eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

Bioactive Plant Compounds Against Viral Diseases: A Reviev

Dr. Suresh Kumar Patel[1], Mr. Roshan Lal[2]
[1]Assistant Professor Chemistry, Shaheed Mangal Pandey Government Girls Post Graduate College, Meerut
[2]Assistant Professor Chemistry, Shaheed Mangal Pandey Government Girls Post Graduate College, Meerut

Received: 24 October 2024, Accepted: 28 October 2024, Published online: 31 October 2024

Abstract

Infectious diseases arise due to penetration of the body tissues by microorganisms such as bacteria, virus, fungus, and parasite. In modern era, viral infections are one of the main causes of disease globally, due to the increase of migration, global transport and urbanization. There are many antiviral drugs and vaccines available against viruses, but these have several side effects and active mutation of viruses also create drug resistance. In developed countries, 80% of the population depends on traditional medicines for their primary health issues, according to the World Health Organization (WHO). Relatedly, India is one of the highest medicinal herbs producing country. Long-term use by human, low toxicity and abundance of bioactive plant compounds led scientists to search herbs as a source for the discovery of more efficient new antivirals. In this review, we focus on the importance of plant extracts and their isolated pure compounds and their potential application in treating or preventing viral diseases.

Keywords: HIV, HSV, Hepatitis C virus, influenza virus, COVID-19, phytochemicals.

Introduction

Viral infections represent one of the main causes of disease due to their complexity and diversity, which make very difficult to counteract their effects and diffusion, which lead often to pandemic events [1]. The increase of migration, global travel, and urbanization have made viruses outbreaks a crucial point for public health, especially when vaccines and antiviral therapies are still not available [2]. Viral infections and associated diseases are responsible for a substantial number of mortality and public health problems around the world. Each year, infectious diseases kill 9.0 million people worldwide [3]. A virus is a tiny parasite that has no capacity to replicate itself. Once infected in a host agent or living cell, it produces more viruses using host machinery. They have RNA or DNA as genetic material with single or double-stranded nucleic acid. Using unique physical properties such as phospholipid layers, ligands, and configurations, they invaded into host cells easily [4]. They show numerous invasion strategies on host cells due to their genetic variation, unique configuration of surface molecules and efficient replication linked to the host resources [5]. Viral infections can lead to acute as well as chronic conditions. Human use of plants as medicine, including viral infections, dates back 60,000 years to the Paleolithic age [6]. The antiviral agent's development started immediately after the end of the Second World War with an increase of in vitro and in vivo studies on antiviral activity of medicinal plants especially during the last 30 years [7]. Furthermore, the failure of several conventional drugs against viral infections and the onset of specific viral resistances has led to an increasing interest for plants as promising antiviral agents [8]. Several plants, essential oils as well as isolated bioactive compounds, such as phenolic acids, flavonoids, terpenes, lignans, coumarins, alkaloids, or proteins showed a potential role as antiviral agents [9]. The aim of this review is to provide an update on the antiviral role of different plants and their isolated compounds, elucidating their mechanism of action and potential interactions against various viruses such as the corona virus, human immunodeficiency virus (HIV), herpes simplex virus (HSV), influenza, and hepatitis c.

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

2. Methodology- We searched for relevant literature using terms like "infectious disease, viral infections, phytochemicals, SARS-CoV-2, HIV, HSV, influenza, hepatitis C, HIV integrase, HIV-reverse transcription, HIV-protease, virucidal action, viral attachment, HCV infection replication, etc." Relevant databases, including Google Scholar, PubMed, SciELO, and others, were searched using these keywords. Between 1975 and 2024, we have gathered data from conference abstracts, books, chapters, research articles, reviews, PhD theses, and books.

3. Therapeutic Natural Compounds against Viruses

a. SARS-CoV-2,

A new coronavirus subtype known as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is currently causing an outbreak that is killing and infecting millions of people globally. Since December 2019, the novel coronavirus illness 2019 (COVID-19), which is caused by SARS-CoV-2, has raised concerns about world health. SARS-CoV-2 are spherical positive single-stranded RNA viruses that are identified by the presence of S proteins projecting from the virion surface [10]. The antiviral properties of few phytochemicals on SARS-CoV-2 are listed in table 1.

