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Review of Some Herbal Agents Having Antiviral Activity

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ABSTRACT: Antiviral is such as an agent, defined as used to treat the targeted virus, or vaccine to produce an antibody against the virus. It gives a proactive therapeutic effect. On the other hand, there is a long traditional use of herbal medicine in the medical platform. The herbal medicine is ornamented with a wide therapeutic window and its side effect is less. The synthetic drug sometimes invites some adverse effects, which is more important that is it occurs more frequently. This gives the opportunity to the researchers to get the noble drug based on the herbal formulation. This review reveals the many herbal plants with their use against the specific virus with the experimental method, based on the knowledge of the Indian traditional system of medicine. The recent database shows the growing research with the herbal medicine, with their therapeutics, especially this time of the society, suffering from the covid -19 (Coronavirus disease), because the doctors have no other options except steroid. So traditional plants open a new chapter in the research of the new antiviral drug.

KEYWORDS: Anti-viral, Herbal formulation, Less side effect, Therapeutic window, Traditional medicinal plant.

INTRODUCTION:

Medicine, protecting from various diseases, is the lifesaving element in the world. The man of the present year living various adversities, stress, strains, and anxiety, especially men are exhausted with covid-19 in the present situation. For this, the physiological condition of humans contributes the most to the disease due to a lack of immunity. Worldwide mortality and morbidity have a major responsibility in the viral disease. Public health is in threat for infectious viral disease. In staid of vaccine, there is no specific treatment for the viral disease throughout the world [1]. There are some aliphatic medicines is available but contain lots of side effects. In Morden, pharmaceutical technology shows greater interest in herbal medicines has increased considerably both at home and abroad as persons believed that herbal medicines are less toxic than synthetic medicines. 80% to 90% of the population use, herbal medicine for their primary health care need.

The WHO (World Health Organization), IUCN (International Union for Conservation of Nature), and WWF (World Wildlife Fund) decided that it is perfect in the collaboration of offering an international Consultation about the conservation of medicinal plants bringing together leading its branches in the fields like ethnos medicine, pharmacology, environmental sciences economics to exchange the views with the administrator, policymaker in health and conversation on this problem to determine priorities and make recommendation fraction.

India has the world's longest, richest, and most diverse cultural legacy involving the use of medicinal plants in the form of traditional medical systems. India is the botanical gardens of the whole world and a goldmine of well-recorded and well-practiced knowledge of herbal medicine.

Documentation of the knowledge through ethnobotanical study is essential for the conversation, which will also improve the biological resources. Ethnopharmacology has an important value through the process of conventional medicine and is likely to become increasingly important in the years to come [2,3].

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Mechanisms of action of antiviral drugs [4]

1. Adsorption of the virus by antibodies or particular ligands must be avoided in order to prevent viral entrance into the cell.
2. After endocytosis, prevent viral uncoating.
3. Prevent DNA or RNA replication throughout the inhibition of DNA- or RNA-polymerases.
4. Interfere in Virus replication.
5. Suppress virus maturation and discharge.

Assays for new antiviral drug screening:

For the development of antiviral drugs, drug screening is necessary. The majority of in vitro antiviral assays are cell-based, such as the cytopathic effect assay (measurement of plaque reduction) and the MTT assay (measurement of cell variability). Other assays, like ELISA (Enzyme-linked immunoassay), are commonly employed to determine the presence of viral protein in drug cytotoxicity studies. Though these antiviral assays are unstandardized and time-consuming, alternative novel approaches for drug screening are becoming more popular such as the RT-PCR (Real-Time Reverse Transcription) method, Biosensor Method using Capacitance Sensor Arrays, and Computation Method [5].

Antiviral activity of medicinal plant:

Lots of Phytochemicals are found in abundance in plants like phenolic compounds, alkaloids, tannins, flavonoids, saponins, coumarins, lignans, etc. The mechanisms of action of herbal medicines are complex and generally unexplored. The review article focuses on medicinal herbs and plants that are used to treat viral infections in particular, which are inexpensive and easily readily available. Since viral infections can be one of the worst night terrors for medical practitioners and patients [6].

