REVIEW ARTICLE

Management of the Post-COVID Condition with Ashtadashanga Churna (Poly herbal Ayurveda medicine)

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Abstract

Ethnic Pharmacological Relevance: The post-COVID sequel in COVID 19 survivors led to a new strain on health-care professionals at the end of the pandemic. Although the pathogenesis of which is not fully understood symptoms that are mostly seen in post-COVID sequel are fatigue, shortness of breath or difficulty in breathing, loss of memory and concentration, sleep problems, persistent cough, chest pain, trouble speaking, muscle ache, loss of smell or taste, depression or anxiety, fever, decrease quality of life, and olfactory and gustatory dysfunction. Ashatadashanga Churna (AC) an Ayurvedic polyherbal formulation is taken into consideration for targeting these post-COVID sequelae. **Aim of this Review:** Ashtadashanga churna can be a potent drug in the treatment of post-COVID sequela classical polyherbal formulation mentioned in the Yogratnakara textbook under the jwara (fever) chapter, one of the authoritative Ayurvedic textbooks. It contains 18 herbal drugs. Each drug of the formulation as an individual and whole formulation is studied to provide a comprehensive insight into its action on post-COVID sequelae and general health improvement. **Materials and Methods:** To examine the impact of each ingredient on post-COVID symptoms, we compiled the information for this article using electronic searches utilizing PubMed, Google Scholar, and Web of Science. **Results:** This medicine's different probable modes of action are scavenging free radical species, inhibiting inflammatory markers, immunomodulation, and protective effect. It is found to be indicated in similar signs and symptoms which is taken into consideration. It is found that all contents contribute to treating disease either individually or in a synergistic way. **Conclusion:** AC medicines may be potential as supplements or substitutes for treating post-COVID sequelae and for improvement of health. Ashtadashanga churna can be a potent drug in the treatment of post-COVID sequel so further research is needed in this formulation.

Key words: Ayurveda, Ashtadashanga Churna, Post – COVID, Polyherbal medicine, Therapeutic mechanism

INTRODUCTION

On 11 March 2020, the World Health Organization (WHO) declared COVID-19 as a global pandemic. Globally, 7,028,881 fatalities and 752,517,552 confirmed cases of COVID-19 have been reported to the WHO as of February4, 2024. A total of 13,156,047,747 doses of vaccines have been given as of January 23, 2023. According to the WHO, the post-COVID-19 condition affects people who have had SARS-CoV-2 infection in the past, usually 3 months after the onset of COVID-19, and has symptoms that last at least 2 months and cannot be accounted for by another diagnosis. Fatigue, shortness of breath or difficulty breathing, memory, concentration, or sleep issues, persistent cough, chest pain, difficulty speaking, muscle aches, loss of smell or taste, depression or anxiety, fever, decreased quality of life, and olfactory and gustatory dysfunction are the symptoms that are most commonly seen in post-COVID sequelae.[1] The term "post-COVID" was also created by the Centres for Disease Control and Prevention (CDC) to describe medical symptoms that persist for more than 4 weeks following COVID-19 infection.[2]

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Ayurveda has gained immense popularity and acceptance in recent years. These herbal and Herbo metallic products treat symptoms and causes of the disease that boost our immunity and improve our overall health condition. During the pandemic period, allopathic practitioners have made many trials, the same goes for Ayurvedic medicines.[3] Ayurvedic medicines have shown better effects in treating mild and moderate COVID cases during COVID period. In the present work, the review study is done to evaluate the potential of Ashtadashanga churna, a polyherbal classical Ayurvedic medicine mentioned in Yogaratnakar, it is a combination of 18 different herbs and as per classical text, it is therapeutically effective in swasa (dyspnea), Kasa (cough), Sotha (inflammation), jirna jawara (chronic fever), and aruchi (tastelessness). Since similar symptoms are also seen in post-COVID sequel we are investigating this formulation and significance of its contents for the treatment of post-COVID condition.

MATERIALS AND METHODS

Several widely used databases were used to find published articles, including SciFinder, Google Scholar, MEDLINE, PubMed, and Science Direct. Using these specific keywords post-COVID, pathogenesis, mechanism, prevalence, *Draksha, Vitis vinifera, Amrita, Tinospora Cardifolia, Sati, Hedychiun spicatum,* Karkatakashringi*, Pistacia lentiscus, Musta, Cyperus rotundus, Rakta Chandana, Pterocarpus santalinus, Sunthi, Zingiber officinale, Katukarohini, Picrorhiza kurroa, Patha, Cissampelos pareira, Bhunimba, Andrographis panicultata, Duralabha, Fagonia cretica,* Usira, *Vetiveria zizaniodes, Padmaka kasta, Prunus cerasoides, Dhanyaka, Coriandrum sativum,* Haribera, *Coleus vettiveroides, Kanthakari, Solanum surattense, Pushakarmula, Inula racemose, Nimbatwak, Azadirachta indica*, phytochemistry, anti-inflammatory, antioxidant, antifibrosis, neuroprotective, phytoconstituents, medicinal properties mechanism of action, using the conjunctions OR/AND, we looked for and extracted published literature.