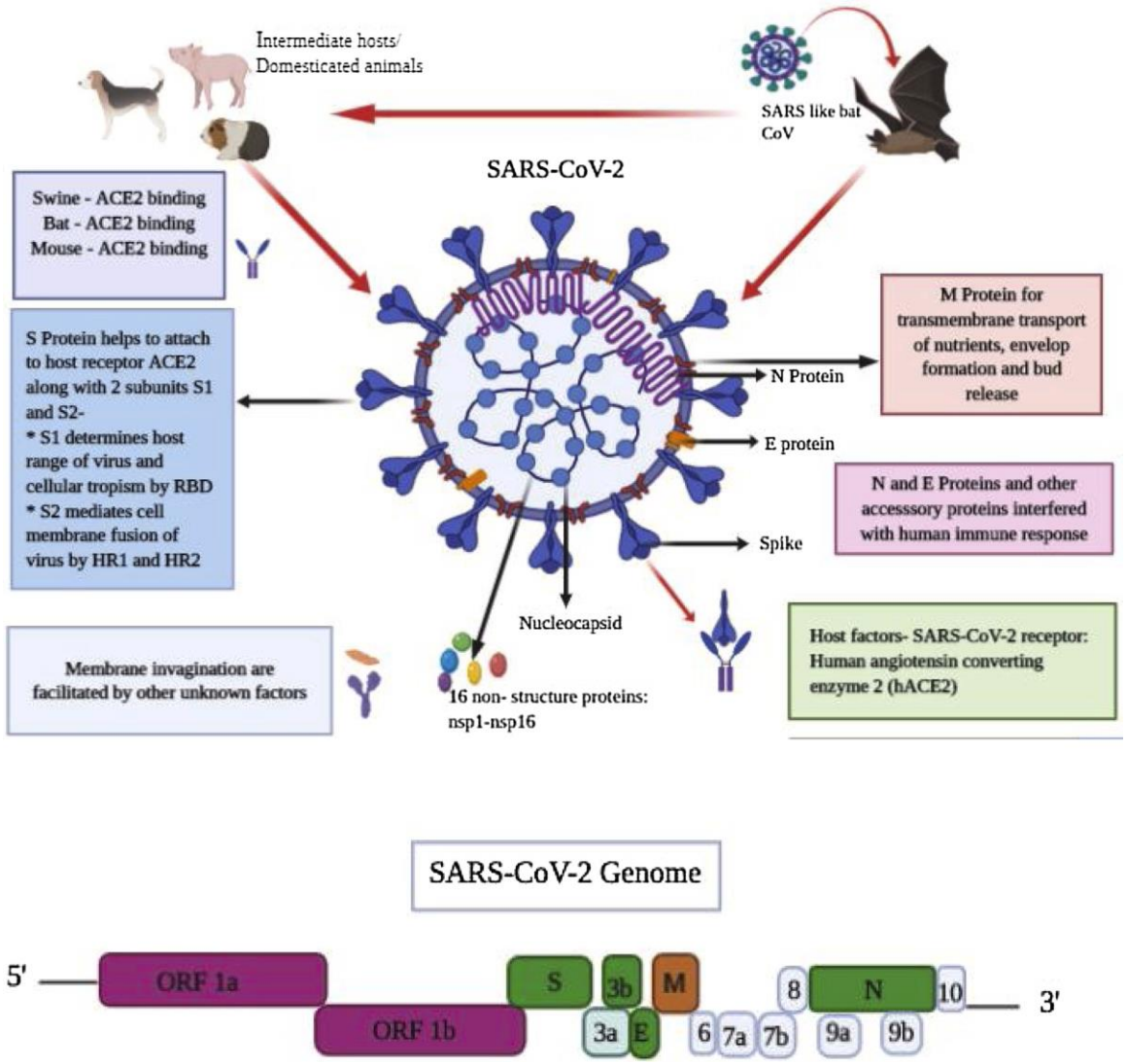


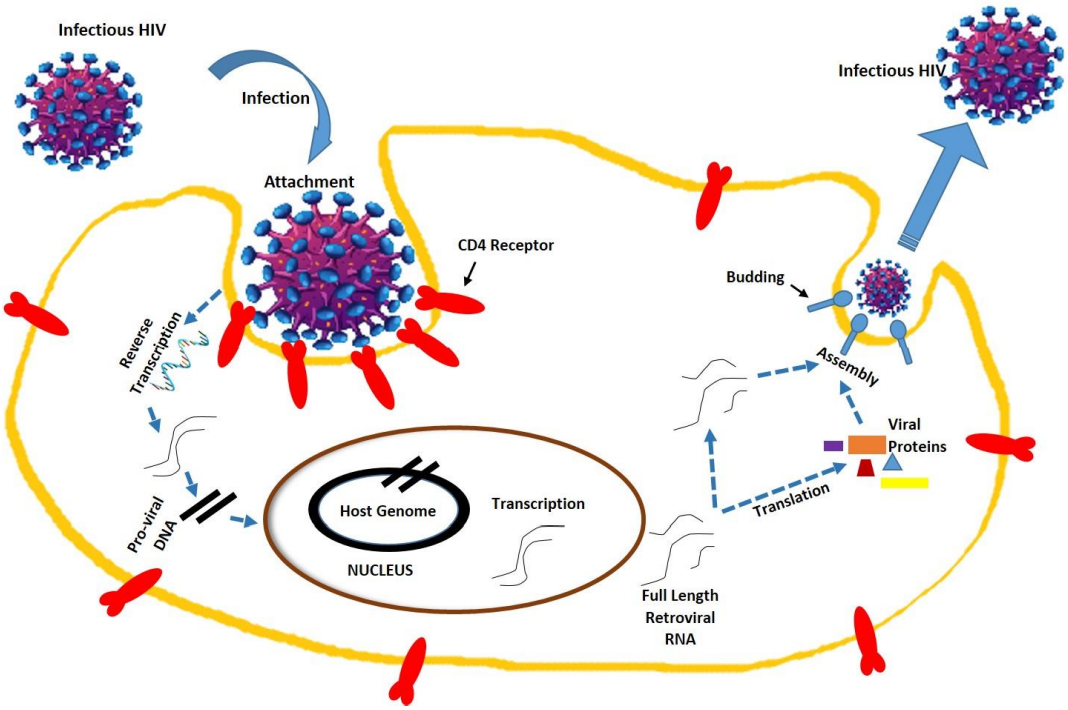
Figure:1 *SARS-CoV-2 structural and genomic organization. (Riya Bhattacharya et al. 2021)* [31]

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

b. Human Immunodeficiency Virus (HIV)

HIV is a member of the genus Lentivirus, part of the family Retroviridae [11]. HIV contains two copies of single-strand RNA, which is the contributory agent of acquired immunodeficiency syndrome (AIDS) by a progressive decline of the immune system. In this condition, the infections take advantage of the weaker immune system, where the immune system is no longer in a stage to fight back. HIV is an enveloped positive-sense virus, which is meticulously focused on the immune system by infecting $CD4^+$ T cells [12]. This T helper cell is the core of the immune system, whereby it handles signal transduction toward the rest of the immune cells and thereby protects the whole system against life-threatening infections and endangering subjects.

The treatment for HIV involves antiretroviral therapy (ART), which is a combination of HIV medicines. ART



has become more important, since there is no vaccine available against HIV. However, again, ART is not a panacea for HIV due to the various side effects and resistance. [13]. Saquinavir, indinavir, ritonavir, and nelfinavir are a few examples of approved protease inhibitors by the WHO [14]. Hence, significant attempts have been employed by natural product biologists to find an alternative for