Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2021; 10(3): 428-431
Received: 07-03-2021
Accepted: 09-04-2021

Drisya MK
Division of Pharmacognosy and Phytochemistry Research Laboratory, Nehru College of Pharmacy, Pampady, Thiruvilwamala, Thrissur, Kerala, India

Nowfa Firoskhan
Division of Pharmacognosy and Phytochemistry Research Laboratory, Nehru College of Pharmacy, Pampady, Thiruvilwamala, Thrissur, Kerala, India

Corresponding Author:
Drisya MK
Division of Pharmacognosy and Phytochemistry Research Laboratory, Nehru College of Pharmacy, Pampady, Thiruvilwamala, Thrissur, Kerala, India

A review on natural antiviral herbal medicine

Drisya MK and Nowfa Firoskhan

Abstract
Viral Infections play a significant role in human diseases. Recent outbreaks in the advent of globalization, their prevention is a critical issue in safeguarding public health. Despite the progress made in immunization, there is a lack of preventive vaccines and efficient antiviral therapies for many viruses, which are often beset by the generation of viral escape mutants. Thus, it should be essential for identifying novel antiviral drugs from natural products as an excellent source for such discoveries.

Keywords: virus infection, herbal medicines, viral diseases, natural products, antiviral

Introduction
The virus causes a variety of human pathogens including cancer. Several viral infections are very hard to cure diseases and also some syndromes including Alzheimer's disease, Type 1 Diabetes, and Hepatocellular Carcinoma [1, 2, 3]. Not only that the epidemic outbreaks caused by emerging and reemerging viruses and also due to increased global travel and rapid urbanization shows a critical threat to public health, but particularly vaccines, as well as antiviral therapies, are also still unavailability for some viral diseases. However, only a few antiviral drugs are licensed for clinical practice and so many viruses are remaining without effective immunization. Hence, provide management for control of viral infections when vaccines and standard therapies are lacking and also urgent need to discover novel antivirals that are highly efficacious and cost-effective. We have known for a long time that herbal medicines and purified natural products are a rich resource for novel antiviral drug development. Detection of antiviral mechanisms from these natural agents has shone the light on where they intervene with the viral life cycle such as viral entry, replication, assembly, and release. This review summarizes some antiviral activities diseases and activities from several natural products and some herbal medicines against that pathogens.

Corona Virus (CoV)
Coronavirus is a type of virus, enveloped, positive-sense single-stranded RNA (ssRNA) virus. It belongs to the family Coronaviridae. Coronavirus is a family of viruses consisting of several species and causes severe acute respiratory syndrome (SARS) and gastrointestinal infection in mammals and birds. In humans can cause common cold but complication that occurs including pneumonia and SARS [4].
Saikosaponins (A1B2, C &D) are naturally occurring triterpene glycosides and are isolated from medicinal plants like Bupleurum species, heteromorpha species and Scrophularia species attribute antiviral activity against HCOV-22E9. Natural extracts from *Lycoris radiata, Artemisia annua, Lindera aggregata* displayed an anti-SARS-COV effect from a screening analysis. Myricetin, scutellarein, phenolic compounds from *Isatis indigotica* and *Torreya nucifera* are identified as natural inhibitors against SARS COV enzymes [5].

Coxsackie Virus (CV)
CV are RNA viruses that consist of mainly two subgroups including Subgroup A (CVA) and B(CVB). It belongs to the family Picornaviridae. It is also a non-enveloped positive sense SSRNA mainly transmitted through the fecal-oral route and also contacts with respiratory secretions. This virus may cause hand, foot, mouth diseases (HFMD) and as well diseases of muscles, lungs, heart. Mainly occurs in young children and this can be avoided by self-limited, so no treatment is required. The infected patient shows the symptoms like fever, malaise, common cold, rashes, and also severe causes like aseptic meningitis, encephalitis, and paralysis [6].
The aqueous extract and ethanol extract of bioactive compounds including linalool, apigenin, and ursolic acid from the herb *Ocimum basilicum* possess antiviral activity against CVB1.

Raoulia australis contain raoulic acid and has been reported as a potent antiviral agent against CVB subtypes [7].

Dengue Virus (DENV)

DENV is a mosquito-borne, enveloped positive sense SSRNA virus of the family Flaviviridae. DENV is the cause of dengue fever and is transmitted by mosquito bites, typically by Aedes aegypti [8]. The face closely related dengue virus is found in the same regions of the world. They are DEN-1, DEN-2, DEN-3, DEN-4 and these are roughly spherical structures composed of capsid proteins and viral genome surrounded by an envelope and shell of proteins. The infected persons show symptoms like fever, headache, nausea, vomiting, myalgia, and specifically life-threatening disease like hemorrhage and dengue shock syndrome (DSS) [9]. There is no specific treatment only prevent the disease by mosquito control and relieving symptoms in infected individuals.

