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THE ROLE OF *"ASHWAGANDHA"*: AS AN IMMUNOMODULATOR IN POST-COVID MANAGEMENT

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ABSTRACT

COVID-19 is a worldwide respiratory illness caused by "Severe Acute Respiratory Syndrome Corona virus 2." Acute post COVID syndrome occurs more than three weeks after the initial infection, whereas chronic post COVID syndrome occurs more than three weeks after the initial infection. Post COVID symptoms include fatigue, dyspnea, low-grade fever, cough, tastelessness, anosmia, chest pain, myalgia, and sleep and mental disturbances. The exact cause of post-COVID syndrome is unknown. The symptoms of Covid-19 are similar to Vatakaphapradhan Sannipataj Jwara, and there will be Dhatu-Kshayaand Agnimandya Avastha inpost-COVID19infection, according to Ayurvedic concepts. As a result, agnideepana, amapachana, brimhana, andrasayanachikitsa areindicatedinthiscondition. Ayurveda is the best option because it includes both preventive and curative measures. Manyherbshavebe enmentionedin Ayurvedic texts that have immunomodulatory properties or work as immunostimulants. Ashwagandha is a well known or ancient drug that is mentioned inAyurvedic texts as a Rasayan with Immunomodulatory activity. Ashwagandha can be used topreventpost-covidsymptomsbecauseithas propertiesthat promotehealth longevity byincreasing defence mechanism many studies on Ashwagandha have been conducted todemonstrate its immunomodulatory, antioxidant, anti-inflammatory, and neuroprotective properties. Ithas antistressproperties.

KEYWORDS: Immunomodulatory, neuroprotective, anti-inflammatory, Ashwangandha, dhatu-kshya.

INTRODUCTION

COVID-19, a global pandemic has affected individuals to varying degrees, ranging from a few days ofmild symptoms to respiratory distress requiring intensive care unit (ICU) treatment including ventilatorsupport, and even death. Early in the pandemic, it was believed that COVID-19 was a short-term illness. In February 2020, the World Health Organization reported that from the onset to clinical recovery formild cases the duration was approximately 2 weeks and that recovery took 3–6 weeks for patients with the severe or critical disease.[1] However, recently it has become clear that in some patients debilitating symptoms persist for weeks or even months. This means that a subset of people who have recovered from COVID-19 continue to experience symptoms that remain beyond testing negative forthe virus. "Long-COVID" or "COVID long-haulers" or post-COVID Syndrome generally describes thosepersons with COVID-19 who experience symptoms for >28 days after diagnosis.[2] Similar to acuteCOVID-19, patients with long-COVID may experience multiple symptoms that involve the lungs andother parts of the body. The common symptoms experienced by COVID long-haulers are cough (maybedry or wet), fatigue, exertional dyspnea, mild to moderate grade of headache, myalgia, disturbed sleeppatterns, neuropsychiatric and depressive symptoms.[3] 5 The reason for Post COVID Syndrome is mayberoleofSARSCOV-2virusinfunctioningof the body by continue to lingerinbody and destabilizesthe Immuneresponse.[4] Thesepersistentsymptomspresentnewchallengestohealth-careproviders.

Ayurveda has an advantage in dealing with health problems, including the recent Post-COVIDSyndrome, duetoitsholisticapproachtohealthanddiseaseandcosteffectiveness.

Ayurveda, which focuses on disease prevention rather than treatment, has stated a number offormulations that directly act on an individual's immune system and help him cope with the afterEffects. Itdescribes Rasyanasinitsancienttexts, whicharenothingmorethan immunomodulatorswiththe ability to enhance and boost one's immune system if consumed correctly and for a set period oftime. Immunomodulation is a fundamental concept in Ayurveda that has been practised by Ayurvedistsfor centuries. Immunity enhancement in Ayurveda is accomplished through the use of Rasayana andVajikaranatherapies, aswell asOjovardhakaremedies.

Ayurvedaclassifiesanumber of drugsas Rasayanas, which claimtohaveimmunomodul atoryproperties. Like Aswagandha, Amalaki,Guduci,andother Rasayanshavebeen

studiedscientifically and found to have immunomodulatory properties. immunomodulatory effect ofayurvedicformulationsinthepost-covidcondition. Itisbelievedthatthissmallattemptat treating post-covid complications entirely through ayurvedic Rasayana therapy will undoubtedlybenefit patients suffering from mild covid complications. It is believed that this small attempt attreating post-covid complications entirely through ayurvedic Rasayana therapy will undoubtedlybenefit patients suffering from mild to moderate cases and will prove to be a boon in thepreventionandmanagementofpost-COVID carethroughtraditional medicineinthecommunity.

