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INDIGENOUS KNOWLEDGE BASED HERBAL MEDICINE FOR CORONA (COVID-19) TREATMENT

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Abstract

Current Corona virus Covid-19 crisis has infected more than 1.8 million humans in last three months and it is increasing exponentially every day. Some of the allopathic medicines (Cholroquine, Lopinover, Oseltamivir and Retenover etc.) used for other purposes like Malaria have shown good results in Corona. Plants species were reported to be effective in coronavirus (SARS-CoV), which causes a serious type of pneumonia. In similar way**,** Plant materials are a good source of bioactive compounds/phytochemicals that can be utilized not only for strengthening our immune system but also killing the pathogens. Due to chemical diversity and natural affability of natural products, either in the form of standardized extract or as a pure compound based on ethnopharmacological properties plays a s significant role in new drug development. Though, we have summarized medicinal plants that have a role in anti-viral activities, but there is an immediate need to find out more and more medicinal plants for anti-viral activities.

Key words: Corona virus, Cholroquine, Herbal medicine, Viral infection

Introduction

Traditional medicines are used for centuries to cure various ailments including treatment of pathogens (Ahmad *et al.,* 2020). Ethno-medicinal research contributes to discover new therapeutics drugs from indigenous medicinal plants (Mustafa *et al.,* 2017). Many of the plant species are also source of modern medicines (Yaseen *et al.,* 2019). The emerging viral infections resistant to already reported available antiviral drugs is a serious threat to human health and need immediate steps to overcome viral infections (Akram *et al.,* 2018). Already available antibiotics are ineffectual against viral infections due to their replicating machinery which is totally different from that of bacteria (Amber *et al*., 2017). However, plants derived active compounds are known as viral inhibitors from long ago (Serkedjieva *et al*., 1990).

Current crises of Corona virus have taken life of almost one hundred five thousand humans within last three months and about 1.8 million infected (WHO, 2020). In this precarious situation, we should learn from our previous efforts on other viral infections and find solutions through our indigenous knowledge too, as some species have already proven good results in other pathogens like leishmaniasis (Shah *et al.,* 2019). *Silybum marianum* that is proved, being used to treat Hepatitis virus and has given good results in nanoparticles too (Hameed *et al.,* 2019). It is also expected to be useful against corona virus too. Herbal products have also hepato protective and proposed possible mechanism of actions (Ali *et al.,* 2018).

Medicinal plants for viral hepatitis: Hepatitis is serious threat to global health. Hepatitis C virus is reported to have about 170–300 million carriers worldwide (Rehman *et al*., 2018). Currently approved treatments for HCV are limited to interferon (INF-α) and ribavirin which have less than 50% chance of cure and still there is no vaccine available (Zuo *et al*., 2005). Plant extracts of *Artocarpus heterophyllus* leaves, *Acacia nilotica, Taraxacum officinale* and *Nymphaea alba* possess promising anti-HVC potential (Akram *et al.,* 2018; Hafid *et al.,* 2017; Rehman *et al.,* 2018). *Phyllanthus urinaria* extract contains active compound loliolide inhibitor which stops hepatitis C virus entry into the cell (Chung *et al.,* 2016). Polyphenols and multigallated esters of D-glucose extracted from *S. melanocentra* have strong anti-HCV potential by inhabiting HCV NS3 serine protease (Zuo *et al.,* 2005).

Hepatitis B virus (HBV) causes about ~2 billion cases of liver infection worldwide and about ~40% of them result in developing hepatocellular carcinoma and cirrhosis (Arbab *et al*., 2017). Plant extracts of *G. senegalensis, F. parviflora, P. crispa, Boehmeria nivea, Polygonum cuspidatum* are reported to have promising anti-HBV potential (Arbab *et al.,* 2017; Chang *et al.,* 2005; Huang *et al*., 2006).