The Baicalein is a flavone that shows potent activity against DENV adsorption the host and also some natural products like Quercetin and Narasin and marine seaweed extracts have significant potent activity against DENV. *Terminalia chebula* contains two hydrolyzable tannins such as chebulagic acid and punicalagin shows antiviral properties. They can directly inactive the DENV particles during early viral entry [10].

Enterovirus 71 (EV 71)

It is a non-enveloped positive sense SSRNA genome belonging to the Picornaviridae family. It is transmitted through the fecal-oral route and also by respiratory droplets. It is the major cause of HFMD (Hand Foot Mouth Disease) in children and notable for its role in causing epidemics of several neurological diseases. At present in the development and palliative care used medication and preventive vaccines to ameliorate the symptoms [12].

Several natural products and herbal medicines act as inhibitory activity against EV 71 injection. *Ocimum basilicum* extracts and pure constituents effectively block infection and replication of EV 71 injection. Raoulic acid is an effective inhibitor of CVB. *Woodfordia fruticosa* flower contain phytoconstituent like gallic acid have shown exert antienterovirus 71 activity and also epigallocatechin gallate from Green tea has been identified to interfere with EV 71 replication [11].

Hepatitis B Virus (HBV)

HBV is a prototype, enveloped virus possessing a relaxed circular, partially double-stranded DNA (dsDNA) genome belonging to the family Hepadnaviridae. This disease is spread most commonly by exposure to infected bodily fluids and by using blood products like unclean needles or unscreened blood, or by having unprotected sexual contact and transmitted by mother to baby by pregnancy. The infected persons show symptoms like yellowing of eyes and dark urine and abdominal pain. Hepatitis B can be prevented by vaccination but if you have the condition it is not curable. In severe chronic cases liver, transplantation is the only method to protect the patient [13].

The interferon -α. [peg-IFN –α] and nucleotide or nucleoside analogs such as lamivudine, adefovir, tenofovir, telbivudine, entecavir show an effective treatment against HBV. The herbal medicine and natural products like isochloeogenic acid A from Laggera alata and amide alkaloid from piper longum and dehydrocheilanthifoline from *Corydalis saxicola* show anti-hepatitis activity. Curcumin has been shown the inhibit gene replication by down-regulating the peroxisome proliferator activated receptor gamma coactivator 1 –alpha [PGC-1α] the coactivator of HBV transcription [14].

Hepatitis C Virus (HCV)

Hepatitis C is an enveloped positive-sense SSRNA caused by the hepatitis c virus. This is infection or inflammation of the liver can cause both acute and chronic hepatitis range in severity from a mild illness lasting a few weeks to serious lifelong illness. Most people have shown symptoms like nausea, loss of appetite, and yellowing of eyes and skin. This can be transmitted through sharing drug injection equipment, by birth, health care exposure, unregulated tattoos or body piercing, sex with an infected person, blood transfusing, and organ transplant. This can be treated with antiviral medication and some current treatments usually involve 8-12 weeks of oral pills and cause over 90% with few side effects and also liver transplantation [15].

Natural products like *Silybum marianum* (silymarin) and its flavonolignans have shown the exert anti-hepatitis activity *in vitro* [16]. Curcumin has been detected as a potential inhibitor of HCV replication. Other natural compounds like epigallocatechin gallate, griffithsin, ladanein and tellimagrandine show effectiveness against entry of HCV [17].

Herpes Simplex Virus (HSV)

Herpes Simplex virus is enveloped dsDNA virus belonging to the family Herpesviridae are of two members 1& 2 also known by their taxonomical names like Human alpha herpes virus 1 & 2 that produce viral infections in major of humans. This can be mainly transmitted through oral to oral contact to cause 'oral herpes' that the symptoms known as "cold sores" and also cause genital herpes, that may symptoms shows small ulcers. The first episode shows the symptoms like fever, muscle pain, headache, swollen lymph nodes, and also other disorders like herpetic whitlow when it involves the finger, herpes of the eye herpes infection of the brain, and herpes of neonatal when it affects a newborn [18]. Currently, there is no design or vaccines available against HSV that can be prevented or reduce the risk of developing and passing by avoiding sex while the symptom is present and using barrier protection such as condoms and also avoiding kissing and oral sex when there is a cold sore around the mouth and other parts and washing the hands thoroughly after touching the affected area.