Epidemiology

On the 95th day following the commencement of symptoms, Professor Paul Garner, from Liverpool School of Tropical Medicine and the Co-ordinating Editor of the Cochrane Infectious Diseases Group, penned an opinion, he claimed, I could not work more than 3 h out of bed. I get palpitations, buzzing in my ears, and periodic cognitive fog.[4] British Medical Association's online survey of medical professionals according to their findings, one third of the 3729 clinicians who responded to a question about patient's ongoing symptoms following COVID-19 claimed they have dealt with or observed patients struggling with post-COVID sequelae.[5] In this regard, Han *et al*. prospective's analysis of 114 very ill COVID-19 patients revealed that 35% of patients had lung fibrotic-like alterations up to 6 months after infection.[6] Contrarily, Latronico *et al*. demonstrated that only a small percentage of critically ill COVID-19 patients (12%) had persistent respiratory symptoms at 6 months, even though residual abnormal chest-X ray were found in roughly 70% of them at 3 months.[7] Compared to other critically ill patient populations (1–10%), COVID-19 patients had pulmonary vascular micro and macro thrombosis in the range of 20–30%.[8-10] 60 mild-critical COVID-19 patients are prospectively evaluated for the presence of brain microstructural abnormalities by Lu *et al*. After 3 months, they discovered alterations in 50% of patients who had recovered.[11] In addition, anecdotal evidence highlighted hypometabolism of the olfactory/rectus gyrus in both patients, demonstrating the long-term damage to the brain in two COVID-19 patients.[12] Further investigations examining diverse groups of COVID-19 patients with mild to severe symptoms indicated that persistent anosmia could last for up to 6 months after symptoms first appeared.[13-16]

More importantly, it showed that among a subset of 44,759 patients without a history of mental illness, the estimated overall probability of being diagnosed with a new mental illness within 90 days of receiving a COVID-19 diagnosis was 5.8% (depression anxiety disorder = 4.7%; mood disorder = 2%; insomnia = 1.9%; and dementia [among those under 65 years old] = 1.6%). In compared control cohorts of patients with influenza and other respiratory tract illnesses, these values were all shown to be significantly higher than those in the study population. After acute COVID-19, cardiac arrhythmias and chronically high blood pressure have also been documented[17,18] Women were shown to be more likely than men to report fatigue and anxiety/depression at the 6-months follow-up in the post-acute COVID-19 Chinese trial, which is consistent with findings from SARS survivors.

MECHANISM BEHIND THE DEVELOPMENT OF POST COVID SYMPTOMS

Mechanism

The pathological hallmark of ARDS, diffuse alveolar damage (DAD), is distinguished by an initial acute inflammatory exudative phase with hyaline membranes, which is followed by an organizing phase and a fibrotic phase.[19]

Cytokine storms produced by an abnormal immune mechanism can lead to the initiation and promotion of pulmonary fibrosis. Epithelial and endothelial damage occurs during the inflammatory phase of ARDS due to the uncontrolled release of matrix metalloproteinases. Exudative, proliferative, and fibrotic phases are anticipated to overlap as ARDS progresses along its pathologic course.[20] The exudative phase causes alveolar flooding and respiratory discomfort by releasing

proinflammatory cytokines such as IL-1, TNF-α, and IL-6, allowing neutrophils to adsorb, and disrupting the endothelial-epithelial barrier.[21] Following the exudative phase is the fibroproliferative phase, which sees the accumulation of fibrocytes, fibroblasts, and myofibroblasts in the alveolar compartment and the excessive deposition of matrix components such as fibronectin, collagen I, and collagen III.[22] The precise reason why not all patients experience fibrosis is still unknown, despite the fact that ARDS appears to be the main predictor of lung fibrosis in COVID-19.[19] Numerous research revealed that COVID-induced ARDS is distinct from the classical ARDS (High and low elastance type). The pulmonary fibrosis in COVID-19 differs from that of IPF and other fibrotic lung illnesses, particularly in light of pathological results that indicate the site of injury was the alveolar epithelial cells rather than the endothelium cells.[23] Some of the mechanisms responsible for the persistence of cardiovascular sequelae in post-acute COVID-19 viral infections include - direct viral invasion, immune response that damage the structural integrity of the myocardium, pericardium, and conduction system, high levels of circulating cytokines and toxic response mediators, such as nitric oxide, IL-6, TNF-α, and calcium channel activity modulation, sarcomere rupture and fragmentation, enucleation, transcriptional alterations, and a strong local immunological response.

In post-acute COVID-19, endocrine symptoms may result from iatrogenic complications, immunological and inflammatory damage, and direct viral harm, all these causes pancreatic β-cell damage, inflammatory alterations in the hypothalamic-pituitary axis, thyroid, and adrenal cortex.[24-26] The relationship between COVID-19 and diabetes appears to be bidirectional in two ways: First, diabetes pre-existing as a risk factor for COVID-19 severity, and second, hospitalization in COVID-19 infection causing new-onset of diabetes during the long-COVID course.[24-27]

Some of the mechanisms that are responsible for thrombo-inflammation are Endothelial injury, complement activation, platelet activation and platelet-leukocyte interactions neutrophil extracellular traps, the release of pro-inflammatory cytokines, disruption of typical coagulant pathways, and hypoxiathey cause disseminated intravascular coagulation and the onset of thromboembolic states, which can aggressively affect a variety of tissues, especially those that are more vulnerable to ischemic processes, such as the pulmonary, cardiovascular, and cerebrovascular tissues.[28]

It is seen that SARS-CoV-2 mediates tubular pathogenesis and AKI by directly infecting the human kidney.[29] Viral tropism, or the binding of spike protein to ACE2, which is abundantly expressed in the kidneys, allows SARS-CoV-2 to directly impact the kidney. Other direct mechanisms proposed include endothelial dysfunction, coagulopathy, direct activation of viral complement, and high levels of circulating cytokines, nephrotoxic medications and volume depletion.

Post-acute sequelae of COVID-19 (PASC) have been documented to have prominent neuropsychiatric symptoms, with typical symptoms including cognitive decline, sleep problems, depression, posttraumatic stress disorder, and substance use disorders. They might include neurodegeneration brought on by acute COVID-19's side effects, and autoimmune processes with. They might also comprise static brain injury acquired during acute COVID-19.[30] Common chronic inflammation, viral persistence in tissue reservoirs, or reactivation of other latent viruses and complex multifactorial sequelae of COVID-19 are some possible reasons.

