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 stead 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].
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 immunosassay), 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

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Plant Name</th>
<th>Family</th>
<th>Part Used</th>
<th>Type Of Extraction</th>
<th>Model Used, Method</th>
<th>Targeted Virus</th>
<th>Result &amp; Discussion</th>
<th>Referenc es</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alobarbadnesis</td>
<td>Liliaceae</td>
<td>Leaves</td>
<td>Hot glycerine extraction</td>
<td>African monkey's kidney cell (Vero cell line) is cultured in bulbaceous minimum media, confirm virus by specific fluorescent monoclonal antibody test, Stock was determined by karber method</td>
<td>Herpes simplex virus (Type 2)</td>
<td>It shows promising antiviral effect against Herpes simplex virus (Type 2)</td>
<td>[7]</td>
</tr>
<tr>
<td>2</td>
<td>Aframomum melegueta</td>
<td>Zingiber aceae</td>
<td>Seed</td>
<td>Ethanolic extraction</td>
<td>Antiviral assays, Cytotoxicity assays</td>
<td>Measles virus</td>
<td>It possesses antiviral properties that are effective against the Measles virus. In the treatment of measles infections and</td>
<td>[8]</td>
</tr>
<tr>
<td>Item</td>
<td>Species</td>
<td>Family</td>
<td>Part</td>
<td>Extraction Method</td>
<td>Assay</td>
<td>Conclusion</td>
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<tr>
<td>3</td>
<td><em>Azadirachta Indica</em></td>
<td>Meliaceae</td>
<td>Leaves</td>
<td>Aqueous extraction</td>
<td>In vivo virus inhibition</td>
<td>Newcastle disease virus</td>
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<td></td>
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<td></td>
<td>The conclusion of this study is that the aqueous extract of <em>Azadirachta indica</em> leaf has antiviral activity against the Newcastle disease virus.</td>
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</tr>
<tr>
<td>4</td>
<td><em>Allium sativum</em></td>
<td>Amaryllidaceae</td>
<td>Fresh garlic bulbs</td>
<td>Aqueous extraction</td>
<td>MTT assay ((3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay), RT-PCR (Real-Time Reverse Transcription))</td>
<td>Influenza (H1N1)</td>
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<td>The bio chemical and molecular methods are evaluated and it will be said that garlic is a suitable anti-viral agent.</td>
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<tr>
<td>5</td>
<td><em>Andrographis paniculata</em></td>
<td>Acanthaceae</td>
<td>Leaves</td>
<td>Ethanolic extract</td>
<td>RT-PCR analysis</td>
<td>Retrovirus (SRV)</td>
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<td>It shows higher activity against the virus than negative control</td>
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<tr>
<td>6</td>
<td><em>Artocarpus Heterophyllus</em></td>
<td>Mulberry</td>
<td>Leaves</td>
<td>n-hexane, Ethanolic extract</td>
<td>Antiviral activity assay, Virucidal activity assay, Effect on a host cell expression assay, Immunoblotting, RT-PCR, MTT assay</td>
<td>Hepatitis C (HCV)</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>It is good to protect our body from HCV</td>
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<tr>
<td>7</td>
<td><em>Andrographis Paniculata</em></td>
<td>Acanthaceae</td>
<td>Leaves</td>
<td>Ethanolic extraction</td>
<td>Plaque forming assay</td>
<td>Herpes simplex (type -1)</td>
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<td>It shows highest inhibitory activity against herpes simplex type 1</td>
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<tr>
<td>8</td>
<td><em>Bambusa vulgaris</em></td>
<td>Poaceae</td>
<td>Leaves</td>
<td>Ethanolic extraction</td>
<td>Antiviral assays, Cytotoxicity assays</td>
<td>Measles virus</td>
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<td></td>
<td>It possesses antiviral properties that are effective against the Measles virus.</td>
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</tr>
</tbody>
</table>
Nigerian herbalists have long used it to treat measles infections.

