URF PUBLISHERS
connect with research world

Journal of Alternative Complementary & Integrative Medicine

https://urfpublishers.com/journal/alternativemedicine

Vol: 1 & Iss: 1

Review

Post Invasional Host Interaction Consequences of Monkey Pox Virus and Its Advanced Treatment: A Mechanism Based Review

Darshana Rathi*, Laxmi Sahu, Anjali Minj and Trilochan Satapathy

Columbia Institute of Pharmacy, Village Tekari, Near Vidhansabha, Raipur-493111, C.G, India

Citation: Rathi D, Sahu L, Minj A, Satapathy T. Post Invasional Host Interaction Consequences of Monkey Pox Virus and Its Advanced Treatment: A Mechanism Based Review. *J Altern Complement Integra Med 2024;* 1(1): 26-33.

Received: 16 November, 2024; **Accepted:** 02 December, 2024; **Published:** 04 December, 2024

***Corresponding author:** Darshana Rathi, Columbia Institute of Pharmacy, Village Tekari, Near Vidhansabha, Raipur-493111, C.G, India. Mob: +919039014155, Email: darshanarathi20018@gmail.com

ABSTRACT

The present study has been undertaken to explore and explain the post invasional consequences of monkeypox (Mpox) virus. This infectious disease occurs in humans as well as other animals with the symptoms such as rash, blisters, which in term causes fever and enlargement of lymph nodes, muscle aches. Other complication includes pneumonia, encephalitis, sepsis, eye infection that leads loss of vision also. Various majors such as supportive treatment and therapeutic majors such as antivirals like Tecovirimat, Brincidofovir, Cidofivir, etc. Apart from therapeutic majors the prevention is the best way and can be achieved by Mpox vaccine. There are two FDA approved vaccine for monkeypox i.e., JYNNEOS and ACAM2000 available in the market that shows positive response towards monkeypox virus. In this review, we have devoted our efforts to comprehensively discuss the mechanism through which the antiviral agents and vaccines exert their pharmacological response to fight with monkeypox virus.

Keywords: Monkeypox Orthopoxvirus, Tecovirimat, JYNNEOS Vaccine, ACAM2000

1. Introduction

The monkeypox virus, which belongs to the Orthopoxvirus genus in the Poxviridae family, is the cause of the uncommon viral illness known as monkeypox[1]. Although the virus was initially identified in 1958 in laboratory monkeys (hence the term "monkeypox"), rodents and other small animals are thought to represent the virus's natural reservoir[2]. The disease is mainly seen in central and west Africa and the first human case was discovered in the Democratic Republic of the Congo in 1970[3]. The main ways that monkeypox is transmitted are via eating bushmeat or coming into touch with diseased animals, such as rats and primates[4]. Direct contact with an infected person's bodily fluids, skin lesions or respiratory droplets, particularly during close contact, can also result in human-to-human transmission. Additionally, contaminated goods and surfaces, such clothing or bedding, can transmit the infection[5]. A rash that typically begins on the face and extends to other areas of the body, such as the hands, feet and genital area, is a hallmark of monkeypox[6]. The rash develops in phases, beginning as flat red spots and progressing to elevated, fluid-filled vesicles, crusting over and finally healing. Monkeypox is usually a mild illness that goes away on its own in a few weeks. Nonetheless, the illness can occasionally be rather serious, particularly in young children, expectant mothers or those with compromised immune systems. Sepsis, pneumonia, subsequent bacterial infections and in rare instances, death, are examples of complications. Depending on the virus strain and the population afflicted, the fatality rate of monkeypox might vary from 1% to 11%[7]. Although monkeypox has traditionally only been found in specific parts of Africa, incidences outside of Africa have noticeably increased in recent years[8]. A major worldwide outbreak of monkeypox was documented in 2022, including instances in nations that

had never before seen widespread monkeypox transmission[9]. Increased public health awareness resulted from this and public health initiatives and vaccine campaigns were used to try to stop the spread. Monkeypox does not currently have a specific antiviral treatment. However, if given prior to exposure, smallpox vaccinations, which are quite effective against monkeypox, can offer protection[10]. In actuality, healthcare professionals and those who are at high risk of exposure are frequently advised to get the smallpox vaccine. For severe cases, antiviral medications like tecovirimat may be utilized. Isolating affected people, maintaining proper hygiene, avoiding contact with animals that might be infected and utilizing personal protective equipment (PPE) for healthcare personnel are all examples of preventive strategies.