Ashtadashanga churna (AC) - A polyherbal Ayurvedic medicine

We can say that persistent hyperinflammation caused during COVID infection, any remnant part of the virus, any other infection, and comorbidity which are exaggerated by COVID infection, weak immune system are some probable reasons for post-COVID sequel. Its full mechanism is being searched so that precise treatment can be given to patients. Considering all these symptoms we have selected a classical Ayurvedic polyherbal formulation Ashtadashanga churna for its treatment after reviewing its properties and indication of its contents [Table 1].

Draksha (*V. vinifera*)

Resveratrol, mangiferin, quercetin, and DHQ administration to mice prevented the development of edema and body weight loss while minimizing the histological damage to the lungs brought on by bleomycin (BLM).[64] When compared to the CCl4-intoxicated rats, the rats in the VVPF (*V. vinifera* polyphenols) group significantly ($P < 0.05$) decreased the fold expression of the pro-inflammatory mediators in lung tissues, particularly for NFκ-B, iNOS, and TNF-α. The lungs showed percentage reductions of 90.817%, 96.590%, and 96.438%.[65] Resveratrol a polyphenol present in high concentration in skin of red wine grapes was found to regulate ACE2 expression and function and thus could decrease the severity of SARS-COV-2 disease.[65] In comparison to mice fed a high diet alone those fed a high-fat diet supplemented with resveratrol displayed elevated ACE2 expression and higher ACE2 protein levels. Such a finding indicates that polyphenols may influence the severity of COVID-19 by altering the mount of ACE2.[66,67]

Amrita (*Tinospora cordifolia*)

In relation to COVID-19, Guduchi have been documented to show a variety of noteworthy properties, including antipyretic, anti-inflammatory, antioxidant, anti-infective, anti-neoplastic, and immuno-modulatory effects.[68] *Tinospora cordifolia* has been shown to contain several important

Table 1: Contains Ayurveda name with other details including botanical name, part used, reference showing the therapeutic activity

Ayurveda Name	Botanical name	Used Part	Reference showing the therapeutic activity
Draksha	*Vitis vinifera*	Fruit	Antiviral and anti-inflammatory activity[31-33]
Amrita	*Tinospora Cardifolia*	Stem	Antiviral, anti-inflammatory, immunomodulatory activity[34-36]
Shati	*Hedychiun spicatum*	Tuber	Antiviral activity[34]
Karkatakashringi	*Pistacia lentiscus*	Gall	Antimicrobial, Anti-inflammatory Activity[37,38]
Musta	*Cyperus rotundus*	Tuber	Antiviral, antibacterial, anti-inflammatory activity[39-41]
Rakta chandana	*Pterocarpus santalinus*	Heartwood	Anti-inflammatory activity[42,43]
Sunthi	*Zingiber officinale*	Tuber	Antiviral, anti-COVID and antituberculosis[44,45]
Katukarohini	*Picrorhiza kurroa*	Root	Antiviral activity[34]
Patha	*Cissampelos pareira*	Root	Antiviral, Anti-COVID activity[46-48]
Bhunimba	*Andrographis panicultata*	Whole plant	Antiviral and anti-COVID activity[34,48]
Duralabha	*Fagonia cretica*	Whole plant	Antibacterial and antifungal Activity[49,50]
Usira	*Vetiveria zizaniodes*	Root	Antituberculosis, anti-COVID activity[51,52]
Padmaka kasta	*Prunus cerasoides*	Bark	Antibacterial activity[53,54]
Dhanyaka	*Coriandrum sativum*	Fruit	Antibacterial, antifungal, anti-COVID and anti-inflammatory[55-59]
Hribera	*Coleus vettiveroides*	Root	Antibacterial, Antioxidant activity[60,61]
Kanthakari	*Solanum surattense*	Whole plant	Anti-COVID and antibacterial activity[62,63]
Pushakarmula	*Inula racemose*	Root	Antiviral activity[34]
Nimbatwak	*Azadirachta indica*	Bark	Antiviral activity[34]

phytochemicals, including tinosporine, tinocordiside, diterpenoid furano lactone, tinosporaside, cordifolide, cordifol, syringin, clerodane furano diterpene, tinosporidine, columbin, and heptacosanol. Immunomodulatory action has been observed for syringin and cordifolioside, *A. tinosporin*, a diterpenoid, has been specifically touted for treatment of the targeted viruses, such as the herpes simplex virus (HSV), HTLV, and HIV-1 and HIV-2 retroviruses in all subgroups. In the *in-silico* study model of phytochemicals of giloy it has been reported tinocodiside, a compound present in giloy, dock with ACE2-RBD complex. Tinocordiside-rich extracts of Giloy, according to the author, would be one additional effective method for preventing COVID-19 from entering host cells, and Giloy's overall immunomodulatory properties would strengthen innate immunity against COVID-19 infections.[69] In LPS-induced Raw 264.7 macrophages, a rat model of neuroinflammation, and an arthritic model, tinospora cordifolia extract (TCE) inhibits the production of pro-inflammatory cytokines such as IL-1, IL-6, IL-17, and TNF-α.[34,70] The polysaccharide G1-4A from *T. cordifolia* exhibits anti-microbial activity by preventing the survival of Mycobacterium tuberculosis (MTB) strains that are drug-sensitive as well as multiple drug resistant under both *in vitro* and *in vivo* conditions by modulating the host immune system in a TLR4-dependent manner.[35,70] These results, therefore, imply that *T. cordifolia* possesses antiviral and anti-inflammatory effects.[34,70] It has been seen that *T. cordifolia* (Tc) extract has a preventive effect in the murine asthma model against oxidative stress, the release of pro-inflammatory mediators, and redox signaling. The Tc extract exhibits medicinal potential for inflammatory lung disease treatment including asthma.[71]

Sati (*H. spicatum*)