ART. The screening of many plants has delivered plenty of secondary metabolites with anti-HIV properties. They include alkaloids, triterpenoids, flavonoids, coumarins, phenolics, tannins, saponins, phospholipids, xanthones, quinones, etc. [15]. Some of them have been found to inhibit HIV integrase and some show RT inhibition (Table1).

Figure 1. *Human immunodeficiency virus structure and replication mechanism (Syam Mohan et al. 2020)* [30]

c. Herpes Simplex Virus (HSV)

HSV is a member of Herpesviridae and composed of double-stranded DNA and an icosahedral capsid, which is surrounded by an amorphous tegument and an envelope containing viral glycoproteins [16]. It causes oral and genital infections associated with herpes labialis or cold sore in both human and animals. The herpes simplex virus (HSV) infection, otherwise known as genital herpes (GH), is the most frequent cause of genital ulceration worldwide. There is a starting treatment for HSV with Acyclovir, Valacyclovir, or Famciclovir for

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

7–10 days for primary HSV infections with either unwanted drug side effects or drug resistance [17]. Many herbal compounds have been investigated in the past for their effectiveness against HSV. An important natural antiviral agent against herpes is represented by Curcumin, which can inhibit the HSV-1 replication [18]. The Quercetin inhibits the infection of HSV-1, HSV-2 and Acyclovir-resistant HSV-1 mainly by blocking viral binding and host cell penetration [19].

