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A CONCEPTUAL STUDY OF *AGAD YOGA* AS PROBABLE ANTIVIRAL MEDICINE FOR COVID-19

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ABSTRACT

The worldwide corona virus disease outbreak, generally known as COVID-19 pandemic outbreak affected the whole world on December 2019 and resulted in a major health crisis. The transmission and mortality rate of COVID-19 appear more severe and uncontrollable and new variants still affecting the population despite being vaccinated. The major complications of COVID-19 are respiratory failure and cardiovascular diseases. Several therapeutic management were put forward but till date there are no specific treatment or medicine developed for this viral infection. The present review summarized the Ayurveda *agad yoga* mentioned in Charak samhita, Sushrut samhita,Aashtanga samgraha, Ashtanga hridaya emphasizes the role of herbs and herbs-derived secondary metabolites in inhibiting SARS-CoV-2 virus. Plant-derived phytochemicals have already been reported to prevent the viral infection by inhibiting the viral replications or terminating their cell life cycle. In this review, we explored 11 *Agad yoga* which are indicated in *jwar(fever), kasa(cough), swasha(difficulty in breathing)* and *janapadodhwamsa vyadhi(epidemic disease)* entioned in Charak samhita, Sushrut samhita, Ashtanga samgraha and Ashtanga hridaya and summarized the mechanistic approaches of their contents as antiviral activity. Reports on the antiviral activity of the contents of *agad yoga* belong to the can be explored for the development of safe and efficacious products targeting COVID-19.

Key Words: SARS-CoV-2, *Agad yoga*, Antiviral activity, *Janapadodhwamsa*.

INTRODUCTION: COVID-19 cases are still increasing day-by-day worldwide and the new variant still affecting the world population. Due to structural differences in S protein, the transmission of SARS-CoV-2 infection is very fast. The patients may die due to acute respiratory distress syndrome (ARDS) caused by systemic inflammatory reactions due to the excessive release of pro-inflammatory cytokines and chemokines by the immune effector cells. In India too, it is transmitting at full speed, although the case fatality rate is below 1.50% **(https://www.statista.com),** which is remarkably less than in other countries, despite the dense population and minimal health infrastructure in rural areas. This may be due to the routine use of traditional AYUSH formulations/drugs, having immunity enhancing potential, by the Indian people.

According to different samhitas and contemporary view points, the newly identified COVID-19 can be categorized under *agantuja vyadhi* (exogenous disease) by inception, caused by *bhoota* (micro-organisms), and transforming to *nija* (endogenous) doshas leading to imbalance of *tridoshas* and causes mainly *pranavaha* (cardio-pulmonary system), *rasavaha*

(cardio-vascular system) and *raktavaha* (vascular and RES) *srotas dushti* vitiation of channels) symptoms. The basic and foremost principle of treatment in ayurveda is designed on the basis of the nature of the disorder, etiology and location. Hence taking into account *rasayana* drugs for enhancing the immunity, *dosha* (mainly *kapha* and *vata*) conciliate drugs i.e *deepana* (stomachic), *pachana* (digestive), *shwasahara* (anti-dyspnea) and *kasahara* (anti-cough) will be effective in this condition. Apart from this, to combat the residual effect of virus on the body, the ministry of ayush suggested *vishaghna chikitsa* (www.ayush.gov.in). The qualities of *visha* is discordant to *ojas* and thus curtail the strength (*ojas*) of the body and may endanger life. The potential of *Agad yoga* (Anti-toxic) are being highlighted as their probable anti-viral action because the contents of *agad yoga* are effective in subsiding vitiated doshas mainly *kapha, vata* and protecting or strengthening the *ojas* (immunity) by virtue of their broad spectrum of pharmacodynamic properties.

Furthermore, the toxicities and ineffective responses to resistant strains of synthetic antiviral drugs have emphasised the search of effective and alternative treatment options,such as plant-derived antiviral drug molecules. Therefore, in the present review, an attempt has been taken to summarize the medicinal plants which are contents of *agad yoga*, reported for exhibiting antiviral activities along with discussing the mechanistic insights into their bioactive components against three most hazardous viruses, namely SARS-CoV-2,HIV,HBV,INFLUENZA. The review covers 11 *Agad yoga* in which their contents reported antiviral activity .