The rhizome extract, which has been recommended for treating bronchitis, indigestion, eye disease, and inflammations, has reportedly been found to include essential oil, starch, resins, organic acids, glycosides, albumin, and saccharides. In addition, it is employed as a laxative, stomachic, carminative, stimulant, brain tonic, and in cases of diarrhea. According to studies essential oil has anti-microbial properties that are effective against bacteria and fungi.[72,73] Rhizome has 4% of its weight in essential oil. Rootstock has a variety of aphrodisiac, emmenagogue, expectorant, stimulant, stomachic, and tonic properties.[74] Recurring paroxysmal bouts of dyspnea (bronchial asthma) in 25 patients were helped by a daily dose of 10 mg of powdered rhizome and were fully alleviated in 4 weeks.[75] Patients with tropical pulmonary eosinophilia were treated with *H. spicatum* powder in clinical research, and after 4 weeks of treatment, the eosinophil count was reported to have decreased by 60.54%.Chlorpheniramine maleate at 2 mg/kg increased preconvulsive dyspnea time by 71.3%, whereas aqueous and ethanolic extracts of *H. spicatum* at various doses (100, 200, and 400 mg/kg) demonstrated dose-dependent protection against histamine-induced bronchospasm in Guinea pigs

increases in pre convulsive dyspnea time from 39.2 to 75.1% and 25.8 to 65.1%, respectively. The results showed that both extracts had equivalent effects with CPM, a well-known H1 blocker.[76]

Karkatshringi (*P. lentiscus*)

P. lentiscus oil therapy corrected all bleomycin-induced changes in oxidative stress markers, it was suggested that *P. lentiscus* oil may have powerful antioxidant characteristics that contribute to its ability to protect against bleomycin-induced fibrosis.[77] In a mouse model of asthma brought on by ovalbumin, mastic significantly decreased airway hyperresponsiveness, decreased the production of inflammatory cytokines (IL-5 and IL-13), and suppressed the release of chemokines (eotaxin, eotaxin2, and regulated on activation, normal T-cell produced and released) in bronchoalveolar lavage fluid.[78] *P. lentiscus* hydrosol demonstrated anti-inflammatory efficacy by inhibiting the release of proinflammatory cytokines IL-1, IL-6, and TNF-α in lipopolysaccharide (LPS)-activated primary human monocytes. It inhibited NF-κB, a crucial transcription factor in the inflammatory cascade, in LPS-activated U937 cells, controlling the expression of both the mitochondrial citrate carrier and the ATP citrate lyase genes. *P. lentiscus* hydrosol inhibited these two crucial steps in the citrate pathway. As a result, the levels of inflammatory mediators downstream the citrate route, including ROS, NO, and PGE2, were decreased. Results revealed *P. lentiscus* hydrosol's metabolic profile and anti-inflammatory effects, shedding light on its potential as a therapeutic agent.[37]

Musta (*Cyperus rotandus*)

The inflammatory cytokine IL-6 production and mRNA expression were both suppressed by α-cyperone. In addition, treatment with α -cyperone reduced the nuclear translocation of the p65 NF-κB subunit and the transcriptional activity of NF-κB in LPS-induced RAW 264.7 cells.[79,80] α-Cyperone inhibited the NF-κB and NLRP3 signaling pathways, primarily by upregulating SIRT1, to show a protective effect on LPS-induced ALI(acute lung injury) in mice. This offers a prospective medication for the management of ALI brought on by LPS.[81] In a study by administering a suspension of dried Brewer's yeast subcutaneously to albino rats, pyrexia was induced, and the alcoholic extract of *C. rotundus* shown highly significant ($P < 0.001$) antipyretic action. The 6-OHDA-induced production of reactive oxygen species, nitric oxide, decreased mitochondrial membrane potential, and caspase-3 activity was all reduced by a water extract of the rhizome of *C. rotundus*. In primary mesencephalic culture, a water extract of *C. rotundus* rhizoma is also shown a notable protective effect against harm to dopaminergic neurons.[79].

Rakta Chandan (*P. santalinus*)

Studies conducted *in vitro* and *in vivo* revealed the heartwood and bark had hepatoprotective, antibacterial, anti-inflammatory, and anti-diabetic properties. Savinin, calocedrin, and eudesmin were three specific lignans found in *P. santalinus* heartwood extract. TNF-α was shown to be inhibited by these substances, and they also had an antiproliferative impact with an IC50 value of 40 g/mL.[82-84] According to early phytochemical screening, the extract contains flavonoids and polyphenolic chemicals, which may be what gives the extract its anti-inflammatory and antioxidant properties. The potent antioxidant flavonoid has also been linked to analgesic effects, especially through focusing on prostaglandins, according to research. As a result, it is reasonable to assume that cyclooxygenase (COX) inhibitory activity in conjunction with antioxidant activity may lower the production of free arachidonic acid from phospholipid or may inhibit the enzyme system responsible for the synthesis of prostaglandins, which would then relieve pain sensation.[85] Phloridzin has also been demonstrated to have anti-inflammatory properties via reducing PGE2 and IL-8 synthesis and structural characteristics of phloridzin interact with COX-1, COX-2, PGES-1, and 5-LOX, indicating that it has the potential to be a strong inhibitor of these enzymes it exhibits antipyretic properties.[86]

Sunthi (*Zingiber officinalis*)

Alcohol extracts improve mice's immunological health by increasing macrophage phagocytosis, whereas crude extracts also improved humoral and cell-mediated immune responses. The bioactive components of ginger, such as nevirapine, β-sitosterol, 6-gingediol, germacrene, methyl-6-shogaol, 6-gingerol, α-linalool, 6-shogaol, gingerdion, and zingiberene, are known to inhibit viral replication; sitosterol is one of these and is the most potent RT enzyme inhibitor; its TNF- α, also referred to as an anti-influenza cytokine, is said to be present in ginger. The ginger rhizome and its primary compounds, such as gingerols, and shogaols, prevent the creation of prostaglandins and leukotrienes, as well as cyclooxygenase and lipoxygenase activities and pro-inflammatory cytokines.[87-89]