Withania somnifera Dunal (ashwagandha, WS) is widely used in Ayurvedic medicine, the traditionalmedical system of India. It is an ingredient in many formulations prescribed for a variety ofmusculoskeletal conditions (e.g., arthritis, rheumatism), and as a general tonic to increase energy,improve overall health and longevity. Withania somnifera, commonly known as Ashwagandha (wintercherry), is an important medicinal plant that has been used in Ayurvedic and indigenous medicine formore than 3,000 years. Some herbalists refer to Ashwagandha as Indian ginseng. The plant extract hasmany bioactive compounds and thereby exerts antioxidant, anti-inflammatory, and immunomodulatoryactivities. The plant extract and its bioactive compounds are used in the prevention and treatment ofmany diseases, such as arthritis, impotence, amnesia, anxiety, cancer, neurodegenerative andcardiovasculardiseases.

MATERIAL AND METHODS

This literature review was limited to published articles and books in the English language. Differentcomputerizedmedicaldatabaseweresearchedfortheentiredurationofeachdatabaseasav ailableonthe C OVID computer search service and other search resources following keywords were used for thesearch: ashwagandha and common misspellings (ashwaganda, aswaganda, aswagandha), Withaniasomnifera, withaferin, sitoindoside, solanaceae, Indian ginseng andCOVID 19 POST- COVIDManagement, immunomodulatory action, recent researches of ashwagandha, Results of thesesearches were reviewed to identify relevant articles A lot of numbers of articles were found using thesearchmethoddescribedabove.

REVIEW OF LITERATURE

W. somnifera Dunal (Solanaceae), also known as Ashwagandha or winter cherry, is one of the most valuable plants in the traditional Indian systems of medicine. Itisasmall evergreen shrubthat grow storoughly four to five feet tall. In India, it is cultivated, on a commercial

scale, in the states of MadhyaPradesh, UttarPradesh, Punjab, Gujaratand Rajasthan.[5] Ashwagandhaisoneoftheprimedrugsof Ayurvedamaterialmedica. Acharya Charakaincludeditin BalyaandBrimhana-gana.[6] ItisattributedwithBalya, Vrishyaand Rasayanapropertiesandsuggestedassubstituteof Kakoli andKshirakakoli.

The species name somnifera means 'sleepinducing' in Latin, indicating that to it are attributed sedatingproperties, but it has been also used for sexual vitality and as an adaptogen. Some herbalists refer toAshwagandha as Indian ginseng. In Ayurvedic medicine, its root is used as an anti-inflammatory drug forswellings, tumours, scrofula and rheumatism; and as a sedative and hypnotic in anxiety neurosis. Leafpossessesanti-inflammatory,hepatoprotective, antibacterialproperties.

Chemical constituents of WS are always of an interest for the researchers. The biologically activechemicalconstituentsarealkaloids (ashwagandhine,cuscohygrine,anahygrine,tropineetc), steroidalcompounds, includingergostanetypesteroidallactones,withaferinA,withanolidesA-y, withasomniferin-A, withasomidienone, withasomniferols A-C, withanone etc. Other constituents includesaponins containing an additional acyl group (sitoindoside VII and VIII), and withanolides with a glucoseat carbon 27 (sitoindoside IX and X).[7,8] Apart from these contents plant also contain chemicalconstituentslikewithaniol, acylsterylglucosides, starch,reducingsugar, hantreacotane, ducitol,avariety of amino acids including aspartic acid, proline, tyrosine, alanine, glycine, glutamic acid, cystine,tryptophan,andhighamountofiron. WithaferinA, chemicallycharacterizedas4b, 27-dihydroxy-5b-6b-epoxy-1- oxowitha-2, 24-dienolide, is one of the main withanolidal active principles isolated from theplant. WSshowedchemogeneticvariationandsofarthreechemotypeI, IIandIIIhadbeenreported.[9]

The search method described above yielded a large number of articles. According to research, ashwagandha has anti-inflammatory, antitumor, antistress, antioxidant, immunomodulatory, hemopoetic, and rejuvenating properties. Ashwagandha appears to be beneficial to the endocrine,cardiopulmonary, and nervous systems. Few articles on the mechanism of action for these COVID 19effectswerediscovered. Severalpreliminaryanimal studieshavebeencarriedout. There sultsof thesestudiesaresummarisedbelow.

Antioxidanteffect

Thebrainandnervoussystemarerelativelymoresusceptibletofreeradicaldamagethan other tissues because they are rich in lipids and iron, both known to be important in

generatingreactiveoxygenspecies.