2. Monkeypox Classification

The monkeypox virus, a species of the genus Orthopoxvirus, is the cause of mpox, formerly known as monkeypox. Clade I, which includes subclades Ia and Ib and Clade II, which includes subclades IIa and IIb, are the two separate clades of the virus. The clade IIb strain of m-pox produced a worldwide outbreak in 2022-2023. The monkeypox virus (MPXV) is the cause of m-pox. In the Poxviridae family, which also contains variola, cowpox, vaccinia and other viruses. Clade I, which includes subclades Ia and Ib and Clade II, which includes subclades IIa and IIb, are the two separate clades of the virus. The orthopoxvirus genus contains the variola virus, which caused smallpox, an infectious human disease, before it was eradicated with the development of the smallpox vaccine. The WHO has classified several members of the poxvirus family, including the monkeypox virus, as potentially epidemic or pandemic illnesses. Both the United States and the European Union (EU) have classified the monkeypox virus as a potentially high or serious danger disease. Clade I, which has traditionally been linked to the Congo Basin and Clade II, which has historically been linked to West Africa, are the two subcategories or clades. Clade II was responsible for a worldwide pandemic in 2022-2023[11]. The coding area of MPV is 96.3% the same as that of the variola virus however, the regions of the genome that encode for virulence and host range are different. MPV is not a direct descendant of the variola virus, according to a phylogenetic study. The virus has a kingdom called Varidnaviria. The phylum Nucleocytoviricota of the Bamfordvirae family is a member of the Class Pokkesviricetes and the Order Chitovirales, which is a member of the Family Poxviridae. The genus Orthopoxvirus is known as Orthopoxvirus monkeypox[12,13]. Other synonyms for Clades include MPV, MPXV and hMPXV. Clades are further separated into Clades I and II, which are further classed as Clade Ia and Clade Ib for Clade I and Clade IIa and Clade IIb for Clade II[14].

3. Genome and Structure

Like other poxviruses, the monkeypox virus is oval in shape and has an outer membrane made of lipoproteins. The virus's transcription factors, DNA and enzymes are shielded by the outer membrane. DNA viruses typically rely on the machinery of their host cell to reproduce and express their genome in the nucleus of eukaryotic cells. However, the majority of the proteins that monkeypox viruses need to proliferate in the cytoplasm are encoded in their genome[13]. The 200 kb of double-stranded DNA that make up the monkeypox virus's genome code for 191 proteins. Monkey pox virions have big oval envelopes, just like other poxviruses. The DNA and the enzymes that help break down the protein coat and replicate are located in the core of each virion. Genes in the viral genome's extremities are more closely linked to interactions between the virus and the host cell, such as spike protein properties, whereas genes in the genome's centre code for essential processes like viral transcription and assembly[15]. **(Figure 1)**

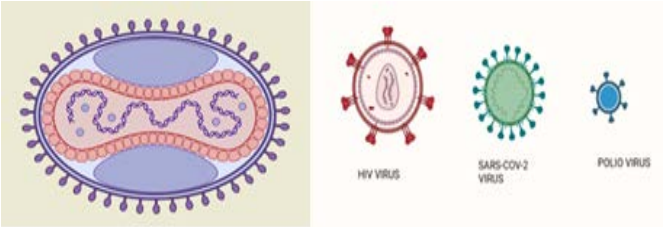

Figure 1: Genome and Structure of Monkeypox virus.

4. Physical Properties of Monkey Pox Virus

Monkey pox virus is an enclosed virus, which means that its centre is encased in a lipid membrane. Its capacity to infect cells may be influenced by this envelope, which is produced from the host cell[16]. As is typical of many poxviruses, the virus usually has an oval or brick-like form. With a diameter of between 200 to 400 nanometres, the monkeypox virus is comparatively large in comparison to many other viruses[17]. Its double-stranded DNA genome provides for a more robust replication process and is more stable than RNA genomes. Outside of a host, the virus can persist for a long time, particularly in dry, chilly conditions. Heat and other disinfectants, however, can deactivate it.