Several natural products and herbal medicines such as epiafzelechin (4α →8)- epiafzelechin extracted from *Cassia javanica* inhibit the replication of HSV -2 and hippomanin A, geranin,1,3,4,6 –tetra –o-galloyl –beta –d –glucose and exoecarianin isolated from *Phyllanthus urinaria* can potently impede HSV infection [34]. *Houttuynia cordata* contains constituents such as Houttuynoids A-E flavonoids found to be potent anti-HSV -1 activity. The aqueous extract from *Rhododendron ferrugineum* L., blackberry extract, and proanthocyanidin enriched extract from *Myrothamnus flabellifolia* Welw show inhibition of HSV-1 infection. The natural products from the marine environment represent while biodiversity in which algae and sponges contain active metabolites to fight against HSV activity [20].

Human immunodeficiency Virus (HIV)

HIV is an enveloped antivirus belonging to the family Retroviridae. These viruses targeting of the immune cells for infection and reverse transcription of their SSRNA genome and also integrate into the host chromosomal DNA. This can be transmitted through the exchange of virus-containing blood

and body fluids, through childbirth as well as breastfeeding, and also sharing of contaminated needles or other surgical items. This virus destroying the WBC that harms the immune system. The infected persons show symptoms within a few weeks such as fever, sore throat, fatigue, loss of appetite, night sweats, malaise, severe unintentional weight loss. The treatment for HIV involves only taking medicine reduces the amount of HIV in the body. The combination of drugs used to treat HIV is antiretroviral (ART) therapy [21].

The crude extracts of *Artemisia annua* and *Artemisia afra* have effective potent activity against HIV medicines. Colophyllum species consists of several coumarins that show exert an inhibitory effect. *Calophyllum brasiliense*, stem bark contain tricyclic coumarin shows inhibition of HIV replication *in vitro* model by suppressing nuclear factor-kappa [NF –KB] activation [22].

Influenza Virus

The influenza virus is enveloped, negative-sense SSRNA belonging to the Family Orthomyxoviridae. It consists of mainly A, B, C viruses (IFA, IFB, IFC). The infected person shows the symptoms like respiratory infection including fever, headache, sore throat, sneezing, muscle, joint pain, and also cause pneumonia [23]. It is transmitted by airborne respiratory droplets like cough or sneezes or by touching a contaminated surface, by saliva (kissing or shared drinks), by skin contact (handshakes, hugs). The normal treatment for influenza virus is rest and plenty of liquids and also includes ways to prevent spreading such as proper washing of hands, keeping clean surfaces, and avoid coughing or sneezing into arm or sleeves. Antiviral medication and annual vaccine are given to prevent this [24].

These liquid extracts of standardized elderberry (*Sambucus nigra*) exert the *in vitro* against antiviral effects like IFA, IFB, and also respiratory bacterial pathogens. The extract from *Pelargonium sidoides* roots inhibits the entry of FDA and also the neuraminidase activity and improves the symptoms of influenza-infected mice. The chalcones from *Glycyrrhiza inflata* xanthones from *Polygala karinsium* and homo isoflavanoids from *Caesalpinia sappan* have attributed as potential influenza inhibitors [25, 26].

Measles Virus (MV)

This is a virus enveloped, negative-sense SSRNA virus of Morbillivirus belonging to the family Paramyxoviridae. This virus is caused by the Rubeola virus.it is a highly contagious sickness caused by a virus that replicates in the nose and throat of an infected child or adult. The infected persons show the symptoms of pain in the muscles, fever, malaise, loss of appetite, dry cough, runny nose or sneezing, swollen lymph nodes. There is no specific treatment and symptoms usually go away within 7 to 10 days. The doctor prescribes Vit A if a child needs treatment in the hospital and also recommends vaccination like MMR (measles, Mumps, Rubella) in two doses of vaccine after one year of age [27].

The plant bioflavonoids isolated from *Rhus succedanea* and *Garcinia multiflora*, calcium spirulan from the blue-green algae spirulina platens is, Crotalus durissus terrific us snake venom, and Rwandan and ugandan medicinal plants extracts made at identifying their natural product that inhibit Measles [28]. *Olinia rochetiana* (olkirenyi) and *Warburgia ugandensis* (osokonoi) and plant extracts of cajanus cajan possess antimeasles activity [29]. Chebulagic acid and punicalagin are two tannins shows effective against measles infection.

