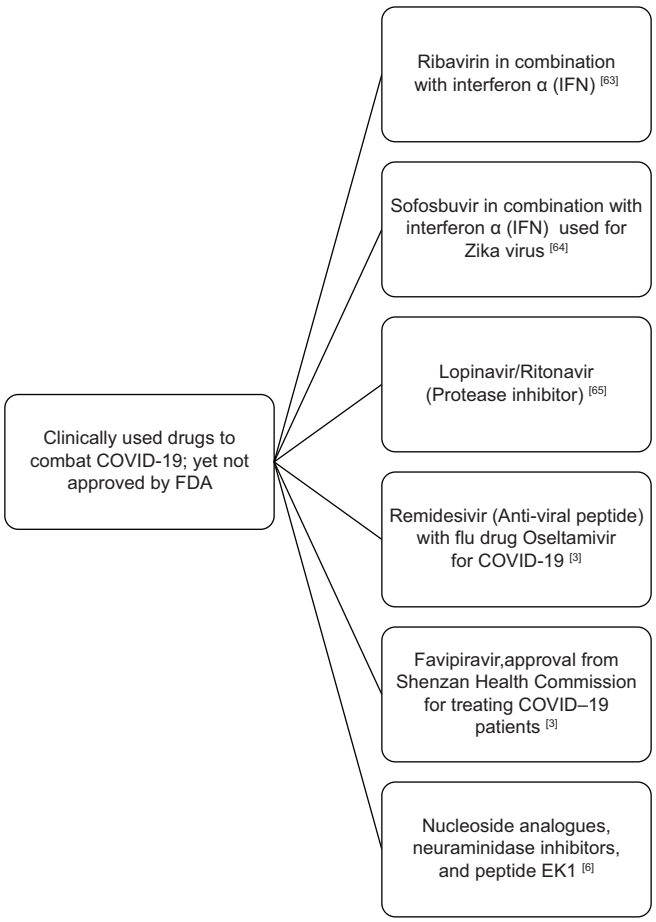


Figure 3: Drugs in the present practice to treat SARS-CoV-2[3,6,63-65]

In the wake of existing global pandemic COVID-19, no approved treatment is deemed fit in modern medicine except repurposed drugs based on symptomatic clinical evidence. Medicinal plants offer a ray of hope as potential Botanical Therapeutics or Green Medicine. Bio-prospecting of traditional herbal medicines and their purified phyto-constituents should be carried out to screen for potential virucidal candidates. This would depend on the structural configuration of natural compounds that exhibit anti-viral activity.[30] A single herb may possess multitude of phytochemical constituents that function singly or in combination to elicit desired pharmacological effect.[72] Efficient, precise, and rapid bioassay systems have been used for rapid screening of anti-viral compounds from plant extracts and their sub-fractions.[73] Screening for plant based novel anti-viral compounds is often considered unsatisfactory because of viral resistance, latency and chances of recurrent infection in immuno-compromised patients.[74] In addition, challenging task is amalgamation of complex biosynthetic pathways with characterization of molecular targets aimed to prevent and treat fatal and complex life-threatening diseases. Likewise, evaluating the compatibility of multifunctional phyto-chemicals and complex multi-component plant extracts for specific disease management also remains cumbersome.[67]

Screening strategy of natural compounds

Strategically, two approaches are being used to screen for potential plant derived anti-viral molecules [Figure 4].

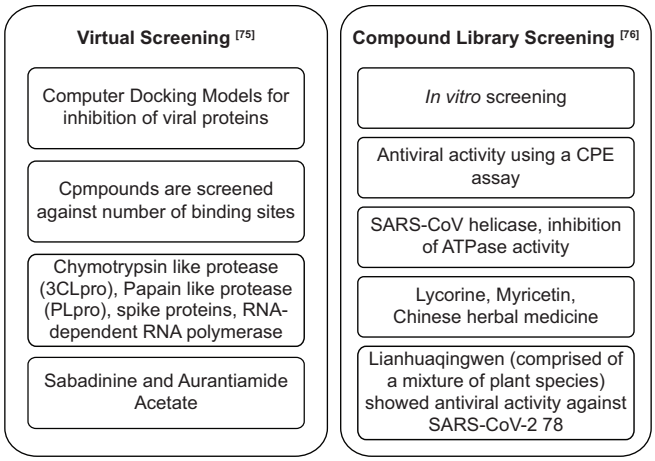


Figure 4: Screening strategy of plant based compounds/ molecules[75-77]