5. Chemical Properties of Monkey Pox Virus

The orthopoxvirus that causes monkeypox has a number of noteworthy chemical and biological characteristics. It has a complicated structure with a lipid sheath and a genome made of double-stranded DNA[18]. The membrane of the host cell serves as the model for the viral envelope, which contains proteins that allow access into host cells. Although the virus is comparatively persistent in the environment, heat, UV light and common disinfectants can all deactivate it. Monkeypox virus uses the host's transcription and replication machinery to replicate in the cytoplasm of host cells. It can trigger a number of immunological reactions, such as cytokine production. One significant component of its pathogenicity is its capacity to elude the immune system[19]. The virus can spread through contaminated items and through direct contact with respiratory secretions, lesions or bodily fluids that are infected.

6. Life Cycle and Replication

Since MPV is an Orthopoxvirus, all of its replication takes place in the cytoplasm of the cell within "factories" that are formed from the host's rough endoplasmic reticulum (ER), where transcription and translation of viral mRNA also occur. Additionally, DNA replication, gene expression and mature virion (MV) assembly take place in the factories[15]. Viral proteins enable MPV virions (MVs) to adhere to the cell surface. A neutral pH is necessary for virus entrance into the host cell's plasma membrane; if not, entry happens through an endocytic pathway that is pH-dependent. The Entry Fusion Complex (EFC) on the monkeypox virus's MV enables it to enter the host cell upon attachment. The host ribosomes convert the viral mRNA into

structural virion protein. When MPV releases enzymatic factors and viral proteins that render the cell inoperable, gene expression starts. Viral matures are contagious. But until they are moved from the factories to the Golgi/endosomal compartment, they will remain inside the cell. The factory's ER membrane can disassemble thanks to protein synthesis and tiny lipid-bilayer membranes will form to enclose the genomes of newly formed virions, which are now extracellular viruses (Evs)[8]. Wrapping the virus and creating Evs require the GARP complex's VPS52 and VPS54 genes, which are crucial for transport. Together with other enzymes and genetic information required for the replication cycle to take place, DNA concatemers break down the genomes that are present in new virions[20].

7. Pathogenesis and Transmission

The MPXV can infect its host by via the nasopharynx oropharynx and subcutaneous portals. At the site of entrance, MPXV multiplies before moving on to neighbouring lymph nodes. After an initial stage of infection, the virus travels to specific other organ systems. In appearance, MPXV is similar to other known Orthopoxviruses. MPXVs have an oval or brick-shaped outer membrane composed of lipoproteins. The MPXV completes its life cycle in the cytoplasm even though it is a DNA virus. Several proteins are required for viral DNA replication, transcription and virion packaging. MPXV can use macropinocytosis and fusion to infiltrate or pierce the host cell. Both the respiratory and the cutaneous routes are possible for monkeypox viruses to reach the host[21]. The illness's manifestation may vary depending on the virus's clade and point of entry. The monkeypox virus can infect airway epithelial cells in the respiratory system, while it can infect keratinocytes, fibroblasts and endothelial cells in the skin, resulting in a cytopathic and productive infection. Through direct viral access to lymphatic channels and the migration of antigen-presenting cells, the monkeypox virus travels from the original site of infection to draining lymph nodes. The monkeypox virus can target other large organs, the spleen and the liver after first replicating in the lymph nodes, causing a low-grade primary viraemia. There, it amplifies and causes a second major viraemia wave, which may then enable the virus to spread to other distant organs like the lung, kidneys, intestines and skin[22].

Transmission can happen between humans and animals. The precise animal reservoir of the monkeypox virus remains unknown, despite the fact that it has been isolated from a number of rodents and non-primate mammals in Africa, including rope squirrels, tree squirrels, Gambian rats, dormice and monkeys. Humans and monkeys have been proposed as inadvertent hosts of the illness[23,24]. Both non-invasive exposures to infected animals (such as touching the animal, cleaning its cage and killing or processing its meat) and bites or scratches from infected animals can result in animal-to-human transmissions, however the former is less likely to happen. Numerous zoonotic spills over into human populations have been identified by genomic analysis, indicating that the monkeypox virus may continue to exist in wildlife reservoirs and sporadically infect people. The virus that causes monkeypox can spread from person to person through respiratory secretions, direct touch, vertical transmission, percutaneous contact or indirect contact through fomites. When big respiratory droplets from the transmitter host land on the recipient host's mouth and nose mucous membranes, respiratory transmission takes place. For transmission to take place through this pathway, prolonged in-person interaction, such as within the home, may be necessary. Activities that cause dried material from lesions to be re-suspended, such as shaking infected linens, may also be dangerous and therefore to be avoided. The 2022 outbreak's main method of transmission has been direct contact with infected sores or lesions on mucosal membranes. Activities involving close, intimate contact with an infected person can spread the monkeypox virus and a breach in the recipient's skin or mucosa such as microscopic abrasions during sexual activity may aid transmission[24]. **(Figure 2)**.