Freeradicaldamageofnervoustissuemaybeinvolvedinnormalagingand neurodegenerative diseases, e.g., epilepsy, schizophrenia, Parkinson's, Alzheimer's, and other diseases. Simultaneousoraladministrationof WSextractpreventedanincreaseinlipidperoxidation.[10]

Anxiety and depression: The investigations supported the use of ashwagandha as a mood stabilizer inclinical conditions of anxiety and depression in Ayurveda.[11] WS, however, has an advantage overPanaxginsengin thatitdoesnotappeartoresultinginseng-abusesyndrome, aconditioncharacterizedbyhighbloodpressure, waterretention, muscletension,andinsomnia.[12]

Antiparkinsonianproperties

Parkinson'sdiseaseisaneurodegenerativediseasecharacterizedbytheselective loss of dopamine (DA) neurons of the substantia nigra pars compacta. Ashwagandhasignificantly inhibited haloperidol or reserpine-induced catalepsy and provide hope for treatment ofParkinson'sdisease.[13]

Antiinflammatory properties: The effects of WS, as anti inflammatory in a variety of rheumatologic conditions, have been studied by several authors.[14] Studies have been conducted on the mechanism of action for the anti inflammatory properties of ashwagandha.

Immunomodulation and hematopoiesis: The role of ashwagandha as immunomodulator has beenextensivelystudied. Inamousestudy, Ashwagandharootex tractenhancedtotalwhitebloodcellcount. In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocyticactivity of macrophages when compared to a control group.[15] Recent research suggests a possiblemechanismbehindtheincreasedcy totoxiceffectofmacrophage sexposed toashwagandhaextracts. Nitricoxidehas beendeterminedtohaveasignificant effectonmacro phagecytotoxicityagain stmicroorganismsandtumorcells.

Antibacterial effect: Both aqueous as well as alcoholic extracts of the plant (root as well as leaves) werefoundtopossess strongantibacterialactivity againsta range ofbacteria,as revealed byinvitroAgarWell Diffusion Method. The methanolic extract was further subfractionated using various solvents andthe butanolic sub-fraction was possessed maximum inhibitory activity against a spectrum of bacteriaincluding Salmonella typhimurium. Moreover, in contrast to the synthetic antibiotic (viz.chloramphenicol), theseextractsdidnotinducelysis

onincubation withhumanerythrocytes,advocatingtheir safety to the living cells. Oral administration of the aqueous extracts successfully obliteratedsalmonella infection in Balb/C mice as revealed by increased survival rate as well as less bacterial load invariousvitalorgansofthetreatedanimals.[16]

Adaptogen Ashwagandha acts as a plant which helps the body to adapt to stress in order to correct theimbalanceamongimmuneandneuroendocrinesystem. Itnormalizesthebody functionsaffectedbytheinfluenceofstressbytargetingthehypothalamic-pituitary-adrenalglandaxis. Ashwagand hadecrease cortisollevelsinapersonunderchronicstress, restoringthehealthyadrenalfunction and thusnormalizingthesympatheticnervoussystem.[17]

DISCUSSION

The experimental trends generated from healthy and disease models indicate that WS has a potentialfor 1) maintaining immune homeostasis, 2) regulating inflammation, 3) suppressing pro-inflammatorycytokines, 4) organ protection (in the nervous system, heart, lung, liver, and kidney), andanti-stress,antihypertensive, andantidiabeticactivities.

Ashwagandha (Withania somnifera) (WS) is one of the most extensively experimented Ayurvedamedicinal plants and has been used in Ayurveda practice since centuries. Ashwagandha has beenselected owing to its properties like immune-modulatory, anti stress and antiviral efficacy. In-silicostudies have shown its high binding affinity to ACE2–RBD interface which may stop SARS COV 2 entryinto cells. The WS root extract has shown good results against protracted social isolation induced stressand anxiety which makes it a good medicine for prophylactic use. Furthermore the medicine also hasvery good pulmonary protective function and hence is beneficial in post covid care, there are substantialnumber of studies on Ashwagandha published in reputed peer reviewed journals to establish its efficacy,safety and protective action. Ashwagandha has been shown to reduce symptoms of other conditionsthat are similar to those of long COVID, so we are hopeful that it will be an effective way to combat thecondition."