Plants and their sub components have been used as raw material for drug formulation instead of their chemical analogs most of them being used as lifesaving drugs.[78,79] Active biomolecules of plant origin have been explored for their pharmacological relevance and subsequently modulated into drugs for various diseases.[80] *In silico* and biological processing have been used to screen for small molecules from natural compounds as inhibitors against viral proteins of SARS-CoV or MERS.[81] Typically, computer models assess free binding of energy between a ligand and a receptor, with a free binding energy on a lower side is indicative of a stronger bond between the ligand and receptor. In these processes, consistency has been a challenge computer modeling nevertheless allows for comparison of the relative binding affinity of bank of molecules toward the receptor in question.[82,83] An *in silico* integrative model of Absorption, Distribution, Metabolism, and Excretion for screening of 230 Chinese herbs had been validated by oral route of administration.[26] Criteria for screening included evaluation of oral bioavailability, Caco-2 permeability, drug-like value, and drug half-life, with their respective threshold values indicating effectiveness being >30%, ≥0.4, >0.18, and >3 h.[48]

Attributed to the fact that SARS-CoV-2 shares both genomic and proteomic similarities with its predecessor SARS-CoV, it is foreseen that previously screened Chinese herbs can be vital in looking for probable anti-SARS-CoV-2 candidates. Chinese natural drugs offer a wide array of prospective pharmaceutical ingredients for anti-viral therapeutic purposes.[84] Traditional Chinese herbal medicine therapy for viral infections is a combination of herbs prescribed by herbalists depending on the differentiation of the patient's syndrome according to devised diagnostic patterns (inspection, listening, smelling, inquiry, and palpation).[85,86] This therapy works on two underlying principles:

1. Oral effectiveness and
2. Traditional usage compatibility

This is followed by sequential selection procedure for screening compounds with high anti-SARS-CoV-2 potential.[87]

1. Drug likeness
2. Evaluation of oral bioavailability
3. Molecular docking,
4. Network pharmacology analysis
5. Other methods

Notably, half of all anti-viral drugs approved between 1981 and 2014 had been derived from natural compounds.[88] Furthermore, in the present outbreak of COVID-19, recent study suggested that almost 92% of 135 hospitalized patients in Northeast Chonqing (China) were given a combination therapy pertaining to Chinese herbs and Western medicine.[12] Chinese medicine has been used both as a preventive measure[89] and for treatment of COVID-19.[90] A recent report of COVID-19 being cured completely by Chinese herbal medicine on January 24, 2020, has been well authenticated.[91]

Plausibly, combinatorial therapy encompassing Chinese herbs and Western medicine obliterated adverse effects induced by glucocorticoids, antibiotics, and antiviral treatment.[92,93] A contradictory report suggests that there is dearth of enough scientific evidence about anti-viral preventive efficacy of these Chinese herbs and additionally they are known to cause side effects.[94]

Importance of Indian traditional medicine (ITM) in amelioration of COVID-19

India is known to possess an age old rich tradition of herbal medicine as evident from ancient Ayurvedic practices.[95] According to Botanical Survey of India, India is a home to 8,000 medicinal plant species.[96] About 25,000 plant based formulations have been used in folk remedies in Indian medicine.[97] Comprehensively, few insights about Indian traditional herbal system are mentioned.[98]

- India one of 17 mega biodiversity countries.
- Contribute about 7% of world biodiversity.
- India has 15 Agro-climatic zones.
- Medicinal plants found from Himalayan to marine and desert to rain forest ecosystems.
- More than 7000 plants species have known used as medicinal plants out of 17000–18000 flowering plants species in India.
- Ayurveda – more than 3000 years old system of medicine has widespread acceptance.
- Ayurveda, Siddha, and Unani systems of medicine have more than 90% formulations which are plant based.

Traditional Indian medicinal practices include AYUSH, which are successfully practiced for treating various diseases.[99] Holistic approach of AYUSH systems of medicine is based on preventive measures for immune-competency.[31]

- Lifestyle modification
- Dietary management
- Prophylactic interventions

Anti-SARS properties of medicinal plants based on ethno-pharmacological studies have been conducted to strengthen immune-competency and immune-modulation [Table 1].