Kutiki (*P. kurroa*)

It is known that *P. kurroa* extract may prevent inflammatory cells including mast cells, neutrophils, and macrophages from proliferating. The findings of a study demonstrated that *P. kurroa*'s anti-inflammatory activity is achieved through modulating NF-κB signaling, which inhibits the generation of mediators and cytokines produced by macrophages. The existence of bioactive components linked to antibacterial activity was shown by phytochemical study of *P. kurroa* Benth rhizomes. Different chemical tests and TLC (thin-layer chromatography) analyses on various

extracts of *P. kurroa* rhizomes confirmed the presence of glycosides, sterols, and phenolic substances. The ethanolic and methanolic extracts of *P. kurroa* have been shown to have antibacterial activity against Gram-positive bacteria such as Bacillus subtilis, Staphylococcus aureus, and Micrococcus luteus as well as Gram-negative bacteria like *E. coli* and *Pseudomonas aeruginosa*. Cucurbitacins were discovered to be cytotoxic and to have anticancer effects in another investigation.[90-92] D-mannitol, kutkiol, kutkisterol, apocyanin, phenol glucosides, androsim, picein iridoid glycosides, resins, sugar, tannins, kutkin, picroside I, II, and III, kutkoside, minecoside, picrorhizin, andarvenin III are the main chemical constituents. Kutkin is the primary active ingredient of *P. kurroa*.[93] Apocynin decreased the synthesis of thromboxane A2 in concentration-dependent manner while increasing the release of prostaglandins E2 and F2. Apocynin also greatly reduced the aggregation of bovine platelets brought on by arachidonic acid, possibly by preventing the synthesis of thromboxane. These results suggest that apocynin may be a useful tool for the development of novel anti-inflammatory or antithrombotic drugs, in addition to its anti-inflammatory effects.

Patha (*Cissampelos pareira*)

The roots of *C. pareira* were extracted in 50% ethanol, and it was discovered to be highly polyphenolic (1, 1-diphenyl-2-picrylhydrazyl), and to have strong antioxidant properties both *in vitro* and *in vivo*.[94] Treatment with *C. pareira* extract reduces oxidative stress caused by thyroxine and heart hypertrophy, likely through improving calcineurin activity and increasing antioxidant enzyme activities, so it can be helpful in cardiac injury also.[95] The whole plant extracts of *C. pareira* (aqueous and alcoholic) were shown to be able to inhibit the virus at least up to 60% *in vitro* tests for viral inhibition of SARSCOV-2. Whole plant hydroalcoholic extract displayed a 98% inhibition. The single molecules that make up *C. pareira* were likewise capable of inhibiting viral particles, with pareirarine exhibiting the maximum level of 80% inhibition. This demonstrated that *C. pareira* can prevent the SARS-CoV-2 virus from replicating *in vitro*.[96] It has been seen Higher concentrations of alkaloids (bebeerines, hayatidin, hayatin, and hayatin) and flavonoids in the hydroalcoholic extract of *C. pareira*'s roots, and these compounds exhibited hepatoprotective effect against CCl4-induced liver damage in rats.[94]

Bhunimba (*A. paniculata*)

Positive antiviral, anti-inflammatory, immunomodulatory, and antipyretic properties of *A. paniculata* and its active components may be helpful for treating COVID-19.[97]. The plaque assay revealed that post-infection treatment with *A. paniculata* and andrographolide greatly reduced the production of infectious virions in Calu-3 cells infected with SARS-CoV-2, with IC_{50} values of 0.036 g/mL and 0.034 M, respectively.[98] In a study according to computational results, andrographolide effectively interacts with important prospective therapeutic targets of viral entry points such furin (−10.54 kcal/mol), TMPRSS-2 (−9.50 kcal/mol), ACE2 (−8.99 kcal/mol), and cathepsin L (−8.98 kcal/mol) that are connected with human hosts. In addition, it inhibits the inflammatory regulators TLR4-MD2 and IL-6, which encourage virus-induced inflammation and cause a cytokine storm in the body of the host.[99] Active components of *A. paniculata* have shown promising effects against 3CLpro and its virus-specific target protein, human hACE2 protein, according to recent *in vitro* and *in silico* investigations. They also suppress the generation of infectious virion.[98] There have also been reports of antivenom, analgesic, anticancer, antidiabetic, antifertility, anti-inflammatory, antimalarial, antimicrobial, antioxidant, antipyretic, antiviral, antiretroviral, and neuroprotective properties. The majority of pharmacological activity are caused by andrographolide, a key distinctive active principle.

Duralabha (*F. cretica*)

In the rat hippocampus cells that had been exposed to oxygen glucose deprivation, *F. cretica* L. demonstrated an oxidative stress-suppressing action at the molecular level (cytosolic enzymatic level and nuclear gene expression level), in addition to directly quenching free radicals.[100] In rat hippocampal slices that had undergone ischemic reperfusion injury, it is examined the up-regulation of VEGF and direct platelet aggregation as well as the down-regulation of COX2 and VCAM genes.[101] The majority of the antioxidants isolated from higher plants are polyphenols (such as phenolic acids, tannins, coumarins, anthraquinones, and flavonoids) with redox properties, which allow them to act as reducing agents, hydrogen donors, singlet oxygen quenchers, and possibly chelate metal ions.