There are some identified medicinal herbs that are being screened for antiviral properties (Table-1)

Table 1: Some Identified Medicinal Herbs That Are Being Screened For Antiviral Properties

Sl. No.	Plant Name	Family	Part Used	Type Of Extraction	Model Used, Method	Targeted Virus	Result & Discussion	References
1	*Alo barbadnesis*	Liliaceae	Leaves	Hot glycerine extraction	African monkey's kidney cell (Vero cell line) is cultured in bulbaceous minimum media, confirm virous by specific fluorescent monoclonal antibody test, Stock was determined by karber method	Herpes simplex virus (Type 2)	It shows promising antiviral effect against Herpes simplex virus (Type 2)	[7]
2	*Aframomum melegueta*	Zingiber aceae	Seed	Ethanolic extraction	Antiviral assays, Cytotoxicity assays	Measles virus	It possesses antiviral properties that are effective against the Measles virus. In the treatment of measles infections and	[8]

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							helminthics infections traditionally it is used by Nigerian herbal practitioners	
3	*Azadirachta Indica*	Meliaceae	Leaves	Aqueous extraction	In vivo virus inhibition	Newcastle disease virus	The conclusion of this study is that the aqueous extract of *Azadirachta indica* leaf has antiviral activity against the Newcastle disease virus.	[9]
4	*Allium sativum*	Amaryllidaceae	Fresh garlic bulbs	Aqueous extraction	MTT assay ((3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay), RT-PCR (Real-Time Reverse Transcription)	Influenza (H1N1)	The bio chemical and molecular methods are evaluated and it will be said that garlic is a suitable anti-viral agent.	[10]
5	*Andographis paniculata*	Acanthaceae	Leaves	Ethanolic extract	RT-PCR analysis	Retro virus (SRV)	It shows higher activity against the virus than negative control	[11]
6	*Artocarpus Heterophyllus*	Mulberry	Leaves	n-hexane, Ethanolic extract	Antiviral activity assay, Virucidal activity assay, Effect on a host cell expression assay, Immunoblotting, RT-PCR, MTT assay	Hepatitis C (HCV)	It is good to protect our body from HCV	[12]
7	*Andrographis Paniculata*	Acanthaceae	Leaves	Ethanolic extraction	Plaque forming assay	Herpes simplex (type -1)	It shows highest inhibitory activity against herpes simplex type 1	[13]
8	*Bambusa vulgaris*	Poaceae	Leaves	Ethanolic extraction	Antiviral assays, Cytotoxicity assays	Measles virus	It possesses antiviral properties that are effective against the Measles virus.	[8]

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							Nigerian herbalists have long used it to treat measles infections.	
9	*Bauhinia variegata*	Leguminosae	Leaves	Methanolic extraction	Virucidal assay, Cytotoxicity assay	Rotavirus	It has a strong antiviral impact in the case of rotavirus infection.	[14]
10	*Curcuma longa*	Zingiberaceae	Dried rhizomes	Polyphenol extract	Cell focusing assay, MTT assay	DENV-2	*Curcuma longa* potentially used as anti-viral against dengue with low toxicity level.	[15]
11	*Cimicifuga foetida*	Ranunculaceae	Whole plant	Ethanolic extraction	XTT Assay (2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide), Plaque Reduction Assay, Time Course Assay, Attachment Assay, Internalization Assay	Human Respiratory Syncytial Virus	It exhibits dose-dependent effects against RSV	[16]
12	*Clerodendrum serratum*	Lamiaceae	Whole plant	Methanolic extraction	Antiviral assays, Cytotoxicity assays	Yellow fever virus	It shows promising antiviral effect against yellow fever virus	[17]
13	*Calotropis giganeta*	Apocynaceae	Latex	95% EtOH filtration	Cytotoxicity assay, Cytopathic effect inhibition assay, Plaque reduction assay, Time course assay, Western blotting, Indirect immunofluorescence microscopy	Influenza (H7N9)	It is a promising candidate to give anti-viral against influenza	[18]
14	*Camellia Sinensis*	Theaceae	Leaves	Hydroalcoholic extraction	MTT assay	Adenovirus	It is a promising candidate to give anti-viral against adenovirus	[19]

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15	*Echinacea purpurea*	Asteraceae	Leaves & Roots	Ethanolic extraction	Randomized clinical trials	Rhinovirus	It has an antiviral effect against rhinovirus.	[20]
16	*Eclipta alba*	Asteraceae	Whole plant	Aqueous extraction	Fluorescence quenching assay, MTT assay	Hepatitis C virus	*Eclipta alba* extract exhibit anti-HCV activity	[21]
17	*Fructus Gardeniae*	Rubiaceae	Fruits	Ethanol extract	MTT Assay, RT-PCR, Western blotting assay of PACT expression, Dual-luciferase reporter gene assay	Influenza virus	It potentially damaged the H1N1 virus cells	[22]
18	*Ferula Asafoetida*	Apiaceae	The gum resin of roots	Hexane extraction followed by MeOH extraction	Plaque forming assay	HSV-1	It shows an antiviral activity against HSV-1 with a meaning full concentration	[23]
19	*Glycyrrhiza glabra*	Fabaceae	Roots	Aqueous extraction	Anti-viral assay, Assay for combined effect with anti-herpes drugs or interferon, varicella-zoster virus inactivation assay, Cytotoxicity assay	Varicella zoster virus	In vitro antiviral activity of *Glycyrrhiza. glabra* may be based on a direct interaction of the compound with a very early stage of the virus replicative cycle	[24]
20	*Hypericum mysorense*	Hypericaceae	Aerial parts	Methanolic extraction	Assays for cytopathic effect inhibition and viral yield reduction	Herpes simplex virus	It's an effective antiviral against the herpes simplex virus. It has traditionally been used to relieve anxiety and inflammation	[25]
21	*Hypericum hookerianum*	Hypericaceae	Aerial parts	Methanolic extraction	Inhibition of cytopathic effect assay and virus yield reduction assay	Herpes simplex virus	It has strong antiviral properties against the herpes simplex virus. It has traditionally been used to	[25]
22	*Rosmarinus officinalis*	Lamiaceae	Leaves	Aqueous extraction	Cytotoxicity assay, Assay of antiviral activities, Assay for	Herpes simplex virus	It showed antiviral effect against HSV-2	[26]