MATERIAL AND METHODS

An extensive literary search on *agad yog* in Brihat-trayee (Charaka Samhita,Sushruta Samhita and Ashtanga Samgraha/Ashtanga Hridaya) along with commentaries, literatures on their contents has been conducted and we have selected some *Agad yog* where they are indicated in *Jwar, Kaas, Swasha* and *Janapadodhwamsa* or *Marak.*

Multiple databases (Science Direct, PubMed, Google Scholar) were also reviewed for their anti-viral activity.

OBSERVATION AND RESULTS

- List of *agad yoga* which are indicated in *Jwar, Swasha, Kaas* and *Janapadodhwamsa*/ *Maraka*:- **TABLE No.1**

S.NO.	*AGADA*	CONTENTS	REFRENCES
1.	***Gandhastinamak Agad***	*Shweta, Vacha, Ashwagandha, Hing, Amrita, Saindhav, Lehsun, Sarsap, Kapitha, Sonapatha, Karanj beej, Vyosh, Shirish pushp, Haldi, Daruhaldi, Vanslochan*, Goat urine, Cow and Horse pitha	Charak Chikitsa 23/95
2.	***RishabhakadiAgad***	*Risbak, Jeevak, Bharangi, Mulethi, Neelkamal, Dhaniya, Nagkesar, Jeera, Sweta aparajita, Kol madhya*	Charak Chikitsa 23/101-104
3.	***Ksharagad***	*Tarun palash shar, Lohit mrid, Haldi, Daruhaldi, Sukla surasa manjarri, Mulethi, Laksha, Saindhav, Jatamansi, Harenu, heeng, shweta, sariva, kushta, vyosh, marich, pippali,*	Charak Chikitsa 23/242-248
4.	***Siddhartakadi Agad***	*Sidharthak, Vacha, Balvach, Hing, Karanj*	Charak

		beej, Devdaru, Manjistha, Triphla, Shweta, Katbhi twak, Sunthi, Marich, Pippali, Priyangu, Shirisha, Haldi, Daruhaldi	Chikitsa 9/69-72
5.	**Sanjivan agad**	*Chandan, Kumkua, Kustha, Kamkashi, Laksha, Priyangu, Musta, Sthauneya, Saileya, Rochana, Madana, Plava, Srivestaka, Vidanga, Ela visala, Ala, Manassila,* Tender leaves of *Surasa, Sprkka, Haldi, Daruhaldi, Valaka, Hingu, Siddhathaka, Padmacarini, Padmakesar,* Flowers and young leaves of *Jati*, Flower of *Arka* and *Shirihsa*, Two *Rodhra*, Two *Brihati, Kaunti, Madhuka, Gandhanakuli, Mudgaparni kana, Syama, Dhyamaka, Nalada, Nata, Sindhuvaraka, Samyaka, Devdaru, Mayuraka*	A.S.40/59-67
6.	***Yapana agad***	*Chandan, Valaka, Musta, Dhyamaka, Katuka, Nata, Dadima, Kumkuma, Sunthi, Kapittha,* Fruit of *Vatsaka*, Seeds of *Karanja, Maricha, Utpala petals of Kamala*, Root of *Nala, Apamarga, Karavira, Anjana, Laksa, Malati, Ahicchatra, Nagapuspa, Amlavetasa, Visala, Rocana, Syama, Sankhpuspi, Priyanguka, Ajaji, Sariva, Kustha, Ajamoda, Kurandaka, Vayastha, Sinduvara, Ela, Kayastha, Vaca, Karkati, Putna, Kesi, Shweta, Girikarnika, Golomi, Simhalomi, Varsabhu, Gajapippali*	A.H.40/68-72
7.	***Chandrodya agada***	*Anjana, Tagar, Kusta, kooth, Hartaal, Manshila, Phalini, Trikatu, sprikka, nagkesar, kesar, harenu, madhuka, jatamansi, rochana, kaaknasa, srivestak, sarjras, balamool, tamalpatra, talishpatra, bhojpatra, khash, haldi, daruhaldi,*	A.H.35/24-32
8.	***Himavana agada***	*Panchval kal, Haritki, Bahera,Amla, Mulethi, Nagkesar, Eluwa, Jivak, Rishbak, Khash, Mishri, Kamal*	A.H.36/63-64
9.	***Lodhradi agada***	*Lodhra*, Flower of *Shirisha, Samanga, Hingu, Renuka, Kana, Usaana Ela, Nepali, Vacha, Yashtimadhu, Utpala, Sinduvaraka, Root of Mandara, Seeds of Karanja, Jyotismati, Nata, Kusta, Sveta, Girikarnika*	A.H.42/83-86
10.	***Bilvadi agada***	Root of *Bilva, Fower of Surasa, Fruits of Karanja, Nata,Suravaha, Phalatraya, Vyosa, Two Nisa, Goat urine*	A.H.42/87-88
11.	***Mahan agada***	*Trivrit, Visalya, Madhuka, The two Nisa, The five Lavanas, Manjista, Tryusana*	A.H.42/89