Medicinal plants and HIV/AIDS: Globally about 35 million individual are living with HIV/AIDS and it counts for 10th global death cause specially in under-developed countries (Rebensburg *et al.,* 2016). Pakistan is on 4th rank in Asia where HIV positive cases are continuously increasing since 1990 (Bergenstrom *et al.,* 2015). There are about 160,272 confirmed HIV cases in Pakistan including 75,000 cases from Punjab province (Mallhi *et al.,* 2019). Certain medicinal plants are reported to have strong anti-HIV potential (Cary & Peterlin, 2018; Sun *et al.,* 1996; Xu *et al.,* 1996). *Carpobrotus edulis* (L.), *Carpobrotus edulis* (L.), *Rhus chinensis, Tuberaria lignosa* and *Sanguisorba minor magnolia* are some reported plants with high anti-HIV potential (Bedoya *et al*., 2001; Omoruyi *et al*., 2012; Wang *et al*., 2006). Methanollic and aqueous extracts of *Carica papaya* have remarkable antiviral activity against HIV-1 (Rashed *et al*., 2013). In an *In vitro* study, extract of *Cistus incanus* inhibited clinical HIV-1 and HIV-2 isolates and virus isolate with multiple drug resistances (Rebensburg *et al.,* 2016).

Table of species used in viral infections:

S. No.	Plant name	Common name	Family	Part used	Extraction solvent	Active compound	Effective against virus	reference
1.	*Abutilon figarianum* Webb	Gargadan, texas Indian-mallow	Malvaceae	Whole plant	Methanol and dichloromethane (DCM) extracts	flavonoids, alkaloids, fatty acid and phenolic compounds	HBV	(Saleem *et al.*, 2020)
2.	*Ajuga bracteosa* Wall. ex Benth	Bugleweed	Lamiaceae	Whole Plant			Antiglycation, cytotoxic, phytotoxic, antioxidant, antiplatelet and antimicrobial activities against various pathogens.	Begum *et al.*, 2016
3.	*Allium sativum* L.	Garlic	Alliaceae	Bulb			Antiviral activity against influenza A and B, HIV, HSV-1, viral pneumonia, and rhinovirus, which causes the common cold.	Bayan *et al.*, 2014
4.	*Alysicarpus monilifer* (L.) DC.	Necklace-pod alyce clover	Fabaceae	Stem and leaves			Antibacterial activity against MRSA	Kasithevar *et al.*, 2017
5.	*Artemisia annua* L.	Annual wormwood	Asteraceae	Whole plant	Ethanol	Artemisinin, deoxyartemisinin, artemisinic acid, arteannuin-B, stigmasterol, friedelin, friedelan-3-β-ol, artemetin, and quercetagetin 6,7,3′,4′-tetramethyl ether	SARS-CoV	Notka *et al.*, 2004; Tan *et al.*, 2013
6.	*Astilbe rivularis* Buch. Ham.	River astilbe Hindi: gosy, pothee	Saxifragaceae	Rhizome	Methanolic extracts	Alkaloids, flavonoids, coumarins and glycosides	HSV-1/Vero cells and influenza virus	Amber *et al.*, 2017
7.	*Azadirachta indica* A. Juss	Neem, nimtree or Indian lilac	Meliaceae	Leaves	Bark extract	Deacetyl-3-cinnamoyl-azadirachtin	Newcastle disease virus (NDV), Hepatitis C virus (HCV)	Mohamed *et al.*, 2020
8.	*Bergenia ciliate* (Haw.) Sternb.	Zakham-e-Hayat, bud mawa	Saxifragaceae	Rhizome	Methanolic extracts	Bergenin, tannic acid, gallic acid, catechin	HSV-1, influenza virus A	Amber *et al.*, 2017
9.	*Caesalpinia pulcherrima* L.	pride-of-barbados, peacock flower, guletura	Fabaceae	Fruits, seeds, stem, and leaves	Aqueous extract	Glycosides, pulcherrimain, homoisoflavonoids, caesalpin, beta-sitosterol, quercetin, methoxy-bonducellin, rhamnetic, ombuin, and brazilide	Herpesvirus −1 and 2 and adenovirus (ADV)-3, ADV-8, and ADV-11	Li *et al.*, 2005; Zheng, 1994; Akram *et al.*, 2018;
10.	*Coronopus didymus*, (L.) Sm	Jangli halon; bitter cress	Brassicaceae	As vegetable	Aqueous extract		Malaria, cancer, digestive, antipyretic, expectorant	De Ruiz *et al.*, 1994

Table (Cont'd.).