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					virus titter, Direct plaque assay			
23	*Justicia adhatoda*	Acanthaceae	Whole Plant	Methanolic extraction	Simultaneous Treatment assay, Post Treatment assay, Hemagglutination assay, Statistical Analysis	Influenza Virus	It showed Potentially inhibition of duplicating the cell of influenza virus	[27]
24	*Kalanchoe pinnata*	Crassulaceae	Leaves	Methanolic extraction	Antiviral assays, Cytotoxicity assays	Chikungunya virus	It shows antiviral effect against Chikungunya virus	[17]
25	*Lawsonia inermis*	Lythraceae	Fruits	Ethanolic extraction	Swiss mice and chick embryo models	Sembiki forest virus	It shows 100 to 65 % activities after 10 to 25 days of virus challenge	[28]
26	*Mangifera indica*	Anacardiaceae.	whole plant	Phenolic extraction	Cell culture and virous propagation (ccvp), PCR	Influenza	Potentially inhibit the duplication the cell of virous	[29]
27	*Melissa officinalis*	Lamiaceae	Leaves	Aqueous extraction	Cytotoxicity assay, assay of antiviral activities, assay for virus titter	Herpes simplex virus	It shows promising antiviral effect against HSV-2	[30]
28	*Nerium Oleander*	Apocynaceae	New soots	Hot distillation	Cell culture, Virus titration, MTT assay, Anti-viral activity assay	Parainfluenza-3	It has potent anti-viral effect against the para influenza	[31]
29	*Ocimum basilicum*	Lamiaceae	Whole plant	Aqueous and Ethanolic extraction	Cytopathic effect reduction assay	Human adenovirus	It is a promising candidate to provide antiviral effect against the Human Adenovirus	[32, 33, 34]
30	*Origanum vulgare*	Lamiaceae	Whole plant	Ethanolic extraction	Cytopathic effect (CPE) assay	RSV, CVB3 and HSV-1	It is a promising candidate to provide antiviral effect against RSV, CVB3 and HSV-1	[35]
31	*Plantago major*	Plantaginaceae	Whole plant	Aqueous and Ethanolic extraction	XTT assay	Human adenovirus	It has shown antiviral activity against Human adenovirus virus	[36-39]
32	*Panax ginseng*	Araliaceae	Roots	Fermentation	Virus Microneutralization	Influenza virus	When mice were co-inoculated	[40]

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					and Plaque Assays, Hemagglutinin Assay, Neuraminidase Assay, Statistical Analysis Methods		with influenza virus and ginseng sample, a fermented ginseng extract with higher saponin component ginsenosides enhanced survival rates and prevented body weight loss.	
33	*Psidium gua java*	Myrtacea e	leaves	Methanolic extraction	Influenza growth inhibition assay	Influenza Virus	It contains antiviral properties that are effective against epidemic and pandemic influenza viruses. The main reason of antiviral activity of guava extract is protein degradation ability.	[41, 42, 43]
34	*Prunus dulcis*	Rose	The skin of the nut	Hexane methanol reflux	Plaque forming assay, Quantification of viral DNA	Herpes simplex virus	It shows the effect against the HSV-1	[44]
35	*Punica Granatum*	Punicace ae	Peel	Alcoholic extraction	Cell culture and influenza virous propagation, cytotoxicity assay, cytopathic effect reduction assay, hemagglutination assay, TCID50 virus titration	Influenza virus	It can inhibit the growth of Influenza A virus	[45]
36	*Pedilanthus tithymaloide s*	Euphorbi aceae	Leaves	Methanolic extraction	Antiviral assays, Cytotoxicity assays	Chikungu nya virus	It shows promising antiviral effect against Chikungunya virus	[17]
37	*Sambucus nigra*	Adoxace ae	Whole Plant	Methanolic extraction	MTT assay, Focus assay, Statistical data analysis of	Influenza Virus A & B	It showed strong antiviral activity	[46]