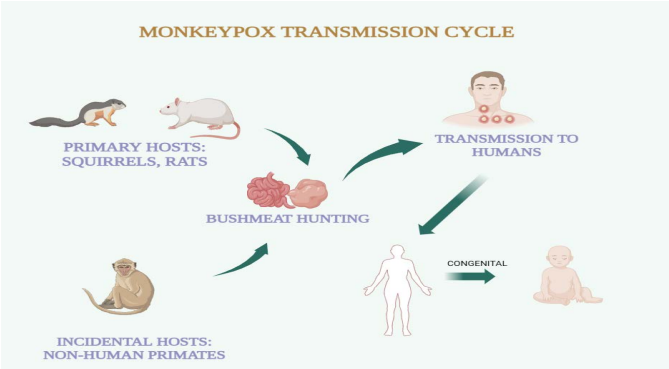

Figure 2: Transmission cycle of Monkeypox virus.

8. Antibody Response Against Monkey Pox

A vital component of the immune system's defence against the virus is the antibody response to monkeypox and knowledge of this response is essential for both disease control and vaccine development[25]. A member of the Orthopoxvirus genus, which is related to smallpox, the monkeypox virus (MPXV) is the cause of monkeypox. Human-to-human transmission is possible even though monkeypox was once thought to be a zoonotic disease (spread from animals to humans), particularly when a person comes into close contact with an infected person or contaminated surfaces[26]. Both innate and adaptive immune responses are started by the immune system when the body is exposed to the monkeypox virus[25]. Interferons and other immune cells, such as macrophages, are the body's first line of defence because they help stop the spread of viruses and stimulate the adaptive immune system. T cells and B cells are activated by the adaptive immune system to react to the virus in a particular way. Antibodies are proteins produced by B cells that either neutralize or mark viruses for death. These usually indicate an acute or early-stage infection and are the first to be produced in response to an infection. These take longer to form and stay in the body, giving long-lasting immunity and assisting the body in identifying and combating the virus more successfully in the event of re-exposure. IgM antibodies usually show up in the first week or so after monkeypox infection. After the first few weeks, IgG antibodies start to increase and are believed to offer long-term protection. The exact length of protection after monkeypox infection is still being investigated, however IgG levels can last for months or even years[27]. The vaccinia virus, a similar virus used in the smallpox vaccine, has been demonstrated to offer cross-protection against monkeypox. Individuals who have gotten a smallpox vaccination, particularly those who did so before to the vaccine's discontinuation in the United States in the 1970s, are less likely to get monkeypox and are more likely to produce an antibody response more quickly if exposed[28]. More recent vaccines, such JYNNEOS (a modified strain of vaccinia Ankara), are being used to prevent monkeypox and smallpox[29]. These vaccinations provide immunity against monkeypox by promoting the development of antibodies against

both viruses. To sustain long-term immunity, booster doses can be required. Antibodies produced during a spontaneous infection may provide protection against the virus in the future. Individual differences may exist in the intensity and duration of this immunity, though. In order to neutralize the virus, antibody synthesis is essential. Antibodies that bind to the virus precisely and stop it from entering human cells are known as neutralizing antibodies. According to some research, people who have had monkeypox or who have been vaccinated against smallpox may produce large amounts of neutralizing antibodies that effectively prevent the virus from spreading[30]. The precise threshold of antibody levels required for complete protection is still being investigated, though. duration of immunity following immunization or illness. T cells' function in enhancing the antibody response perhaps new vaccines or booster shots could be required to prevent epidemics in the future.