Discovered active phytochemicals in this natural herb include carbohydrates, flavonoids, glycosides, steroids, saponins, alkaloids, triterpenoidal glycosides, amino acids, chlorides, sulfates, and anthraquinoids. Fagonia species have a wide range of biological activities, including anti-inflammatory, antimicrobial, antioxidant, and cardio protective effects. The potential efficacy of *F. cretica* extracts and HPLC fractions against MDR GI pathogens was demonstrated.[102]

Usira (*Vetiveria zizanioides*) (Figure 12)

The ethanolic extract of *V. zizanioides* successfully scavenged the production of free radicals O_2, H_2O_2, OH, and NO. The extract demonstrated robust antioxidant activity in a dose-dependent manner in each of these techniques. The results showed that a standardized aqueous root extract of *V. zizanioides* supplement had a considerable dose-dependent nephroprotective efficacy against experimental nephrotoxicity caused by doxorubicin. It is a beneficial

nutritional supplement for treating renal illness so it will be helpful in repreparing of kidney damage caused by COVID -19 infection. Based on the GC-MS chromatogram study, nootkatone, dehydroaromadendrene, isokhusenic acid, vetivone, and isolongifolene were found in the methanol extract of *V. zizanioides*.[103] On connecting with spike protein, laevojunenol from *V. zizanioides* modifies the spike's affinity for ACE-2, potentially acting as a therapeutic drug for SARS-COV-2 by preventing the virus from entering a human cell.[104]

Padmaka kasta (*Prunus cerasoides*)

Extract of *Prunus cerasoides* (PC) may enhance neuroglobin level as it is seen in a model of cerebral ischemia, PC extract (PCE) upregulate neuroglobin (Ngb) levels and has neuroprotective qualities by inhibiting the formation of ROS and apoptosis that are brought on by stroke, this research indicates that PCE may be taken into account for therapeutic applications in situations when elevated Ngb levels would be advantageous, such as reducing the functional damage caused by cerebral ischemia.[105] Flavones glucoside, narigenin, apigenin, β-sitosterol, genkwanin, sakuranetin, prunetin, noctacosane, triacontane, β-sitosterol, ursolic acid, oleic, palmitic, and stearic acids, afzelin, kaempteritrin, and naringenin, etc., are phytoconstituents of plant and it is seen to show diuretic, depurative, antiabortifacient, antipyretic and refrigerant, astringent, and anti-inflammatory activities.[106]

Dhanyaka (*Coriandrum sativum*) (Figure 14)

Findings have shown that *C. sativum* has the ability to lower IL-1, IL-6, and TNF- α. Following ingestion of *C. sativum*, IL-1, IL-6, and TNF-α significantly decreased in direction.[56] According to a study, 9 of CSL's active components may have the ability to inhibit 51 COVID-19-related target genes. EGFR, AR, JAK2, PARP1, and CTSB are the main targets for COVID-19 treatment. The outcomes showed that CSL may have a variety of effects on immune response regulation and viral infection inhibition, suggesting that it may be effective against COVID-19.[58] It has been suggested that the most important mechanism of action against COVID-19 is *C. sativum*'s inhibitory efficacy against angiotensin-converting enzyme. *C. sativum* exhibits a wide range of pharmaceutical potentials, including antidiabetic, antiseptic, anti-inflammatory, antihypertensive, and anxiolytic.[58]

Haribera (*C. vettiveroides*) (Figure 15)

Superoxide radical scavenging activity, hydroxyl radical scavenging activity, and DPPH radical scavenging activity were tested using an *in vitro* antioxidant assay against all three of the tested methods, the extract demonstrated strong antioxidant activity. *P. vettiveroides* demonstrated high effectiveness even at extremely low concentrations. *P. vettiveroides* have strong antioxidant and anticancer properties.[107] Spathulenol, with the chemical formula $C_{15}H_{24}O$, is the substance that *P. vetiveroides* uses as an active ingredient.[108] Treatment with a methanolic *C. vettiveroides* extract in comparison to the control group, Jacob dramatically reversed the alterations seen in the streptozotocin-induced animals the pancreas of rats given methanolic extract showed normal architecture when inspected under a microscope. The findings show that *C. vettiveroides* Jacob's methanolic extract has strong anti-diabetic effect.[109]

Kanthakari (*S. surattense*) (Figure 16)

Methanolic extract of *S. surattense* is proved to show a great nephroprotective agent and have shown strong antifungal activity against dermatophytic fungi *T. rubrum*, *C. albicans* and *E. floccosum* and it also possesses antioxidant activity, so it will check any opportunistic fungal infection as COVID infection make body more vulnerable for such infections. The standard (vitamin C) displayed 96.95% DPPH scavenging activity with an IC_{50} value of 7.6 g mL^{-1}, which was virtually equal to the methanolic extract's 83.15% DPPH scavenging activity and 10.15 g mL^{-1} IC_{50} value. This was almost equal to it. The crude methanolic extract efficiently protected HEK 293 cells against cisplatin by up to 95.31% at a higher dose (500 g mL^{-1}) and was nearly as effective as the common nephroprotective drug rutin.[110] The plant *S. surattense* contains active phytochemicals such as saponins, alkaloids, phenols, solamargine, solasurine, solasonine, gum, ascorbic acid, sterols, torvoside K, torvoside L, khasianine, glycosides, flavonoids, aculeatiside A, glycoalkaloid, steroidal compound, steroidal alkaloids, and polyphenol (caffeic acid). The use of this medicinal plant in pharmaceutics is very common, and it continues to be a rich source of active phytochemicals with a variety of functions, including antibacterial, anti-larvicidal, anthelmintic, antimalarial, antioxidant, antidiabetic, anti-asthmatic, and anti-cancerous.[111] Molecular docking (blind) was carried out with AutodockVina's assistance., research revealed that, of the 13 phytochemicals examined, eight displayed extremely high binding affinities to 3CLpro, while the remaining four displayed moderate to high binding affinities. Furthermore, the bindings were to the region to which the protease inhibitor N3 has been demonstrated to bind, suggesting that they may be useful in preventing COVID infection.[62]

Pushakarmula (*Inula racemose*)