Respiratory Syncytial Virus

Respiratory Syncytial virus is an enveloped negative-strand SSRNA Virus belonging to the Paramyxoviridae family. Respiratory Syncytial virus causes infections mainly in the lungs and respiratory tract. The infected person shows signs about 4 to 6 days after exposure to the virus and symptoms are congested or runny nose, dry cough, sore throat, mild headache, and in severe cases inflammation in lungs, cyanosis, breathing problem, etc. There is no current treatment or vaccine that exist for the virus. Only precautions like washing the hands frequently, avoid exposure, keep things clean, smoking, keep things clean, etc. can help prevent the spread of the infection [30].

The chromone glycoside, uncinodide A and B are isolated from *Selaginella uncinala*, potently inhibit RSV infection [31]. The genkwanol B, genkwanol C, and stelleranol are biflavanoids extracted from *Rodex witstroemia* effective against RSV 6-C monoglycosides are flavone from the leaves of *Lophatherum gracile* show to reduce RSV infection [32]. *Cimicifuga foetida* is a major component of herb-identified anti respiratory syncytial natural medicine [33].

Conclusion

A viral infection is caused by the presence of a virus in the body. Moreover, many viruses remain without preventive vaccines and effective antiviral therapies or treatment, eradicating these viral diseases appear difficult. Nonetheless, natural products are attributed as an excellent source of biodiversity for discovering novel antivirals and also developing effective therapeutic strategies against viral infections. Moreover, many natural products and herbal medicines are identified to possess robust antiviral activity, and also their discoveries can further help to develop the derivatives and therapeutic leads. Furthermore, additional studies should encourage the possibility of combination therapies with natural agents or as a multitarget therapy to reduce the risk of generating drug-resistant viruses. Therefore, natural products will continue to play an important role and contribute an antiviral development.

Acknowledgement

The authors are acknowledging The Chairman and Managing Trustee, Adv. Dr. P. Krishnadas, L. L. B, MBA, BEM, Nehru college of Pharmacy, Pampady, Thiruvilwamala, Thrissur, Kerala, for providing all the support.

References

1. Ball MJ, Lukiw WJ, Kammerman EM, Hill JM. Intracerebral propagation of Alzheimer's disease: Strengthening evidence of a herpes simplex virus etiology. Alzheimers Dement 2013;9:169-75.
2. Hober D, Sane F, Jaidane H, Riedweg K, Goffard A, Desailloud R. Immunology in the clinic review series; focus on type 1 diabetes and viruses: Role of antibodies enhancing the infection with Coxsackievirus-B in the pathogenesis of type 1 diabetes. Clin Exp Immunol 2012;168:47-51.
3. Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: A meta-analysis of observational studies. Ann Intern Med 2013;158:329-37.
4. van der Hoek L. Human coronaviruses: What do they cause? Antivir Ther 2007;12:651-8.