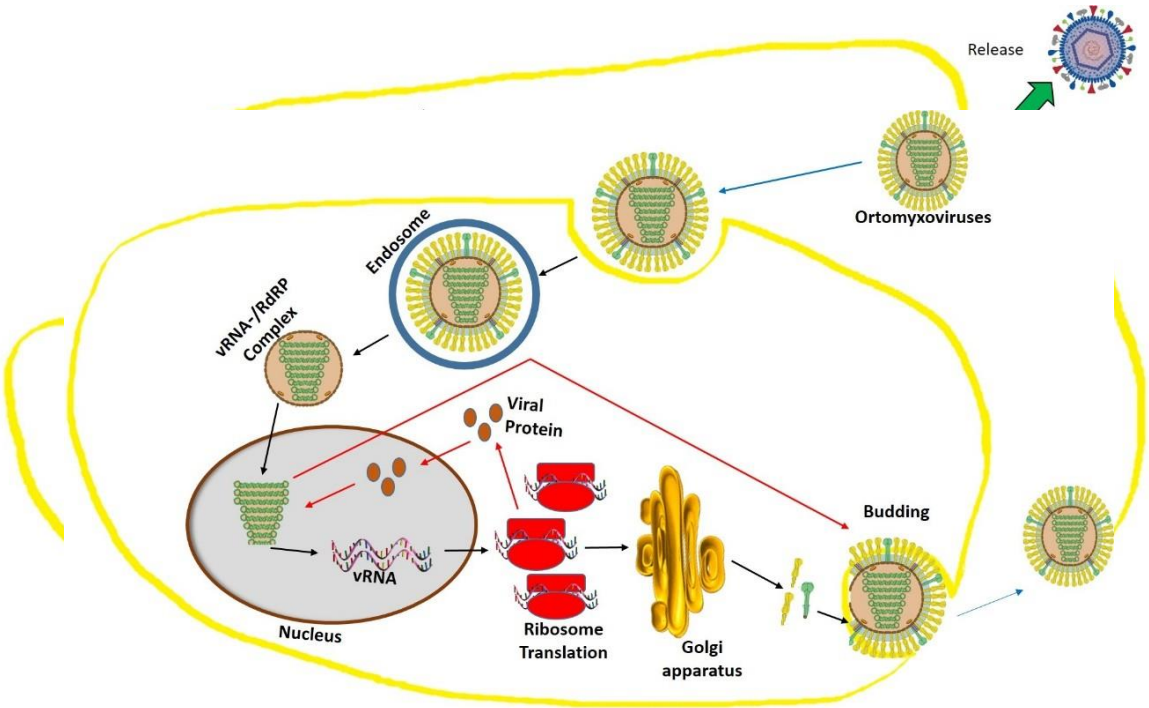


Figure 2. *Herpes simplex virus structure and replication mechanism. (Syam Mohan et al. 2020)* [30]

d. Influenza Virus

The influenza virus, a member of the Orthomyxoviridae family, is a single-stranded RNA virus that infects both mammals and birds. Its genome is negatively sense linearly fragmented and encapsulated in capsids. It includes seven species-Alpha, Beta, Gamma, Delta, Isavirus, Quaranjavirus, and Thogotovirus [20]. Alpha, Beta, Gamma, and Delta, caused mammalian flu. There are 18 various hemagglutinin (HA) subtypes and 11 various neuraminidase (NA) subtypes [21]. Subtypes are named by combining the H and N numbers e.g., A(H1N1), A(H3N2). On the other hand, influenza B viruses are classified into two lineages: B/Yamagata and B/Victoria. Influenza viruses are extremely infective agents due to the frequent epidemics and pandemics Three pandemics happened in the previous century: the H1N1 pandemic (1918), the H2N2 pandemic (1957), and the H3N2 pandemic (1968) [22].