S. No.	Plant name	Common name	Family	Part used	Extraction solvent	Active compound	Effective against virus	reference
11.	*Fagonia indica* L.	Dhamasa	Zygophyllaceae	Leaves	ethanol extract		Antileishmanial effects	Ullah *et al*., 2017a
12.	*Ficus benjamina*	Banyan	Moraceae	Leaves	Etanol extracts	phenolic and flavonoid compounds	Pseudomonas aerugonisa, Escherichia coli and Bacillus cerus	(Ashraf *et al*., 2020)
13.	*Glycyrrhiza glabra* L.	Licorice, Liquorice, *Sweetwood*	Fabaceae	Root & Leaves			Corona virus, type A influenza virus , Japanese encephalitis, herpes simplex, vesicular stomatitis virus, Newcastle disease virus (NDV	(Damle, 2014; Hussain *et al*., 2017); Ashraf *et al*., 2017
14.	*Glycyrrhiza uralensis* Fisch.	Licorice	Fabaceae	Root			Root extract is effective against HIV, RSV, herpes viruses, and severe acute respiratory syndrome-related coronavirus (SARS-CoV), which causes a serious type of pneumonia	Feng *et al*., 2013
15.	*Guazuma ulmifolia* Lam	West Indian elm or bay cedar	Malvaceae	Bark	aqueous (AqF) and ethyl acetate (EtOAcF) fraction	Epicatechin, procyanidins B2 and B5, procyanidin C1; epicatechin-(4β → 6)-epicatechin-(4β → 8)-epicatechin; epicatechin-(4β → 8)-epicatechin-(4β → 6)-epicatechin	poliovirus 1 (P-1) and bovine herpesvirus 1 (BHV-1)	Chiang *et al*., 2005
16.	*Hyoscyamus niger* L.	Black henbane-stinking nightshade; ajwain Kharasani	Solanaceae	Flower	methanol	Acyclovir	*Influenza* A	Cohen *et al*., 1964; Waheed *et al*., 2020
17.	*Hypericum connatum* Lam	St John's wort	Hypericaceae	Flowers			HSV, HIV, influenza, hepatitis, and coxsackievirus	Akram *et al*., 2018
18.	*Hyphaene thebaica* L.	Doum palm	Arecaceae	Fruit	Aqueous	Fe_2O_3 Nanoparticles used for treatment	polio virus-1 and polio virus-2	(Hamza *et al*., 2020)
19.	*Iresine herbstii* Hook. ex Lindl.	Blood leaf or beefsteak plant	Amaranthaceae	Shoot	Ethanol, petroleum ether, Acetonic, dichloromethane	Phytochemicals and other compounds	Newcastle disease virus infection (NDV)	(Andleeb *et al*., 2020)
20.	Isatis tinctoria L.	Dyer's woad, or glastum	Brassicaceae	Leaves		Indole-type glucosinolates	Antibacterial and Antifungal activity; an ancient dye plant	Ullah *et al*., 2017

Table (Cont'd.).