This fact necessitates further screening of anti-SARS-CoV-2 compounds aimed at containment of COVID-19.[106]

Indian preventive and prophylactic medicinal plants recommended by AYUSH for COVID-19 [Table 2]. Extensive reports supporting use of AYUSH based anti-viral compounds/drugs for respiratory ailments are available. A study has shown anti-mouse coronaviral activity (a surrogate of SARS-CoV) by the plants *Indigofera tinctoria*, *Vitex trifolia, Gymnema sylvestre, Abutilon indicum, Leucas aspera, Cassia alata, Sphaeranthus indicus, Clitoria ternatea, Clerodendrum inerme* Gaertn*, Pergularia daemi, and Evolvulus alsinoides* in Tamil Nadu.[107] *V. trifolia* and *S.*

Table 1: Indian medicinal herbs known to possess anti-HCoV properties[7]

S. No.	Plant Source	Mechanism of Action	Target	Virus	Reference
1	*Allium sativum*	Proteolytic activity and hemagglutination	-	SARS	[100]
2	*Andrographis paniculata*	Suppression	NLRP3, capase-1, and IL-1β	SARS and likely SARS-CoV-2	[101]
3	*Boerhaavia diffusa*	Inhibition	ACE	-	[102]
4	*Clerodendrum inerme* Gaertn	Inactivation	Ribosome	SARS-CoV-2	[103]
5	*Strobilanthes callosa*	Blocking	-	HCoV-NL63	[104]
6	*Vitex trifolia*	Reduction	-	SARS-COV	[105]

Table 2: AYUSH recommended medicinal plant extracts for treating COVID-19 (AYUSH Ministry of Health Corona Advisory- D.O. No. S16030/18/2019-NAM; dated- March 6, 2020)[31]

Indian medicinal plant	Form of extract	Practice	Recommended usage	Effective against
Preventive and prophylactic				
Tinospora cordifolia	Aqueous	Ayurveda	Twice a day for 15 days	Chronic fever
Andrograhis paniculata	Aqueous	Siddha	Twice a day for 14 days	Fever and Cold
Cydonia oblonga	Aqueous	Unani	Twice a day for 14 days	Anti-oxidant, immune-modulatory, anti-allergic, and anti-influenza
Arsenicum album 30	Tablet	Homeopathy	Daily once in empty stomach for 3 days (To be repeated after 1 month till infection persists	Effective against SARS-CoV-2, immune modulator
Symptomatic management of COVID-19				
AYUSH-64	Tablet	Ayurveda	Two tablets twice a day	Respiratory infections
Agastya Haritaki	Powder	Ayurveda		Upper respiratory infections
Anuthaila	Oil	Ayurveda	Two drops in each nostril daily morning	Respiratory infections
Adathodai Manapagu	Aqueous	Siddha	10 ml twice a day	Fever
Bryonia alba	Tablet	Homeopathy		Reduces lung inflammation
Rhus toxico dendron	Tablet	Homeopathy		Viral infections
Atropa belladonna	Tablet	Homeopathy		Asthma and chronic lung diseases
Bignonia sempervirens	Tablet	Homeopathy		Asthma
Eupatorium perfoliatum	Tablet	Homeopathy		Respiratory symptoms
Add on interventions to conventional care				
Vishasura kudineer	Tablet	Siddha	Twice a day	Fever
Kaba sura kudineer	Tablet	Siddha	Twice a day	Fever, cough, sore throat, and shortness of breath