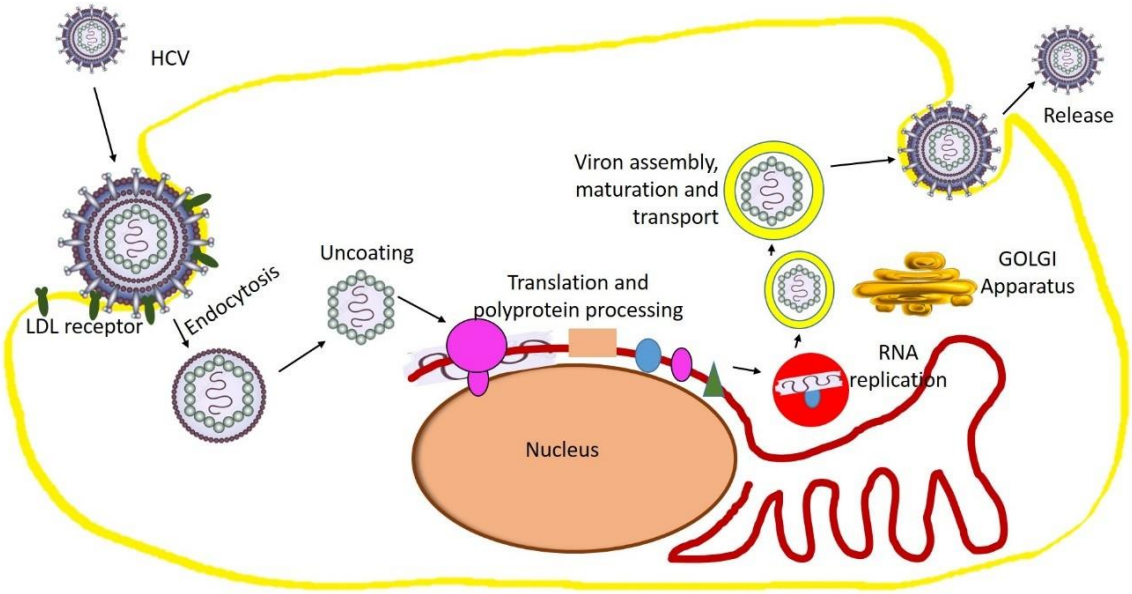
Among viral infections, the viruses of the influenza viral infection have the ability to mutate their genome and become resistant to drugs [23]. Thus, the discovery of phytochemicals against the influenza virus is more challenging compared to other viruses. Among the phytochemicals, alkaloids have shown superior activity against flu virus. It is believed that the alkaloids have the ability to kill virus by the induction of interferon of the immune system [24]. Some alkaloids can increase the phagocytosis by macrophages activity, whereas some can inhibit viral protein synthesis [25].

Figure 2. *Orthomyxovirus virus structure and replication mechanism. (Syam Mohan et al. 2020)* [30]

e. Hepatitis C Virus (HCV)

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

Hepatitis C virus (HCV) is an enveloped virus with a positive single stranded RNA genome with two embedded viral glycoproteins, which belongs to the Flaviviridae family. This tiny virus (55–56 nm) is the causing agent of Hepatitis C, an acute liver inflammatory disease, which can exacerbate and become chronic, leading to high risk of liver cirrhosis and hepatocellular carcinoma development [26]. Hepatitis C virus (HCV) infection is considered as a significant public health problem. It has infected around 180 million people



worldwide [27].

There are synthetic agents available now against HCV, but they have a lack of specific treatment for HCV therapy. Another concern in these cases is the presence of severe side effects and reported poor response rates. To manage and to get these problems under control for better treatment against HCV, new potential agents to be explored.

Natural compounds always serve as a lead to create new drugs. There is substantial increase in the reports on phytochemicals that show anti-HCV properties. Both primary and secondary metabolites have shown promising activities. For instance, alkaloids, flavonoids, polyphenols, coumarins, and peptides have been reported to possess anti-HCV activities [28].

Figure 2. *Hepatitis C s virus structure and replication mechanism. (Syam Mohan et al. 2020)* [30]

Table 1: Some phytochemicals their source active against various viruses [29,30]

S.No	Plant	Virus	Phytocheicals/Extract	Mode of action/Target
1.	*Zingiber officinale*	SARS-CoV-2	6-gingerol	In silico binding affinity to 5R7Y protease
2.	*Psorothamnus arborescens*	SARS-CoV-2	5,7,3′,4′-tetrahydroxy-2′-(3,3- dimethylallyl) isoflavone	Inhibition of 3CLpro
3.	*a) Justicia adathoda L* *b) Carica Papaya* *c) Andrographis paniculata Burm* *d) Ocimum tenuiflorum* *e) Melia azedarach*	SARS-CoV-2	Vasicine Quercetin Andrographolide Ursolic acid Meliacin	In silico binding affinity to Spike (S) protein