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					experiments, Biosafety		against influenza virus A & B	
38	*Silybum marianum*	Asteraceae	Seeds	Ethanolic extraction	Cell sensitivity to virus, Reference virus inactivation test, Titration of the virus control	Poliovirus	It shows promising antiviral effect against poliovirus	[47]
39	*Spinacia oleracea*	Amanantaceae	Leaves	Centrifuged supernatant fluid of the mixer of Phosphate buffer, PMS, EDTA, DDT mixed with crude with proper ratio.	Estimation of antiviral activity, Inhibitory effect of SPF5 protein peak against TMV in vitro, Inhibitory effect of SPF5 protein peak against TMV in infection sites, Inhibitory activity against TMV replication of SPF5 protein peak.	Tobacco Mosaic virus	It has a little inhibitory activity against TMV virus further study required	[48]
40	*Terminalia chebula*	Combretaceae	Leaves	Methanolic extraction	Antiviral assays, Cytotoxicity assays	Enteroviruses.	It has antiviral effect against enterovirus. Indigenously this plant is used to combat of ulcers, bleeding piles and gout.	[17]
41	*Usnea complanta*	Usneaceae	Whole plant	Acetone extraction	Assays for cytopathic effect inhibition and viral yield reduction	Herpes simplex virus	Its antiviral action against the herpes simplex virus is very strong. However, it has typically been used to treat bacterial infections.	[25]
42	*Verbascum thapsus*	Scrophulariaceae	Leaves	Methanolic extraction	Dye uptake study.	Influenza Virus A	It is a promising candidate to give anti-viral against influenza virus A.	[2,49]

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43	*Withanina Somnifera*	Solanaceae	Leaves	Water extract	MTT Assay, RT-PCR, Colony forming assay	Hepatitis C (HCV	PCR shows a marked viral load reduction, colony formation assay gives a significant result against the untreated positive control. So, ASH is a powerful antiviral agent against HCV	[50]
44	*Zingiber officinale*	Zingiberaceae	Fresh clean rhizomes	Aqueous extraction	Animal cell culture model	Chikungunya	In the study it reviles that the effective dose of the extract shows antiviral effect against Chikungunya virus	[51]

Advantages of herbal drugs:

Herbal medications are one of the most popular topics in traditional medicine systems all over the world. Human is completely reliant on plants and plant products for their basic necessities like food, clothing, and shelter, as well as indirectly for their beneficial effects on climate and the preservation of their immediate and distant surroundings, making plants essential for their survival and continuous existence. In 1978, the World Health Organization (WHO) underlined the need for scientific study in herbal medicine, and since then, developing countries around the world have begun research programs to scientifically verify the therapeutic benefit of their native medicinal plants in order to be added to the WHO's list of "essential medications."

Herbal medications and purified natural products are a significant source of material for the development of new antiviral drugs. The discovery of antiviral mechanisms in these natural products has provided insight into how they interact with the life cycle of a virus, including viral entrance, replication, assembly, and release, or even the targeting of virus–host-specific interactions [52]. Herbal medicines are widely prescribed due to their efficiency, lack of adverse effects, and inexpensive cost. Traditional medicine practitioners widely use herbal medicines in their daily practice due to their easy availability and therapeutic applications of medicinal plants in many diseases. According to a World Health Organization (WHO) survey from 1993, traditional medical practitioners of India, Burma, and Bangladesh serve around 80percent of the total patients of their countries. Medicinal plants employed in traditional medicine have proven to be effective in the therapy for bronchial asthma, cold, chronic fever, malaria, cough, dysentery, diarrhoea, convulsions, diabetes, arthritis, emetic syndrome, insect bites, skin illnesses, as well as cardiovascular, hepatic, gastric, and immunological disorders [53,54,55].

CONCLUSION

There are many viral infections in the world for which there is no effective treatment or any vaccines, destroying these viral infections is more challenging. However, these herbal products play as a great source of biodiversity to discover new antivirals, develop effective protection against viral infections. There are more possibilities of obtaining active constituents from the above-mentioned plants which will provide many useful leads to develop effective antiviral agents. These plants must be examined for the formulation of active medicines against numerous viral infections. Herbal extracts also help to strengthen the immune system which supports the body to fight off attacking viruses. Future studies of herbal antiviral drugs may help to understand the mechanism of

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action for better action to control viral infections and to reduce the risk of multi-drug resistant viruses. Additionally, further studies may also help to discover the anti-viral effect of herbal products against (severe acute respiratory syndrome coronavirus 2) SARS CoV-2.

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