CONCLUSION

In the Indian system of Ayurveda, Withania somnifera, also known as Ashwagandha. The Ashwagandhahave been extensively used as a valuable drug in Ayurveda. However, its therapeutic potential asimmunomodulatory, apoptogenic, antioxidant, hypoglycemic and anti-cancer activities have beenreported. The extensive survey of literature revealed that WS is an

important source of manypharmacologically and medicinally important chemicals, such as withaferins, sitoindosides and varioususefulalkaloids.

Thus, the above findings clearly indicate that the use of Ashwagandha for activities such asimmunomodulatoryanti-viral and especially against POST-COVID-19 has a logical and scientific basis. We conclude, there needs some experimental and clinical validation to know the reliability andpreventivemeasurementinpost-covidcomplications.

REFERENCES

1. WorldHealthOrganization.ReportoftheWHO-ChinaJointMissiononCoronavirus Disease 2019 (COVID-19). Geneva: WHO, 2020. Available from: https://www.who.int/docs /default-source/coronaviruse/who-chinajoint-mission-on-cov
2. Mendelson M, Nel J, Blumberg L, Madhi SA, Dryden M, Stevens W, et al. Long-COVID: An evolvingproblemwithanextensiveimpact. SouthAfrMedJ, 2021; 111: 10-12.
3. Levison ME. Commentary: WhatWeKnowSoFar About Post-COVIDSyndrome,MSD Manual Professional Version; September 24, 2020. Available from:https://www.msdmanuals.com/professional/news /editorial/2020/09/23/20/17 /post-covid-syndrome.
4. Timesofindia.imdiatimes.com > long covid: who has the higher risk of developingcovid.22. october/2020. asseseddate, 21/01/2021.
5. Ven Murthy MR, Ranjekar PK, Ramassamy C, Deshpande M. Scientific basis for the use ofIndianAyurvedicmedicinalplantsinthetreatmentofneurodegenerativedisorders:Ashwagandha.CentNervSystAgentsMed Chem, 2010; 10(3): 238–246.
6. Proff.K. Nishteswar, K.Hemadri, Dravyaguna Vijnana, Chaukhambha Samskrit Pratishthana, Firstedition, 121.
7. M. Elsakka, E. Grigorescu, U. Stanescu, U. Stanescu, V. Dorneanu. New data referring to chemistryof Withaniasomniferaspecies. Rev.Med.Chir.Soc.Med.Nat.Iasi, 1990; 94(2): 385-387.
8. M.Ganzera,M.I.Choudhary,I.A.Khan.QuantitativeHPLCanalysisofwithanolidesinWithaniasomnifera.Fitoterapia, 2003; 74(1-2): 68-76.
9. A.Abraham,I.Kirson,E.Glotter,D.Lavie.AchemotaxonomicalstudyofWithaniasomnifera(L)Dunal.Phytochemistry, 1968; 7: 957-962
10. J.N. Dhuley. Effect of ashwagandha on lipid peroxidation in stress-induced animals. J.Ethnopharmacol, 1998; 60(2): 173-178.

11. S.K. Bhattacharya, A. Bhattacharya, K. Sairam, S. Ghosal. Anxiolytic-antidepressant activity of Withaniasomniferaglyco withanolides:anexperimentalstudy.Phytomedicine, 2000; 7(6): 463-469.
12. S.K. Bhattacharya, A.V. Muruganandam. Adaptogenic activity of Withania somnifera: anexperimental studyusingaratmodel ofchronicstress.Pharmacol.Biochem.Behav, 2003; 75(3): 547-555.

A. Kumar, S.K. Kulkarni. Effect of BR-16A (Mentat), a polyherbal formulation on druginducedcatalepsyinmice. IndianJ.Exp.Biol, 2006; 44(1): 45-48.

13. K.Anbalagan, J.Sadique. InfluenceofanIndianmedicine (Ashwagandha) onacutephasereactantsininflammation. IndianJ.Exp.Biol, 1981; 19(3): 245-249.
14. L.Davis,G.Kuttan.EffectofWithaniasomniferaoncellmediatedimmuneresponsesinmice.J.Exp.Clin.CancerRes, 2002;21(4): 585-590
15. M. Owais, K.S. Sharad, A. Shehbaz, M. Saleemuddin. Antibacterial efficacy of Withania somnifera (ashwagandha) an indigenous medicinal plant againstexperimental murine salmonellosis. Phytomedicine, 2005; 12(3): 229-235.
16. Kaushik MK, Kaul SC, Wadhwa R, et al. Triethylene glycol, an active component of Ashwagandha (Withania somnifera) leaves, is responsible for sleep induction. PLoS One, 2017; 12(2): e0172508. https://www.ncbi.nlm.nih.gov /pubmed/28207892.