- List of the ingredients of above described agad yoga, in which there are anti-viral activity are reported:-

TABLE No. 2

S. NO.	PLANT/ FAMILY	PART USED	BIOACTIVE COMPOUND	ANTI-VIRAL ACTIVITY ON VIRUS	MECHANISM OF ANTI-VIRAL ACTIVITY	REFERENCES
	Andrographis paniculata/ Kalmegh/ Acanthacea	Leaf	Andrographo-lide	SARS-CoV-2	Binding potential with active residues of ACE2 that mediate host viral interface	[i]*Dhanshankar* et al
	Justicia adhatoda/ Vasa/ Acanthacea	Leaf	Anisotine	SARS-Cov 2, Influenza virus, HSV	Inhibit Mpro of SARS-CoV-2	[ii]Ghosh et al(2021) [iii]Chavan and Choudhary (2014);
	Achyranthes aspera / Apamarg/ Amaranthacea	Leaf	Oleanolic acid	HSV-I and II	**a)** Inhibited the early stage of multiplication (2–6 h of post infection) of HIV **b)** Inhibit protease enzyme of HIV-I	[iv]Mukherjee et al(2013)
	Allium sativum/ Lehsun/ Liliaceae	Bulb	Ajoene,allicin, allin, methyl allyl thiosulfinat,allitridin,diallyl sulfide, garlicin, lectin	SARS CoV-2	Allyl disulfide, allyl trisulfide, allyl (E)-1-propenyl disulfide, allyl methyl trisulfide, diallyl tetrasulfide, 1,2-dithiole, allyl (Z)-1-propenyl disulfide, 2- vinyl-4H-1,3-dithiine, 3-vinyl- 1,2-dithiacyclohex-4-ene, carvone, trisulfide, 2-propenyl propyl, methyl allyl disulfide, diacetonalcohol, trisulfide, (1E)- 1-propenyl 2-	[v] Thuy et al [vi] Khaerunnisa et al

					propenyl, allyl sulfide, 1-propenyl methyl disulfide, trisulfide, (1Z)-1-propenyl 2-propenyl showed inhibition of the ACE2 protein Allicin (xxv) may act as potential inhibitors of the COVID-19 Mpro	
	Alstonia scholaris/ Saptparn/ Apocynaceae	Leaf	Total alkaloid	IAV,HSV	Aqueous and alcoholic plant extract showed antiviral potential against coxsackie B2, polio virus and herpes simplex virus.	[vii]Antony et al(2014)
	Calotropis gigantea/ Arka/ Apocyanacea e	Latex	Pinoresinol 4-0-(6”-O-vanilloyl)-beta-D-glucopyranoside 6-O-vanilloyltachioside 6-O-vanilloyl-isotachioside	H1N1	Inhibit NF-κB pathway and viral ribonucleoproteins nuclear export of H1N1 virus.	[viii]Parhira et ol(2014)
	Aloe vera/ Asphodelaceae	Leaf	Feralolide,9-dihydroxyl-2-O-(z)-cinnamoyl-7-methoxy-aloesin, aloeresin,quercetin,catechin hydrate and kaempferol	SARS-CoV-2, Infuenza virus	**a)** Inhibit influenza-A virus **b)** Inhibit Mpro of SARS CoV-2 **c)** Quercetin inhibited ACE2 receptor of SARS CoV-2.	[ix]Mpiana et al(2020) [x]Choie et al(2019);
	Eclipta prostrata/ Bhringraj/ Asteraceae	Leaf	Coumestan	HCV	Inhibit HCV NS5B protein leading to RNA replication K.	[xi]Kaushik basu et al (2008)
	Bombax ceiba/ Semal/ Malvaceae	Flower	Kaempferol-3-O-beta-d-glucopyranoside	SARS-CoV-2 and RSV	**a)** Inhibit cytopathic effect of RSV **b)** Inhibit ORF-3a protein of SARS-CoV-2	[xii]Schwarz et al(2014) [xiii]Zhang et al(2015)