The root is used medicinally and is thought to be particularly effective for chest pain, particularly pre-cordial pain, dyspnea, asthma, pleurisy, and tuberculosis.[112] The polyherbal formulation containing *I. racemosa* exhibits antihistaminic, mast cell stabilizing, and spasmolytic effects in an experiment on guinea pig ileum where histamine was used to produce bronchoconstriction. According to Srivastava, an alcoholic extract of the root of *I. racemosa* significantly reduces

mast cell degranulation and passive cutaneous anaphylaxis (PCA) caused by egg albumin in albino rats. 50 patients with ischemic heart disease received 6 g/day of Pushkara guggulu, an extract of *I. racemosa* and Commiphora mukul, in clinical research. Precordial pain, discomfort with effort, dyspnea, and mean serum cholesterol have all improved. The ECG pattern has also shown a noticeable improvement. It has been reported that giving gum guggul along with *I. racemosa* to 200 patients with ischemic heart disease restored their electrocardiogram (ECG) total cholesterol, triglyceride, and total blood lipids to normal.[113,114] The sesquiterpene lactones atlantolactone and isoalantolactone have been shown to be the primary phytochemical substances in various regions of the plant.

Nimbatwak (*A. indica*)

The most adaptable and practical medicinal plant ever discovered is the neem (*A. indica* A. Juss). It contains a wealth of bioactive substances in every portion that have been traditionally used to cure a variety of conditions, including infectious disorders.[115] Nimbin (triterpene) in particular has demonstrated antipyretic, fungicidal, antihistamine, and antiseptic effects. Nimbin is also thought to have anti-inflammatory and antioxidant properties. By lowering the generation of reactive oxygen species, these properties help to lessen damage.[116] Flavonoids, which act as prostaglandin biosynthesis inhibitors, endoperoxides, and enzymes including protein kinases and phosphodiesterases, all of which are implicated in inflammation, are also present in neem.[117] Limonoid is a key bioactive component of neem. Limonoid is a furanolactone that is well-known for its ability to inhibit the production of inflammatory mediators. It is also referred to as a pain reliever because it stimulates the activation of endogenous opioid pathways, including those that produce interleukins and tumor necrosis factor alpha (TNF-α).[115] Numerous studies have shown that neem extracts have the ability to scavenge free radicals and lessen ROS-mediated cell damage. Normalizing lipid peroxidation and reducing ROS-mediated cell death are achievable with neem. In addition, neem extracts can increase the number of CD4 + and CD8 + T-cells and drastically lower the release of proinflammatory cytokines. All these properties contribute in fighting infection and cytokine storm caused by COVID 19 infection.

DISCUSSION

We have faced 3 waves of COVID-19 and finally we learned and developed different tools and techniques to fight this deadly disease with the help of vaccines, medicines, immunity enhancement and by improving our health-care system. Pandemic is gone but survivors of this disease are still facing post-COVID sequel which has created another burden on health care workers. As we have seen above, site of SARS COVID19 has its primary site in lungs on ACE2 receptor but as disease progresses it involves almost all systems of body (cardiovascular, GIT, endocrine, renal, nervous system, etc.). Variation in genome sequence also have been seen, due to various mutations, in receptor binding domains(RBDs) and spike proteins. Many hits and trials had had been tried during this unseen condition still we did not find any right Path for this. These sequelae could be brought on by cellular injury, an active innate immune response that generates inflammatory cytokines, or a pro-coagulant state brought on by SARS-CoV-2 infection. Asthadashanga churna is a classical polyherbal formulation mentioned in Ayurveda text Yogaratanakara in jawar (fever) chapter and it is indicated in fever, inflammation, dyspnea, anorexia, and cough. Almost similar along with some other symptoms are present in COVID-19 infection on this basis we have selected this medicine for post-COVID sequel.

Through the scavenging of reactive oxygen species (ROS) and the inhibition of oxidant-producing enzymes, antioxidants have the power to counteract the effects of oxidants. The frequency, development, and severity of COVID-19 are significantly influenced by the overproduction of ROS and the lack of antioxidant mechanisms. The interactions between transcription factors with opposing effects that lead to oxidative damage and inflammation are explained by interconnected pathways. *V. vinifera* reduces inflammatory markers like TNF-α, IL-6, IL-10, and IL-12, modulate proteins involved in apoptosis and MAP Kinase signaling pathways, improve histopathological and biochemical parameters (ALT, AST, ALP, and others), and improve mitochondrial enzyme activities. *T. cardifolia* inhibit IL-6 and TNF-α inflammatory markers, improves innate immunity, and reduces oxidative stress. *H. spicatum* at various doses demonstrated dose-dependent protection against histamine-induced bronchospasm in Guinea pigs. Patients treated with *H. spicatum* shows reduced eosionophil counts. *P. lentiscus* hydrosol demonstrated anti-inflammatory efficacy by inhibiting the release of proinflammatory cytokines IL-1, IL-6, and TNF-α in lipopolysaccharide (LPS)-activated primary human monocytes. It inhibited NF-κB, a crucial transcription factor in the inflammatory cascade, in LPS-activated U937 cells, controlling the expression of both the mitochondrial citrate carrier and the ATP citrate lyase genes. The inflammatory cytokine IL-6 production and mRNA expression were both suppressed by α-cyperone of Cyperus rotundus. The 6-OHDA-induced production of reactive oxygen species, nitric oxide, decreased mitochondrial membrane potential, and caspase-3 activity was all reduced by a water extract of the rhizome of *C. rotundus*. Phloridzin a content of *P. santalinus* has also been demonstrated to have anti-inflammatory properties via reducing PGE2 and IL-8 synthesis and structural characteristics of phloridzin interact with COX-1, COX-2, PGES-1, and 5-LOX, indicating that it has the potential to be a strong inhibitor of these enzymes it exhibits antipyretic properties. *P. kurroa*'s anti-inflammatory activity is achieved through modulating NF-κB signaling,