- **Bauhinia variegata** (Leguminosae): Leaves, Methanolic extraction, Virucidal assay, Cytotoxicity assay. It has a strong antiviral impact in the case of rotavirus infection. [14]

- **Curcuma longa** (Zingiberaceae): Dried rhizomes, Polyphenol extract, Cell focusing assay, MTT assay. *Curcuma longa* potentially used as anti-viral against dengue with low toxicity level. [15]

- **Cimicifuga foetida** (Ranunculaceae): Whole plant, Ethanolic extraction, XTT Assay, Plaque Reduction Assay, Time Course Assay, Attachment Assay, Internalization Assay. It exhibits dose-dependent effects against RSV. [16]

- **Clerodendrum serratum** (Lamiaceae): Whole plant, Methanolic extraction, Antiviral assays, Cytotoxicity assays. It shows promising antiviral effect against yellow fever virus. [17]

- **Calotropis gigantea** (Apocynaceae): Latex, 95% EtOH filtration, Cytotoxicity assay, Cytopathic effect inhibition assay, Plaque reduction assay, Time course assay, Western blotting, Indirect immunofluorescence microscopy. It is a promising candidate to give anti-viral against influenza. [18]

- **Camellia Sinensis** (Theaceae): Leaves, Hydroalcoholic extraction, MTT assay. It is a promising candidate to give anti-viral against adenovirus. [19]
<table>
<thead>
<tr>
<th>Page No.</th>
<th>Plant Name</th>
<th>Family</th>
<th>Part(s)</th>
<th>Extraction Type</th>
<th>Assays/Tests</th>
<th>Activity/Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td><em>Echinacea purpurea</em></td>
<td>Asteraceae</td>
<td>Leaves &amp; Roots</td>
<td>Ethanolic extraction</td>
<td>Randomized clinical trials, Rhinovirus</td>
<td>It has an antiviral effect against rhinovirus.</td>
</tr>
<tr>
<td>16</td>
<td><em>Eclipta alba</em></td>
<td>Asteraceae</td>
<td>Whole plant</td>
<td>Aqueous extraction</td>
<td>Fluorescence quenching assay, MTT assay, Hepatitis C virus, Eclipta alba extract exhibit anti-HCV activity</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td><em>Fructus Gardeniae</em></td>
<td>Rubiaceae</td>
<td>Fruits</td>
<td>Ethanol extract</td>
<td>MTT Assay, RT-PCR, Western blotting assay of PACT expression, Dual-luciferase reporter gene assay</td>
<td>Influenza virus. It potentially damaged the H1N1 virus cells.</td>
</tr>
<tr>
<td>18</td>
<td><em>Ferula Asafoetida</em></td>
<td>Apiaceae</td>
<td>The gum resin of roots</td>
<td>Hexane extraction followed by MeOH extraction</td>
<td>Plaque forming assay, HSV-1 Plaque forming assay</td>
<td>It shows an antiviral activity against HSV-1 with a meaning full concentration</td>
</tr>
<tr>
<td>19</td>
<td><em>Glycyrrhiza glabra</em></td>
<td>Fabaceae</td>
<td>Roots</td>
<td>Aqueous extraction</td>
<td>Anti-viral assay, Assay for combined effect with anti-herpes drugs or interferon, varicella-zoster virus inactivation assay, Cytotoxicity assay, Varicella zoster virus</td>
<td>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</td>
</tr>
<tr>
<td>20</td>
<td><em>Hypericum mysorense</em></td>
<td>Hypericaceae</td>
<td>Aerial parts</td>
<td>Methanolic extraction</td>
<td>Assays for cytopathic effect inhibition and viral yield reduction, Herpes simplex virus, Varicella zoster virus</td>
<td>It's an effective antiviral against the herpes simplex virus. It has traditionally been used to relieve anxiety and inflammation</td>