	Cyprus rotundus/ Mustak/ Cyperaceae	Rhizome	Humulene epoxide, caryophyllene oxide	SARS-CoV-2,HAV,HSV-I,CVB	Inhibit four target proteins of SARS-CoV-2 such as spike glycoprotein, papain-like protease (PLpro), 3- chymotrypsin-like protease (3CLpro) and RNAdependent RNA polymerase (RdRp).	[xiv]Samra et al(2020) [xv]Amparo et al(2021)
	Albizia procera/ Shirish/ Fabaceae	Bark	Catechin,Protocatechuic acid	IAV,SARS-CoV	**a)** Inhibit integrase enzyme of human influenza virus-I by interacting with Thr66, Gly148, and Glu152. **b)** Inhibit Mpro enzyme of SARS CoV.FPH	[xvi]Panthong et al(2015)
	Butea monosperma / palasha/ Fabaceae	Bark, flower, fruit, root,leaf	5-7-dihydroxy-3,6,4-trimethoxy flavone-7-O-alpha-L xylopyranosyl-O-alpha-L Arabinopyranosyl-O-beta-D Galactopyranoside	EV-71	-	[xvii]Panda et al(2017) [xviii]Tiwari et al(2019)
	Swertia chirayita/ Chirayita/ Gentianaceae	Whole plant	Amarogentin, gentipicrin,7-O-methylswertianin ,Chiraranin	-	Chloroform extract inhibit expression of viral protein R	[xix]Woo et al. (2019)
	Swertia augustfolia/ Gentianaceae	Whole plant	Cycloolivil-4-O-beta-d-glucopyranoside, swertia chiralotone A,swertiachoside A, swertiachirdiol A and Swertiachoside B	HBV HSV-I	Inhibit HBsAg and HBeAg secretion and HBV DNA replication.	[xx]Verma et al(2008) [xxi]Zhou et al(2015)
	Ocimu	Aeri	Ursolic acid,	HSV-I and II	**a)** Inhibit	[xxii]Caamal

	m tenuliflorum / Tulsi/ Lamiaceae	al part	eugenol, 1-8-cineole,rosmarinic acid		replication of HSV-I and II **b)** Inhibit multiplication of HCV	heerera et al(2016)
	Ocimum basilicum	Aerial part	1-8-Cineole, camphor,thymol, eugenol,eugenol epioxide,apigenin,linalool,ursolic acid	HIV-I,HSV.ADV-3,8,11,HVB,EV,CVB-I	**a)** Inhibit ACE2 receptor and 3CLpro of SARS-CoV-2 **b)** Inhibit replication of HBV	[xxiii]Behbahani et al(2013) [xxiv]Kubica et al(2014)
	Ocimum campechianum	Leaf, Aerial part	Beta-caryophyllene and 1-8-cineole	HSV-1 and II,IBV	Inhibit replication of HSV-II and II	[xxv]Maria das gracas et al(2007), [xxvi]Astani et al (2010), [xxvii]Yang et al(2010)
	Ocimum grattisimum	Leaf	Eugenol,Thymol	HSV-1 and II	**a)** Inhibit replication of HSV-I and II **b)** Inhibit multiplication of HCV	[25]Maria das gracas et al(2007), [xxviii]Beneci a and courreges(2000), [xxix]Lai et al(2012)
	Azadirachta indica/ Nimb/ Meliaceae	Bark, Leaf	Gedunin,pongamol, Azadirachtin	SARS-CoV-2,HSV-I,CVB-B4,HBV	-	[xxx]Alzohairy (2016) [xxxi]Rao and yeturu(2020) [xxxii]Nesari et al((2021)
	Zingiber officinale/ Shunthi/ Zingiberaceae	Rhizome	6-gingerol, gingeronone A	SARS-CoV-2,HCV, CHIKV	**6-gingerol-** Inhibit SARS CoV-2 by interacting viral proteases, RNA binding protein and Spike protein **Gingeronone A-** Inhibit 6LU7 and 7JTL of SARS-CoV-2	[xxxiii]Pandey et al(2021) [xxxiv]Kaushik et al(2020) [xxxv]Rathinavel et al(2020)
	Curcu	Rhiz	Curcumin	HBV.SARS-	**a)** combination of	[xxxvi]Kim et