S. No.	Plant name	Common name	Family	Part used	Extraction solvent	Active compound	Effective against virus	reference
21.	*Justicia adhatoda* L.	Bansa, malabar nut, adhatoda,	Acanthaceae	Leaves	aqueous and methanolic extracts	Phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids, and reducing sugars	Influenza virus, Herpes Simplex Virus-2 (HSV-2), HSV-1; Antimicrobial efficacy of drug blended biosynthesized colloidal gold nanoparticles	Afolayan *et al*., 2007; Pant *et al*., 2012; Chavan & Chowdhary, 2014; Emmanuela *et al*., 2017
22.	*Lycoris radiate* (L'Heritier) Herbert.	Red spider lily.	Amaryllidaceae	Stem	Ethanol Chloroform	Lycorine, glycyrrhizin	Severe acute respiratory syndrome-associated coronavirus (SARS-CoV)	Chiang *et al*., 2002
23.	*Melissa officinalis* L.	Lemon balm, balm, or balm mint	Lamiaceae	Whole plant	Hot-water extracts	Terpinene, phenol carbon acid (rosmarinic acid), and flavonglychoside acid	Herpes simplex virus, Semliki Forest virus, Newcastle, vaccinia	Mahmood *et al*., 2018, Ashfaq *et al*., 2006
24.	*Moringa oleifera* Lam.	Moringa, horseradish tree	Moringaceae	Leaves, fruits, seeds	Phenolic	(1) O-ethyl-4- (α-L-rhamnosyloxy) benzyl carbamate; (2) 4 (α-Lrhamnosyloxy)-benzyl isothiocyanate (3) niazimicin; (4) niazirin (5) p-sitosterol; (6) glycerol-1-(9-octadecanoate); (7) 3 -0- 6 -O-oleoyl-β-D-glucopyranosyl-b-sitosterol; (8) β-sitosterol-3-X-O -β -D-glucopyranoside	EBV-EA (Epstein- Barr virus-early antigen)	(Arbab *et al*., 2017; Saleem *et al*., 2020)
25.	*Morus alba* L.	Toot, white mulberry,	Moraceae	Root and leaves	Ethanol	Kuwanon S, mulberroside C, cyclomorusin, eudraflavone B hydroperoxide, oxydihydromorusin, leachianone G and α-acetyl-amyrin	Herpes simplex type 1 virus (HSV-1) FMD virus, Foot-and-mouth disease virus	(Du *et al*., 2003) Yang *et al*., 2007; Akram *et al*., 2018; Cheng *et al*., 2011
26.	*Nigella sativa* L.	Black *seed*, black caraway, roman coriander, kalonji, or fennel flower,	Ranunculaceae	Seed	(Aqueous, Methanol, Ethanol, Cloroform, Butanol, Diethyl ether, n-Hexane and Acetone	Steroids, tannins, flavanoids, coumarins, cardiac glycosides, saponins and diterpenes	Murine cytomegalovirus (MCMV)	Estari *et al*., 2012
27.	*Ocimum basilicum* L.	Mushk, jangli tulsi, kam Kashturi, niazbo, basel	Lamiaceae	Whole plant	aqueous and ethanolic extracts	Apigenin, linalool and ursolic acid	HSV-1, ADV-8, CVB1, EV71, HSV-2, ADV-3	Serkedjieva *et al*., 1990; Hearst *et al*., 2010

Table (Cont'd.).