9. Pharmaceutical Medication for The Treatment of MVP Virus

There are a few drugs and therapies for monkeypox as of the most recent revisions in 2023, but no particular treatment that specifically targets the virus itself exists[31]. Nonetheless, a few drugs and treatments can help control the symptoms and lessen the disease's severity[32]. An outline of the available medications for treating monkeypox is provided below[33]:

9.1. Antiviral Treatment

Some medicines that were first created for other poxviruses or viral illnesses are being evaluated or used under emergency use authorization, even though no antiviral medications have been officially authorized specifically for monkeypox.

9.2. Tecovirimat (TPOXX)

An antiviral medication called tecovirimat, sometimes referred to as TPOXX, is intended specially to treat orthopoxvirus infections, such as smallpox and monkeypox. By stopping the discharge of viral particles from infected cells, the antiviral medication tecovirimat stops the virus from replicating[34]. Although it was first created to treat smallpox, it has also been used off-label to treat monkeypox[35]. Tecovirimat has received an emergency use authorization (EUA) from the U.S. Food and Drug Administration to treat monkeypox[34]. Although there is currently little information on Tecovirimat's specific use for monkeypox, clinical trials and observational data indicate that it is useful in lessening the severity and duration of the illness[36]. The mechanism of action of tecovirimat is the suppression of p37, a vital viral protein[37]. For orthopoxviruses to replicate and proliferate throughout their host, the p37 protein is crucial. Tecovirimat inhibits the production of "extracellular enveloped virions," which are what allow the virus to leave infected cells and disseminate to other cells, by binding to p37[38]. This binding effectively stops the progression of the infection by blocking the maturation and dissemination of the virus. Tecovirimat inhibits the release of viral particles from infected cells by specifically targeting the p37 protein[39]. The virus cannot efficiently move across cells or infect new cells in the host if there are no functioning extracellular virions present[40]. Because mutations in the p37 protein may impair the virus's capacity to infect and multiply effectively, the drug's mechanism of binding to p37 confers a significant barrier to viral resistance[41]. Tecovirimat slows the spread of the disease and lowers the viral load. Even people with impaired immune systems can benefit from tecovirimat because it is generally well tolerated and has minimal known negative effects[42]. It can be given intravenously or orally and it effectively accumulates in the tissues where the monkeypox virus usually replicates[22]. Tecovirimat has demonstrated a beneficial effect on infection duration and symptom intensity in both compassionate use cases and animal trials for monkeypox in people[43].

9.3. Cidofovir

An antiviral medication called cidofovir was first created to treat cytomegalovirus (CMV) infections, particularly in people with weakened immune systems[44]. Cidofovir's wide antiviral mechanism has shown some efficacy against Ortho poxviruses, including the monkeypox virus, despite the fact that it is not specifically authorized for monkeypox[45]. A nucleotide counterpart of the DNA building unit cytosine is called cidofovir. Viral DNA polymerase, the enzyme that copies viral DNA during replication, is hampered by it. Within infected cells, cidofovir undergoes phosphorylation to produce cidofovir diphosphate, its active form that closely resembles cytosine nucleotides[46]. Consequently, it is integrated into the viral DNA chain, leading to mutations that prevent additional DNA synthesis or chain termination[47]. This procedure limits the virus's growth within the host and prevents viral multiplication[48]. Instead of targeting host polymerases, cidofovir selectively targets viral DNA polymerase. Cidofovir slows the growth of the illness by interfering with the viral DNA chain, which prevents the monkeypox virus from efficiently replicating its genome[49]. Premature chain termination results from cidofovir's integration into viral DNA. This lowers the viral load in the infected host by stopping the monkeypox virus from replicating its genetic material and creating new virions[50]. Because of its extended intracellular half-life, the phosphorylated active form of Cidofovir (cidofovir diphosphate) can continue to combat the virus long after treatment has stopped[51]. The wide-ranging antiviral effect of cidofovir can affect host cells as well. Nephrotoxicity or kidney toxicity, may result from this, hence only well monitored individuals may use it[52]. Probenecid, a drug that lowers uric acid, is frequently given in conjunction with this to lessen kidney injury. Because of its poor oral absorption, cidofovir is taken intravenously. When alternative medicines (such Tecovirimat) are unavailable or ineffective, it is used as an off-label treatment for monkeypox.