</tr>
<tr>
<td>21</td>
<td><em>Hypericum hookerianum</em></td>
<td>Hypericaceae</td>
<td>Aerial parts</td>
<td>Methanolic extraction</td>
<td>Inhibition of cytopathic effect assay and virus yield reduction, Herpes simplex virus, Varicella zoster virus</td>
<td>It has strong antiviral properties against the herpes simplex virus. It has traditionally been used to</td>
</tr>
<tr>
<td>22</td>
<td><em>Rosmarinus officinalis</em></td>
<td>Lamiaceae</td>
<td>Leaves</td>
<td>Aqueous extraction</td>
<td>Cytotoxicity assay, Assay of antiviral activities, Assay for Herpes simplex virus, Varicella zoster virus, HSV-2</td>
<td>It showed antiviral effect against HSV-2</td>
</tr>
<tr>
<td>S.No.</td>
<td>Common Name</td>
<td>Family</td>
<td>Part of Plant</td>
<td>Type of Extraction</td>
<td>Assays Conducted</td>
<td>Results</td>
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<tr>
<td>23</td>
<td>Justicia adhatoda</td>
<td>Acanthaceae</td>
<td>Whole Plant</td>
<td>Methanolic extraction</td>
<td>Simultaneous Treatment assay, Post Treatment assay, Hemagglutination assay, Statistical Analysis</td>
<td>Influenza Virus</td>
</tr>
<tr>
<td>24</td>
<td>Kalanchoe pinnata</td>
<td>Crassulaceae</td>
<td>Leaves</td>
<td>Methanolic extraction</td>
<td>Antiviral assays, Cytotoxicity assays</td>
<td>Chikungunya virus</td>
</tr>
<tr>
<td>25</td>
<td>Lawsonia inermis</td>
<td>Lythraceae</td>
<td>Fruits</td>
<td>Ethanolic extraction</td>
<td>Swiss mice and chick embryo models</td>
<td>Sembiki forest virus</td>
</tr>
<tr>
<td>26</td>
<td>Mangifera indica</td>
<td>Anacardiaceae</td>
<td>Whole plant</td>
<td>Phenolic extraction</td>
<td>Cell culture and viral propagation (ccvp), PCR</td>
<td>Influenza</td>
</tr>
<tr>
<td>27</td>
<td>Melissa officinalis</td>
<td>Lamiaceae</td>
<td>Leaves</td>
<td>Aqueous extraction</td>
<td>Cytotoxicity assay, assay of antiviral activities, assay for virus titter</td>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>28</td>
<td>Nerium Oleander</td>
<td>Apocynaceae</td>
<td>New soots</td>
<td>Hot distillation</td>
<td>Cell culture, Virus titration, MTT assay, Anti-viral activity assay</td>
<td>Parainfluenza-3</td>
</tr>
<tr>
<td>29</td>
<td>Ocimum basilicum</td>
<td>Lamiaceae</td>
<td>Whole plant</td>
<td>Aqueous and Ethanolic extraction</td>
<td>Cytopathic effect reduction assay</td>
<td>Human adenovirus</td>
</tr>
<tr>
<td>30</td>
<td>Panax ginseng</td>
<td>Araliaceae</td>
<td>Roots</td>
<td>Fermentation</td>
<td>Virus Microneutralization</td>
<td>Influenza virus</td>
</tr>
<tr>
<td>31</td>
<td>Plantago major</td>
<td>Plantaginaceae</td>
<td>Whole plant</td>
<td>Aqueous and Ethanolic extraction</td>
<td>XTT assay</td>
<td>Human adenovirus</td>
</tr>
<tr>
<td>32</td>
<td>Origanum vulgare</td>
<td>Lamiaceae</td>
<td>Whole plant</td>
<td>Ethanolic extraction</td>
<td>Cytopathic effect (CPE) assay</td>
<td>RSV, CVB3 and HSV-1</td>
</tr>
<tr>
<td>Page</td>
<td>Species</td>
<td>Family</td>
<td>Part</td>
<td>Extraction Method</td>
<td>Assay/Technique</td>
<td>Virus/Infection</td>
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<td>33</td>
<td>Psidium guajava</td>
<td>Myrtaceae</td>
<td>leaves</td>
<td>Methanolic extraction</td>