5. Cheng PW, Ng LT, Chiang LC, Lin CC. Antiviral effects of saikosaponins on human coronavirus 229E *in vitro*. Clin Exp Pharmacol Physiol 2006;33:612-6.
6. Tapparel C, Siegrist F, Petty TJ, Kaiser L. Picorna virus and enterovirus diversity with associated human diseases. Infect Genet Evol 2013;14:282-93.
7. Chiang LC, Ng LT, Cheng PW, Chiang W, Lin CC. Antiviral activities of extracts and selected pure constituents of Ocimum basilicum. Clin Exp Pharmacol Physiol 2005;32:811-6.
8. Black WCt, Bennett KE, Gorrochotegui-Escalante N, Barillas-Mury CV, Fernandez-Salas I, de Lourdes Munoz M *et al*. Flavivirus susceptibility in *Aedes aegypti*. Arch Med Res 2002;33:379-88.
9. Sam SS, Omar SF, Teoh BT, Abd-Jamil J, AbuBakar S. Review of Dengue hemorrhagic fever fatal cases seen among adults: A retrospective study. PLoS Negl Trop Dis 2013;7:e2194.
10. Zandi K, Teoh BT, Sam SS, Wong PF, Mustafa MR, Abubakar S. Novel antiviral activity of baicalein against dengue virus. BMC Complement Altern Med 2012;12:214.
11. Chang LY, Tsao KC, Hsia SH, Shih SR, Huang CG, Chan WK *et al*. Transmission and clinical features of enterovirus 71 infections in household contacts in Taiwan. JAMA 2004;291:222-7.
12. Choi HJ, Lim CH, Song JH, Baek SH, Kwon DH. Antiviral activity of raoulic acid from Raoulia australis against Picornaviruses. Phytomedicine 2009;16:35-9.
13. Liang TJ, Hepatitis B. The virus and disease. Hepatology 2009;49(5 Suppl):S13-21.
14. Kwon H, Lok AS. Hepatitis B therapy. Nat Rev Gastroenterol Hepatol 2011;8:275-84.
15. El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. Gastroenterology 2012;142:1264-73.
16. Polyak SJ, Morishima C, Shuhart MC, Wang CC, Liu Y, Lee DY. Inhibition of T-cell inflammatory cytokines, hepatocyte NF-kappa B signaling, and HCV infection by standardized Silymarin. Gastroenterology 2007;132:1925-36.
17. Ciesek S, von Hahn T, Colpitts CC, Schang LM, Friesland M, Steinmann J *et al*. The green tea polyphenol, epigallocatechin-3-gallate, inhibits hepatitis C virus entry. Hepatology 2011;54:1947-55.
18. Fatahzadeh M, Schwartz RA. Human herpes simplex labialis. Clin Exp Dermatol 2007;32:625-30.
19. Isaac John Umaru, Saad Ismail Shuaibu, Rufaidat Baba Adam, Bilyaminu Habibu, Kerenhappuch Isaac Umaru, David Ephraim Haruna. Bando Christopher David. Effect of herbal medicine and its biochemical implication. Int. J Adv. Biochem. Res. 2020;4(2):46-57. DOI: 10.33545/26174693.2020.v4.i2a.130
20. Chen SD, Gao H, Zhu QC, Wang YQ, Li T, Mu ZQ, *et al*. Houttuynoids A-E, anti-herpes simplex virus active flavonoids with novel skeletons from Houttuynia cordata. Org Lett 2012;14:1772-5.
21. Sierra S, Kupfer B, Kaiser R. Basics of the virology of HIV-1 and its replication. J Clin Virol 2005;34:233-44.
22. Kudo E, Taura M, Matsuda K, Shimamoto M, Kariya R, Goto H *et al*. Inhibition of HIV-1 replication by a tricyclic coumarin GUT-70 in acutely and chronically infected cells. Bioorg Med Chem Lett 2013;23:606-9.
23. Eccles R. Understanding the symptoms of the common cold and influenza. Lancet Infect Dis 2005;5:718-25.
24. Krawitz C, Mraheil MA, Stein M, Imirzalioglu C, Domann E, Pleschka S *et al*. Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and influenza A and B viruses. BMC Complement Altern Med 2011;11:16.
25. Dao TT, Nguyen PH, Lee HS, Kim E, Park J, Lim SI *et al*. Chalcones as novel influenza A (H1N1) neuraminidase inhibitors from Glycyrrhiza inflata. Bioorg Med Chem Lett 2011;21:294-8.
26. Dao TT, Dang TT, Nguyen PH, Kim E, Thuong PT, Oh WK. Xanthones from Polygala karensium inhibit neuraminidases from influenza A viruses. Bioorg Med Chem Lett 2012;22:3688-92.
27. Clements CJ, Cutts FT. The epidemiology of measles: Thirty years of vaccination. Curr Top Microbiol Immunol 1995;191:13-33.
28. Cos P, Hermans N, De Bruyne T, Apers S, Sindambiwe JB, Vanden Berghe D *et al*. Further evaluation of Rwandan medicinal plant extracts for their antimicrobial and antiviral activities. J Ethnopharmacol 2002;79:155-63.
29. Nwodo UU, Ngene AA, Iroegbu CU, Onyedikachi OA, Chigor VN, Okoh AI. *In vivo* evaluation of the antiviral activity of Cajanus cajan on measles virus. Arch Virol 2011;156:1551-7.
30. Hall CB. Prospects for a respiratory syncytial virus vaccine. Science 1994;265:1393-4.
31. Ma LY, Ma SC, Wei F, Lin RC, But PP, Lee SH *et al*. Uncinoside A and B, two new antiviral chromone glycosides from Selaginella uncinata. Chem Pharm Bull (Tokyo) 2003;51:1264.
32. Huang W, Zhang X, Wang Y, Ye W, Ooi VE, Chung HY *et al*. Antiviral biflavonoids from Radix Wikstroemiae (Liaogewanggen) Chin Med 2010;5:23.
33. Wang LJ, Geng CA, Ma YB, Huang XY, Luo J, Chen H *et al*. Synthesis, biological evaluation and structure-activity relationships of glycyrrhetinic acid derivatives as novel anti-hepatitis B virus agents. Bioorg Med Chem Lett 2012;22:3473-9.
34. Cheng HY, Yang CM, Lin TC, Shieh DE, Lin CC. ent-Epiafzelechin- (4alpha-->8)-epiafzelechin extracted from Cassia javanica inhibits herpes simplex virus type 2 replication. J Med Microbiol 2006;55:201-6.