indicus have remarkably exhibited reduction in inflammatory cytokines using the NF-kB pathway which is responsible for respiratory distress in SARS-CoV.[108] *C. ternatea* has been identified as a metalloproteinase inhibitor, ADAM17, a metalloproteinase which shreds ACE2, an event responsible for generation of mature virus particles.[109] Replication of SARS-CoV has been found to be arrested by *Glycyrrhiza glabra* and *Allium sativum* emerging as a prospective candidate against SARS-CoV-2.[110] *C. inerme* Gaertn has significantly inactivated the viral ribosome, further investigations need to be envisaged to target SARS-CoV-2 protein translation.[103] Similarly, *Strobilanthes cusia* has been explored for blocking HCoV genome synthesis and inducing papain such as protease activity.[104] Ethano-medicinal studies to screen for medicinal plant species *Hyoscyamus niger*, *Justicia adhatoda,* and *Verbascum thapsus* in Himalayan forests against bronchitis have been conducted in recent past. Further exploratory studies are required to establish a possible overlap in molecular mechanism of influenza and SARS-CoV-2.[111] *H. niger* has exhibited broncho dilation property and had inhibitory effects on Ca2+ channel which could be targeted for orf3a Ca2+channels that triggers downstream pathways on viral infection.[112] *Coriandrum sativum* is known to possess inhibitory effects against ACE 2, *Punica granatum cassia* had shown to exhibit specific inhibitor mode of action against virus while *Boerhaavia diffusa, Cynara scolymus, Coscinium fenestratum, occidentalis,* and *Embelia ribes* were non-specific inhibitors.[103,113] *Andrographis paniculata* was found to suppress NOD-like receptor protein 3 (NLRP3), caspase-1, and interleukin-1βmolecules which play crucial role in pathogenesis of SARS-COV and most likely SARS-CoV-2 as well *Salacia oblonga*[114] exhibited suppressive effects on angiotensin II, AT1 signal linked to pulmonary damage. Some plants such as *Ocimum sanctum*, *Ocimum kilim* and *Scharicum*, *Solanum nigrum*, and *Vitex negundo* have been known to possess anti-HIV reverse transcriptase activity and hold a promise to possess anti-SARS-CoV-2 reverse transcriptase activity.[115-118]

DISCUSSION

COVID-19 has emerged as the most fatal pandemic with high mortality across the globe and its unprecedented community spread is wreaking havoc. Daunting is the task to screen for promising anti-SARS-CoV-2 candidates catering to prophylactic, therapeutic, and immune-modulatory effects. A high of mutation especially in spike protein has rendered virus to evolve and emerge in due course of time. Mutagenesis has not only contributed to higher rates of transmission but also infectivity. Molecular diagnostics had been revamped to incorporate features of testing and tracking. Along with routine RT-PCR and Rapid Antigen Tests, an innovative and indigenous testing approach, *Feluda Test* is a cost effective and time intensive approach to RT-PCR tests.[119] India has established its own genome surveillance platform Indian SARS-COV-2 Genomics Consortium, an initiative by Ministry of Health and Family Welfare, Government of India.[121] This platform is repository of mutated genomes which along with epidemiological and sero-surveillance data are analyzed for further action plan to minimize the Positivity Rate and Case Fatality Ratio. "Green" therapeutic interventions have been given considerate importance in addition to present therapeutic options available. Novel active ingredients screened and processed from herbal plants are known to deliver multitude of anti-viral properties especially in respiratory ailments. This holds promise as plant derived molecules possess antagonistic and inhibitory properties against both viral structural and functional proteins which arrest viral replication hence preventing its spread within host to distant locations.[120] In addition, a recent joint initiative of the Ministries of AYUSH, Health, Science and Technology through the Council of Scientific and Industrial Research with technical support from the Indian Council of Medical Research has recently began with clinical trials to establish bio-efficacy of four Ayurvedic formulations (Rasayanas) — Ashwagandha, Yashtimadhu, Guduchi, Peepli, and Ayush 64 for the purpose.[121]

CONCLUSION

With this devastating pandemic having crossed all geographical barriers, and frequent mutations to add on to crippling scenario; targeted prophylactic approach needs to be envisaged. With no approved treatment options available, an insight leading to repurposing of drugs and *in silico* screening of plant derived bio-therapeutics holds a promise to mitigate the contagion. With some vaccine candidates being granted Emergency Use Authorization, a vast repertoire of pharmacologically active compounds needs to be explored as a treatment regime. ITM in conjunction with TCM, Traditional Persian Medicine, and other holistic approaches are being deciphered, though still in nascent stages. We believe our AYUSH system is robust and gratuitous for us to get an approved cure against the pandemic. Novel Active Pharmaceutical Ingredients can offer a wide array of therapeutics possessing anti-SARS-COV-2 properties with minimal risk imparting drug resistance.

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