S. No.	Plant name	Common name	Family	Part used	Extraction solvent	Active compound	Effective against virus	reference
28.	*Phyllanthus amarus* Schum. & Thonn.	Black catnip, gulf leaf flower, stone breaker	Phyllanthaceae	Leaves	Aquous and ethanolic extract	Gallotannin, corilagin	HIV, HSV-1 and HSV-II	(Ashraf *et al.*, 2020)
29.	*Phyllanthus emblica* L.	Amla, Indian gooseberry	Leiothrichidae	Fruits	n-hexane, ethyl acetate, and n-butanol		HIV	Andleeb *et al.*, 2020
30.	*Phyllanthus urinaria* L.	Leaf-flower, shatterstone, stone-breaker herb	Phyllanthaceae	Root, leaves	Acetone extract	1,3,4,6-Tetra-O-galloyl-d-glucose (1346TOGDG), Excoecarianin	herpes simplex virus type 1 and 2 (HSV-1;2)	(Porter & Bode, 2017; Serkedjieva *et al.*, 1990)
31.	*Plantago major* L.	Bartang, broad-leaved plantain	Plantaginaceae	Whole plant	aqueous	Caffeic acid, chlorogenic acid	HSV-1, HSV-2, ADV-3, ADV-11	Akram *et al.*, 2018
32.	*Polygonum cuspidatum* Siebold & Zucc.	knotweed and knotgrass	Polygonaceae	Root	Ethanol extract, water extract	Stilbenoids, anthraquinones, catechins	HBV, HIV-1	Chavan *et al.*, 2014; Chavan *et al.*, 2013; Pathak, 1970
33.	*Sambucus nigra* L.	Elder; elderberry	Adoxaceae (previously Caprifoliaceae)	Flowers, fruits	Methanol, Ethanol	Flavonol (Isoquercetin, rutin, Quercetin-3-O-6″-acetylglucoside), Flavanones (Naringenin), Flavones (Luteolin)	Influenza virus types A and B, herpes simplex virus type 1,	(Porter & Bode, 2017; Serkedjieva *et al.*, 1990)
34.	*Sambucus nigra* L.	Elderberry - European elder	Adoxaceae	Flowers	Aqueous extract	Flavonoids, triterpene saponins, phenolic acids, tannins and polysaccharides	Influenza virus types A and B, herpes simplex virus type 1, HIV, HSV, hepatitis,	Du *et al.*, 2003; Imrana *et al.*, 2016; Akram *et al.*, 2018
35.	*Silybum marianum* (L.) Gaertn.	Milk thistle Ount Katara	Asteraceae	Fruit		Silymarin, a mixture of flavanoid complexes	Hepatitis virus; cirrhosis, prostate, skin and breast cancer, cervical cells and kidney ailment	Khan *et al.*, 2014
36.	*Withania coagulans* (Stocks) Dunal	Paneer dodi	Solanaceae	Fruit			Leishmanicidal active withanolides	Kuroyanagi *et al.*, 2012
37.	*Withania somnifera* (L.) Dunal	Ashwagandha, Indian ginseng,	Solanaceae	Root	hydro- alcoholic extract, aqueous		Infectious bursal disease virus (IBDV), simplex virus type 1 (HSV-1), Herpes simplex virus type 2 (HSV-2)	(Serkedjieva *et al.*, 1990)
38.	*Zingiber officinale* Rosc.	Adrak, Ginger	Zingiberaceae	Rhizome	Aquous extract	Ar-curcumene, β-sesquiphellandrene, α-zingiberene and β-bisabolene, flavan and 4, 6-dichloroflavan	*Rhinovirus* IB	Salem *et al.*, 2000 Ishtiaq *et al.*, 2013

Medicinal plant and human influenza virus: Influenza virus is a severe threat to the global health (Iuliano *et al*., 2018). About 10% of world population is infected annually and causes approximately 250,000 death (McCaughey, 2010). Due to emerging drugs resistant strains of influenza virus, search for new, novel and potent anti-viral drugs is the need of time (Rajasekaran *et al.,* 2013). Medicinal plants provide active and potential phytochemicals with promising anti-viral activities (Bodinet *et al.,* 2002; Kernan *et al.,* 1997; Liu *et al.,* 2008). Similarly, *Allium fistulosum* L. extract contains an inulin-type polysaccharide with good anti-influenza activity (Lee *et al.,* 2012) (Table-1).

Anti-viral mechanism of plant extract: Plant extract and plant derived active compound show different antiviral potential mechanism towards different viruses. Some phytochemicals target the viral envelope or the membrane proteins while other stop the viral attachment to host cell. Some phytochemicals denature the important viral enzymes which are necessary for viral genome replication and assembly (Amber *et al.,* 2017). Concentrated juice of elderberry *Sambucus nigra* L. has strong anti-viral potential against human influenza virus tested in mice model (Kinoshita *et al*., 2012). Methanol extracts of *Adenium Obesum* and *Tephrosia Nubica* are reported to have antiviral activity (99.3 and 93.3% inhibition at the concentration of 10 g/ml, respectively (Kiyohara *et al.,* 2012).

Discussions

Our group had already been advocating of Emerging Viral Infections in Pakistan, its potential damages and how can we prepare ourselves for any negative impact. We had been warning that MERS-Cov), or Corona like a pandemic is possible (Khalil *et al.,* 2017). Due to chemical diversity and natural affability of natural products, either in the form of standardized extract or as a pure compound based on ethnopharmacological properties play a significant role in new drug development (Zohra *et al.,* 2019). Traditional medicines have potential of antiviral properties, also through bioactive compounds to green nanoceria (Hamza *et al.,* 2020). Plant materials are a good source of bioactive compounds/ phytochemicals that can be utilized in not only strengthening our immune system but also killing these pathogens.

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