which inhibits the generation of mediators and cytokines produced by macrophages. Apocynin decreased the synthesis of thromboxane A2 in concentration-dependent manner while increasing the release of prostaglandins E2 and F2. In this way, it acts both as anti-inflammatory and antithrombotic agent. Likely through improving calcineurin activity and increasing antioxidant enzyme activities, so *C. pareira* can be helpful in cardiac injury and to reduce oxidative stress. Pareirarine present in *C. pareira* have been demonstrated inhibition of SARSCOV-2. It also possesses hepatoprotective effect. The plaque assay revealed that post-infection treatment with *A. paniculata* and andrographolide greatly reduced the production of infectious virions in Calu-3 cells infected with SARS-CoV-2, with IC_{50} values of 0.036 g/mL and 0.034 M, respectively, therefore act as anti-COVID drug. In rat hippocampal slices that had undergone ischemic reperfusion injury, it is examined the up-regulation of VEGF and direct platelet aggregation as well as the down-regulation of COX2 and VCAM genes by *F. cretica*. The ethanolic extract of V. zizanioides successfully scavenged the production of free radicals O_2, H_2O_2, OH, and NO. The extract demonstrated robust antioxidant activity in a dose-dependent manner in each of these techniques. V. zizanioides modifies the spike's affinity for ACE-2, potentially acting as a therapeutic drug for SARS-COV-2. *C. sativum*'s action against COVID-19 is by inhibitory efficacy against angiotensin-converting enzyme. *C. sativum* has the ability to lower IL-1, IL-6, and TNF- α, following ingestion of *C. sativum*, IL-1, IL-6, and TNF-α significantly decreased in direction. *C. vettiveroides* exhibit antioxidant and antidiabetic properties. The standard (Vitamin C) displayed 96.95% DPPH scavenging activity with an IC50 value of 7.6 g mL^{-1}, which was virtually equal to the methanolic extract of *S. surattense* 83.15% DPPH scavenging activity and 10.15 g mL^{-1} IC50 value. Similar to catechin (standard) scavenging activity, it displayed 89.95% hydroxyl radical scavenging with an IC50 value of 11.89 g mL1. Also act as antiasthmatic drug. Root of *I. racemose* exhibit cardioprotective, antiallergic, analgesic, and hepatoprotective activity. *A. indica* extracts can increase the number of CD4 + and CD8 + T-cells and drastically lower the release of proinflammatory cytokines. With all those above-mentioned activities most of these herbal drugs contain different types of alkaloids, flavonoids, polyphenols, and other active ingredient which helps in fighting and suppressing post-COVID symptoms.For instance, by blocking endogenous antioxidant enzymes such NQO-1 and HO-1, Nrf2 reduces inflammation. The pro-inflammatory cytokines and chemokines IL-1, IL-6, IL-8, PGE-2, COX-2, TNF-α, MMP-3, and MMP-4, on the other hand, are upregulated by NF-κB. Reduced glutathione (GSH), which is decreased in SARS-CoV-2 infection, has a crucial antioxidant role. Almost all contents of this powder more or less exhibit anti-inflammatory, antioxidant activity, and immunomodulatory activity. During this pandemic many have adopted Ayurvedic regimen to fight this disease.

Tinospora cardiofolia, *C. pareira*, *A. panicultata*, *V. zizaniodes*, *C. sativum*, *S. surattense*, *A. indica* all these plants have shown anti-COVID activity in various studies. Corona virus mainly causes respiratory infection and develops ARDS and subsequently involves almost all system of body by causing cytokine storm, or through different mechanisms. Sequel of this infection remains in body and causes post-COVID symptoms. *H. spicatum*, *A. indica*, Inula racemose, *S. surattense*, *C. rotundus* acts on inflamed lungs and helps in bringing down inflammation, repair acute lung injury, decrease bronchospasm, and decreases histamine release. Many patients have developed diabetes and those who already have increased dose of medicine after corona virus infection. *A. panicultata*, *A. indica*, *C. vettiveroides*, and *T. cardiofolia* have antidiabetic effects which will help diabetic patients to control glucose level. *P. cerasoides*, *F. cretica* these drugs have neuroprotective effect which will prevent post-COVID neuronal symptoms. *V. zizaniodes* and *S. surattense* are nephroprotective in nature which will heal kidney in post infection period. *C. pareira*, and *I. racemose* possesses cardioprotective properties. *Z. officinale* increases humoral immunity and helps in inhibition of viral replication. Fever one of the post-COVID symptom can be countered by *P. santalinus*, *T. cardiofolia*, *A. panicultata*, *A. indica*. Thrombosis have also been noticed in some post-COVID patients, *P. kurroa* and some other drugs have antithrombotic properties. *C. pareira* and *F. cretica* are hepatoprotective and GI protective which also heals the damaged parts. Overall, this medicine will be capable of, healing the effected part, preventing further damage and will enhance the immunity and quality of life.

CONCLUSIONS

It is concluded that this post pandemic burden can be tackled by both allopathic and Ayurvedic ways, that is, from integrated approach. 18 herbal drugs of the formulation help directly or indirectly in curing post-COVID symptoms through different mechanisms. Asthadashanga churna acts not only as antiviral drug but it also acts on different systems of body via therapeutic and protective mechanism. Immunomodulation, inhibition of pro inflammatory markers, acting as antioxidant agent are some of its therapeutic mechanisms. Some drugs of this formulation are hepatoprotective, nephroprotective, and neuroprotective in nature which protect these organs from the harmful effect of cytokine storms. Diabetes and cardiovascular damage done during the infection period will also be addressed by this formulation. Various pathways based on the previous studies have been discussed here for its probable mode of action; therefore, further studies and clinical trials of Ashtadashanga churna to evaluate its efficacy are needed.

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