	ma longa/ Harid ra/ Zingib eracea e	ome		CoV-2,HIV,IAV,DENV,CHIKV,VSV,ZIKV and RSV	vitamin C, curcumin and glycyrrhizic acid exhibited COVID-19 Mpro inhibitions. Cucrcumin inhibited human respiratory syncytial virus replication and budding **b)** HIV: Inhibit replication and degrade viral protein **c)** DENV: Inhibit viral entry, replication and protease enzyme **d)** IAV: Inhibit replication **e)** EV 71:	al(2009) [xxxvii]Jennings and park(2020) [xxxviii]Thimulappa et al(2020)
	Aegle marmelos/ Bilva/ Rutaceae	Root, stem, bark, fruit	Seselin	SARS-CoV-2	Inhibit the receptors SARS-CoV-2S protein, COVID19 main protease, and free enzyme of the SARS-CoV2 (2019-nCoV) main protease	[xxxix]Niveditha et al(2021)
	Citrus sinensis/ Nimbuk/ Rutaceae	Fruit	Hesperidin,luteolin, vitamin c	SARS-CoV-2,HAV	Inhibit ACE2 receptor, RdRp, spike protein and Mpro of SARS-CoV-2 (under clinical trials, phase-II)	[xl]Battistini et al(2019)
	Nigella sativa/ Kalonji/ Ranunculaceae	Seeds	Nigellidine and α- hederin	SARS-CoV-2	Nigellidine and α-hederin found to have the best potential in COVID-19	[xli]Umar et.al.(2016)
	Phyllanthus emblic	Fruits			. Phyllaemblicin B (xiv) and phyllaemblinol	[xlii] Yin et al [xliii] Wu et al

	a/ Amla/ Phyllanthaceae				showed binding affinity to Helicase (Nsp13).	
	Solanum nigrum L./ Makoi/ Solanaceae	Seeds		HCV	Chloroform extract decreased the expression or function of HCV NS3 protease in a dose dependent manner and GAPDH remained constant.	[xliv]Javed et al. (2011)
	Valeriana wallichii/ Jatamansi/ Valerianaceae	Roots		HCV	Alcoholic root extract inhibited HCV by binding with HCV NS5B protein.	[xlv]Ganta et al. (2017)
	Vitex negundo/ Nirgundi/ Verbanaceae	Leaves		HIV	Alcoholic extract of leaves inhibits HIV-1 reverse transcriptase activity in in vitro assay thus exhibits anti-HIV activity. D	[45]Ganta et al. (2017)
	Withania somnifera/ Asgand/ Solanaceae	Roots		IBD virus, SARS-CoV-2	**1.**Hydro-alcoholic root extract of W. somnifera showed antiviral properties against IBD virus by cytopathic effect reduction assay. **2.**Withanone and withaferin a have been found effective against SARS CoV 2 in bioinformatics studies and asgandh extract is under clinical trial. (https://www.researchsquare.com/article/rs-	[xlvi]Pant et al. (2012).