<td>Influenza growth inhibition assay</td>
<td>Influenza Virus</td>
</tr>
<tr>
<td>34</td>
<td>Prunus dulcis</td>
<td>Rosaceae</td>
<td>The skin of the nut</td>
<td>Hexane methanol reflux</td>
<td>Plaque forming assay, Quantification of viral DNA</td>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>35</td>
<td>Punica Granatum</td>
<td>Punicaceae</td>
<td>Peel</td>
<td>Alcoholic extraction</td>
<td>Cell culture and influenza virus propagation, cytotoxicity assay, cytopathic effect reduction assay, hemagglutination assay, TCID50 virus titration</td>
<td>Influenza virus</td>
</tr>
<tr>
<td>36</td>
<td>Pedilanthus tithymaloideae</td>
<td>Euphorbiaceae</td>
<td>Leaves</td>
<td>Methanolic extraction</td>
<td>Antiviral assays, Cytotoxicity assays</td>
<td>Chikungunya virus</td>
</tr>
<tr>
<td>37</td>
<td>Sambucus nigra</td>
<td>Adoxaceae</td>
<td>Whole Plant</td>
<td>Methanolic extraction</td>
<td>MTT assay, Focus assay, Statistical data analysis</td>
<td>Influenza Virus A &amp; B</td>
</tr>
<tr>
<td>No.</td>
<td>Plant Name</td>
<td>Family</td>
<td>Part Used</td>
<td>Extraction Method</td>
<td>Experiments, Biosafety</td>
<td>Against Influenza Virus A &amp; B</td>
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<tr>
<td>38</td>
<td><em>Silybum marianum</em></td>
<td>Asteraceae</td>
<td>Seeds</td>
<td>Ethanolic</td>
<td>Cell sensitivity to virus, Reference virus inactivation test, Titration of the virus control</td>
<td>It shows promising antiviral effect against poliovirus [47]</td>
</tr>
<tr>
<td>39</td>
<td><em>Spinacia oleracea</em></td>
<td>Amanantaceae</td>
<td>Leaves</td>
<td>Centrifuged supernatant fluid of the mixer of Phosphate buffer, PMS, EDTA, DDT mixed with crude with proper ratio.</td>
<td>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.</td>
<td>Tobacco Mosaic virus It has a little inhibitory activity against TMV virus further study required [48]</td>
</tr>
<tr>
<td>40</td>
<td><em>Terminalia chebula</em></td>
<td>Combretaceae</td>
<td>Leaves</td>
<td>Methanolic extraction</td>
<td>Antiviral assays, Cytotoxicity assays</td>
<td>It has antiviral effect against enterovirus. Indigenously this plant is used to combat of ulcers, bleeding piles and gout. [17]</td>
</tr>
<tr>
<td>41</td>
<td><em>Usnea complanta</em></td>
<td>Usneacea</td>
<td>Whole plant</td>
<td>Acetone</td>
<td>Assays for cytopathic effect inhibition and viral yield reduction</td>
<td>Its antiviral action against the herpes simplex virus is very strong. However, it has typically been used to treat bacterial infections. [25]</td>
</tr>
<tr>
<td>42</td>
<td><em>Verbascum thapsus</em></td>
<td>Scrophulariaceae</td>
<td>Leaves</td>
<td>Methanolic extraction</td>
<td>Dye uptake study.</td>
<td>It is a promising candidate to give anti-viral against influenza virus A. [2, 49]</td>
</tr>
</tbody>
</table>
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]

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 80 percent 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
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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ties of extracts and selected pure constituents of or extracts and related compounds
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