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

4.	*Euphorbia kansui*	HIV	Ingenol Bryostatin Prostratin	Latency-reversing agents (LRAs)
5.	*Calophyllum lanigerum*	HIV	Calanolides	Reverse trascriptase and Integrase inhibitors
6.	*Syzygium claviflorum*	HIV	Betulinic acid Dihydro betulinic	Maturation inhibitors
7.	*Nostoc ellipsosporum*	HIV	Ascyanovirin-N	Entryinhibitors
8.	*Curcuma longa L*	HSV-1	Curcumin Gallium-curcumin Cu-curcumin	Inhibits immediate-early Gene expression
9.	*Houttuynia cordata*	HSV-1, HSV-2	Quercetin	Blocks viral binding and Suppresses NF-kB activation
10.	*Aloe Vera*	HSV-1	Polyphenols-rich extract	Reduction of cytopathic effect (CPE)
11.	*Litchi chinensis*	H3N2	Oligonol	Blocking (ROS)-dependent ERK phosphorilation
12.	*Green tea*	H1N1	Catechins, Epigallocatechin gallate	Inhibiting RNA polymerase, Haemagglutinin inhibitors
13.	*Mycale hentscheli*	H1N1, H3N2	Pateamine A	Inhibitors of the cellular factor eEIF4A
14.	*Curcuma longa L.*	H1N1	Curcumin	Haemagglutinin inhibitors
15.	*Bupleurum kaoi*	HCV	Saikosaponin B2, Methanolicextract	Inhibition of viral entry
16.	*Anthocyanidin*	HCV	Delphinidin	Inhibition of viral entry
17.	*Alloeocomatella polycladia*	HCV	Ethylacetate soluble fraction	Suppression of the helicase activity of HCV NS3
18.	*Taraxacum officinale*	HCV	Flavonoids	Inhibition of HCV NS5B replicase activity
19.	*Entada africana*	HCV	Methylene chloride-methanol (MCM) stem bark crude extract	Broad antiviral activity
20.	*Flavanone*	HCV	Naringenin	Release/Assembly

4. Conclusions- Viral infections and pandemic have been recorded as a potential risk for human survival. The lack of proper prophylactic vaccines and drugs for many viruses makes the situation worse in health management. Due to rapid mutation capability of virus, it leads to change in strains dynamically, which make it more worsen to develop any drug or effective vaccine. Exploration of novel antiviral compounds for drug development is on prime requirement. In the current review, we have selected SARS-CoV-2, HIV, HSV, Influenza virus and HCV. The purpose of this current review is to identify some plant metabolites that can be used in the prevention and treatment of some viral infections. This review also highlights the importance of replacing synthetic drugs that cause many side effects in the long run, by plants as a natural source of medication. Natural products directly or indirectly support the drug discovery against viruses. Therefore, it is necessary to pay attention to using plants as a safe, natural source for treating many diseases that affect humans and animals.

eISSN 2581-8996
ONLINE
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN MULTIDISCIPLINARY SCIENCES (IJARMS)
A BI-ANNUAL, OPEN ACCESS, PEER REVIEWED (REFEREED) JOURNAL
Vol. 07, Special Issue 02, October 2024

References:

1. Drexler, Madeline; "What you need to know about infectious disease." *Washington (DC): The National Academies Press (US).* (2014).
2. Neiderud, Carl-Johan. "How urbanization affects the epidemiology of emerging infectious diseases." *Infection ecology & epidemiology* 5.1 (2015): 27060.
3. Bhutta, Zulfiqar A., et al. "Global burden, distribution, and interventions for infectious diseases of poverty." *Infectious diseases of poverty* 3 (2014): 1-7.
4. Brito, Anderson F., and John W. Pinney. "Protein–protein interactions in virus–host systems." *Frontiers in microbiology* 8 (2017): 1557.
5. Cohen, Fredric S. "How viruses invade cells." *Biophysical journal* 110.5 (2016): 1028-1032.
6. Solecki, Ralph S. "Shanidar IV, a Neanderthal flower burial in northern Iraq." *Science* 190.4217 (1975): 880-881.
7. Akram, Muhammad, et al. "Antiviral potential of medicinal plants against HIV, HSV, influenza, hepatitis, and coxsackievirus: A systematic review." *Phytotherapy Research* 32.5 (2018): 811-822.
8. Irwin, Kristen K., et al. "Antiviral drug resistance as an adaptive process." *Virus evolution* 2.1 (2016): vew014.
9. Daglia, Maria. "Polyphenols as antimicrobial agents." *Current opinion in biotechnology* 23.2 (2012): 174-181.
10. Neuman, Benjamin W., et al. "Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy." *Journal of virology* 80.16 (2006): 7918-7928.
11. Mohan, Syam, et al. "Bioactive natural antivirals: An updated review of the available plants and isolated molecules." *Molecules* 25.21 (2020): 4878.
12. Soudeyns, Hugo, et al. "Transient T cell receptor β-chain variable region-specific expansions of CD4+ and CD8+ T cells during the early phase of pediatric human immunodeficiency virus infection: characterization of expanded cell populations by T cell receptor phenotyping." *The Journal of infectious diseases* 181.1 (2000): 107-120.
13. Bock, Christoph, and Thomas Lengauer. "Managing drug resistance in cancer: lessons from HIV therapy." *Nature Reviews Cancer* 12.7 (2012): 494-501.
14. Gills, Joell J., et al. "Nelfinavir, A lead HIV protease inhibitor, is a broad-spectrum, anticancer agent that induces endoplasmic reticulum stress, autophagy, and apoptosis in vitro and in vivo." *Clinical cancer research* 13.17 (2007): 5183-5194.
15. Asres, Kaleab, et al. "Naturally derived anti-HIV agents." *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 19.7 (2005): 557-581.
16. Fatahzadeh, Mahnaz, and Robert A. Schwartz. "Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management." *Journal of the American Academy of Dermatology* 57.5 (2007): 737-763.
17. Brady, Rebecca C., and David I. Bernstein. "Treatment of herpes simplex virus infections." *Antiviral research* 61.2 (2004): 73-81.
18. Zandi, Keivan, et al. "Evaluation of antiviral activities of curcumin derivatives against HSV-1 in Vero cell line." *Natural product communications* 5.12 (2010): 1934578X1000501220.
19. Hung, Pei-Yun, et al. "Houttuynia cordata targets the beginning stage of herpes simplex virus infection." *PloS one* 10.2 (2015): e0115475.

20. Nachbagauer, Raffael, and Florian Krammer. "Universal influenza virus vaccines and therapeutic antibodies." *Clinical Microbiology and Infection* 23.4 (2017): 222-228.
21. Ng, Sophia, et al. "Novel correlates of protection against pandemic H1N1 influenza A virus infection." *Nature medicine* 25.6 (2019): 962-967.
22. Jester, Barbara J., Timothy M. Uyeki, and Daniel B. Jernigan. "Fifty years of influenza A (H3N2) following the pandemic of 1968." *American journal of public health* 110.5 (2020): 669-676.
23. Brown, E. G., et al. "Pattern of mutation in the genome of influenza A virus on adaptation to increased virulence in the mouse lung: identification of functional themes." *Proceedings of the National Academy of Sciences* 98.12 (2001): 6883-6888.
24. Ghildiyal, Ritu, et al. "Phytochemicals as antiviral agents: recent updates." *Plant-derived bioactives: production, properties and therapeutic applications* (2020): 279-295.
25. Moradi, Mohammad-Taghi, Ali Karimi, and Zahra Lorigooini. "Alkaloids as the natural anti-influenza virus agents: a systematic review." *Toxin reviews* 37.1 (2018): 11-18.
26. Gao, Jianjun, and Chuanxia Ju. "Research progress on the direct antiviral drugs for hepatitis C virus." *BioScience Trends* 11.1 (2017): 41-45.
27. Soriano, Vincent, et al. "Directly acting antivirals against hepatitis C virus." *Journal of antimicrobial chemotherapy* 66.8 (2011): 1673-1686.
28. Sola, M. A. W. M., et al. "The activity of Sterculia quadrifida R. Br stembark against hepatitis C virus." *Proceedings of the BROMO Conference (BROMO 2018), East Java, Indonesia*. 2018.
29. Musarra-Pizzo, Maria, et al. "Antiviral activity exerted by natural products against human viruses." *Viruses* 13.5 (2021): 828.
30. Mohan, Syam, et al. "Bioactive natural antivirals: An updated review of the available plants and isolated molecules." *Molecules* 25.21 (2020): 4878.
31. Bhattacharya, Riya, Kamal Dev, and Anuradha Sourirajan. "Antiviral activity of bioactive phytocompounds against coronavirus: An update." *Journal of Virological Methods* 290 (2021): 114070.