					17806/v1), (http://www.bioinformation.net/016/97320630016411.pdf)	
	Azadirachta indica/ Neem/ Meliaceae	Leaves			Nimboloid (terpenoid lactone) is effective in regulating the ARDS	[xlvii] Shetty et al [xlviii] Schumacher et al
	Berberis aristata/ Daruharidra / Berberidaceae	Bark		EV71	-	[xlix]Wang et al. (2017)
	Cassia fistula/ Amaltas/ Fabaceae	Fruit, bark, flower leaves		Hepatitis B	Hydroalcoholic extract of C. fistula suppressed extracellular HBV DNA production.	[l]Indrasetiawan et al. (2019)
37.	**Cinnamomum zeylanicum/ Daalchini/ Lauracea**	Stem Bark	Cinnamaldehyde, eugenol, cumic, methyl amyl ketone		Bark etract inhibit SARS-CoV-2	[li] Zhuang et al [lii] Kubo et al
38.	**Glycyrrhiza glabra L./ Mulethi/ Fabaceae**		Glycyrrhizin,Liquirtin, glucoliquirtin apioside, 1-methoxyphaseolin	SARS-CoV-2	-	[liii] Yang et al [liv] Tanemoto et al
39.	**Picrorhiza kurroa/ Kutki/ Planta**	Rhizome, roots	Iridoids, acetophenones	Vpr(viral protein) of HIV	-	[lv]Win et al. (2019)

	ginacea					
40.	**Pongamia pinnata (L.)/ Karanj/ Fabaceae**	Fruit, leaves, root, bark	Karanjin, 3-metho-oxypongapin	Hepatitis B	Aqueous extract interfered with HbsAg.	[lvi]Mathayan et al. (2019)
41.	**Acorus calamus L./ Vacha / Acoraceae**	Whole plant.	Asarones	HSV-1 and 2	Alcoholic etract showed potent antiviral activity.	[82]Umamaheshwari, N. and Rekha, A. 2018. Sweet flag (*Acorus calamus*) – An incredible medicinal herb. *J. Pharmacog Phytochem*. 7(6): 15 - 22.
42.	**Punica granatum L/ Dadim / Punicaceae**	Whole plant.	Triterpenoids,steroid,glycosides,saponins,alkaloids, flavonoids and tannins	HIHV-3	Evaluation of peel extract as anti-adenovirus activity in vitro by report that the peel extraction exhibited strong activity against adenovirus with a selectivity index (SI) value of 8.9 Aqueous extract of Punica granatum, respectively, showed anti-HSV-1 activity probably due to the presence of polyphenolic compounds that contributed to their antiviral activity.	[lvii](Moradi et al., 2016).
43.	**Solanum virginianum**	Fruit	Solasodine,glyco alkaloid (solanosine), steroidal	HIV	-	[lviii]Kumar and Pandey, 2014).

	L./ Solanaceae		compound (carpesterol) and steroidal alkoloids (caffeic acid, coumarins, and triterpinoids)			
44.	**Solanum surattense/ Solanaceae/ Kateri**	Fruit.	(solasonine	PPR virus Reo virus	Fruit extract possesses anti-reverse transcriptase (RT) activity.	[69]Kumar & Pandey (2014)
45.	**Terminalia chebula/ Haritki/ Combretaceae**	Fruit, leaf and bark.	Tannins Chebulic acid, chebulinic acid, chebulagic acid, gallic acid, corilagin and ellagic acid	HSV-2,HIV-1	The fruit extract in 50% ethanolic extract, chebulagic acid, chebulinic acid were found to have direct anti-viral activity against HSV-2. The aqueous extract was found to be effective at a concentration of 25 µg/mL in the thfluorogenic assay against HIV-1 protease.	[lix](Kesharwani *et al*., 2017).
46.	**Tinospora sinensis/ Giloy/ Menispermaceae**	Fruit, leaf and bark.	Tinosporin, tinosporic acid, berberine, Palmitine, tembatarine, mangoflorine , choline, isocolumbin, tetrahydropalmatine.		Berberine (xxi), isocolumbin,magnoflorine (xxii) and tinocordiside have binding efficacy against surface glycoprotein and receptor binding domain and main protease.	[lx] Sagar et al
47.	**Tribulus terrestris/ Gokshur/ Zygophyllaceae**				Methanol fruit extracts showed *in vivo* antiviral potential on newcastle disease virus Haemagglutination titer *in vivo* vero cell line culture. The extract	[lxi] Malik.et.al

					exhibited enormous anti Newcastle disease virus effect in vero cell line	
48.	**Piper longum/ Pippali/ Piperaceae**				Piperlactone A have antiviral potential against SARS-CoV-2	[lxii] Joshi et al

DISCUSSION: Epidemics have not been new to India. Ayurveda has a biggest role in the prevention and management of COVI-19 pandemic, and has recorded its valuable experiences. In this review, we have systematically summarized and analyzed the *agad yoga* and the pharmacological importance of contents, which may be effective against COVID-19. By identifying the antiviral property of certain phytocompounds, it is possible to effectively characterize medicinal herbs that could help to alleviate the SARS-CoV-2 viral infection. In above described *agad yoga* every *agad* formulation contents possessing antiviral activity for instance, anisotine of *vasa* has significantly inhibited the main protease (Mpro) of SARS-CoV-2 and the inhibitory potential of this alkaloid is higher compared to the inhibitory activities of lopinavir and darunavir. Oleanolic acid inhibited the early stage of multiplication, specifically 2–6 h of post infection of the viruses. Ajoene of allium sativum prevents HIV-induced destruction of CD4+ cells and enhances cellular immunity. Allicin and allyl methyl thiosulfinate inhibit the entry of virus by disrupting viral envelope and cell membrane. An in silico study of cyprus rotundus demonstrated that humulene epoxide has remarkable binding affinity to four target proteins,such as spike glycoprotein, papain-like protease (PLpro), 3-chymotrypsin-like protease. A number of antiviral bioactive compounds of ocimum, such as ursolic acid, eugenol, 1,8-cineole, and rosmarinic acid which exhibit potential to inhibit virus cell life cycle. Aegle marmelos plant produces a bioactive compound named seselin having activity against multiple targets of SARS-CoV-2. Solanum extract possess antihistaminic, mast cell stabilizing and decreased capillary permeability effect and hence has potential role in the treatment of asthma and allergic disorders.

Therefore, the metabolites of contents of *agad yoga* possess multiple therapeutic activities. Overviewing the symptoms of COVID-19 mainly respiratory and upper gastro-intestinal parts are involved and *Agad* can combat symptom of COVID-19 because ingredient have *vishaghna,jwarghna,kasahara,kanthya,Shoolaghna,Shwasahara,Deepana,Pachana, anulomana,Grahi,shothahara karma* . Hence, by reviewing the potential of Indian medicinal plants, *agad yoga* might become innovative treatment options and can be penned down to defeat this viral pandemic. The antiviral resistance property and the adverse effect of pharmaceutical drug, there is an urgent need of advanced ayurveda drug. According to *ayush* guidelines, they have suggested *vishghna* treatment to reduce the residual effects of virus hence, Due to

unique combination of drugs in above described *Agad yoga* and their anti-viral, anti-inflammatory, anti-allergic, immunomodulatory potential hence, they can produce synergistic effects and may resulting superior therapeutic outcomes against SARS-CoV-2. This review provides collective information regarding probable pharmacological and therapeutic action of *Agad yoga* against COVID-19. Further laboratory and clinical trials of *agad yoga* are necessary.

CONCLUSION: As a matter of fact, the pandemic is not over yet. There are more questions than answers about diagnosis, treatments, and, what we need most, effective cures and aftercare. This review may serve as reference in traditional herbal medicine in *agad* formulation for COVID-19 treatment. The present review compiled pharmacological information of 11 *agad yoga* with 46 contents possesing anti-viral activity,which may combat the viral infection and post-COVID complications through different mechanisms. Hesperidin, apigenin, luteolin, seselin, 6-gingerol, humulene epoxide, quercetin, kaempferol, curcumin, and epigallocatechin-3-gallate (EGCG) have been reported to inhibit viral replication in a number of in silico investigations. Besides, numerous in silico, in vitro, and in vivo bioassays have been demonstrated that EGCG, anolignan-A, and B, ajoene, curcumin, and oleanolic acid exhibit anti-HIV activity while piperine, ursolic acid, oleanolic acid, (+)-cycloolivil-4′-O-β-dglucopyranoside, quercetin, EGCG, kaempferol, aloin, apigenin, rosmarinic acid, andrographolide, and hesperidin possess anti-HBV activity. Thus, the antiviral medicinal plants and the isolated bioactive be considered for further advanced investigations with the aim of the development of effective and affordable antiviral drugs. *Agad yoga* may be useful in alleviating the disease symptoms or post-covid symptom but it requires research works to unravel their therapeutic potential.

REFERNCES

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