9.4. Brincidofovir

Brincidofovir is an antiviral medication that was created to treat a range of DNA viruses, including orthopoxviruses like the monkeypox virus[53]. It is derived from Cidofovir. Its original purpose was to lessen the nephrotoxicity of Cidofovir and increase its efficacy[54]. As a modified form of Cidofovir with a lipid (fatty acid) tail, Brincidofovir is a lipid conjugate of Cidofovir. This alteration enhances its intracellular uptake, distribution and absorption, enabling it to exhibit potent antiviral activity at less dosages[55]. The active form of brincidofovir, cidofovir diphosphate, is created after it reaches cells and functions as a nucleotide analog that merges with viral DNA[56]. Brincidofovir's lipid conjugate design lessens the medication's effect on the kidneys, which is a major drawback of Cidofovir[57]. Longer treatment courses are made possible without the need for extra protective medications like probenecid, making it a safer choice for patients. Brincidofovir's lengthy half-life and intracellular buildup of cidofovir diphosphate[42], its active

metabolite, give it a sustained antiviral impact that enables longer-lasting action against the monkeypox virus[58]. As a result, fewer doses are needed to maintain therapeutic levels. Unlike Cidofovir, which is taken intravenously, Brincidofovir is administered orally, making its use simpler[59]. Although its efficacy in treating monkeypox particularly is still being investigated, it was employed in several instances during the 2022 outbreak[60]. Although it can be used more safely due to the decrease in nephrotoxicity, some adverse effects, including gastrointestinal problems, have been documented.

9.5. Vaccination

Monkeypox can be prevented in part by vaccinations designed to prevent orthopoxvirus diseases, such as smallpox. Due to outbreaks of monkeypox in different areas, vaccination has emerged as a crucial preventive strategy[61].

9.6. JYNNEOS Vaccine (Modified Vaccinia Ankara-BN)

A more recent and secure variant of the smallpox vaccination is this one. It is authorized to prevent monkeypox and smallpox[62]. Because JYNNEOS is so good at preventing monkeypox, it has been used to reduce outbreaks, especially for high-risk individuals or those who have been exposed to monkeypox[35]. Two doses of the vaccination are given, usually separated by four weeks. Compared to previous smallpox vaccines, JYNNEOS has a better safety record with fewer adverse effects, especially for those with weakened immune systems[63].

9.7. ACAM2000 (Live Smallpox Vaccine)

The vaccinia virus, a cousin of the monkeypox virus, is the source of the live vaccination ACAM2000[64]. It was created as a smallpox prevention measure. It works well against smallpox, but because it can have serious adverse effects, especially in immunocompromised people, it is often used less often for monkeypox[65]. Although ACAM2000 has not been licensed specifically for monkeypox, it may be administered in some circumstances to help suppress outbreaks[66].

9.8. Post-Exposure Prophylaxis (PEP)

If given within four days of being exposed to the virus, vaccines such as JYNNEOS can be used as post-exposure prophylaxis (PEP). If administered within 14 days of exposure, it may still provide some protection in certain situations[67].

9.9. Symptomatic Treatment

Analgesics or painkillers, like acetaminophen or ibuprofen, can be taken for pain management in order to reduce the discomfort brought on by the typical pox lesions[68]. Antibiotics could be recommended if the skin lesions develop secondary bacterial infections. Maintaining enough hydration and administering supportive care (such as intravenous fluids) may be required in cases of severe illness[69]. Some topical therapies may be recommended for skin lesions and itching in order to reduce discomfort or stop secondary infections[53]. **(Table 1)**.

10. Herbal Medication and Treatment of Monkeypox Virus

Table 1: Herbal drugs used for the treatment of virus with their respective uses and therapeutic actions.

S.no.	Herbal Drugs	Uses	Therapeutic Action
1	Echinacea	Echinacea is frequently used to treat respiratory infections and strengthen the immune system. According to certain research, it might lessen the intensity of flu and cold symptoms[70].	Compounds found in echinacea may have antiviral properties and boost the immune system[71].
2	Andrographis (Andrographis paniculata)	Colds, the flu and other viral diseases have long been treated with this herb[72].	It is thought to have immune-stimulating, antiviral and anti-inflammatory qualities[73].
3	Elderberry (Sambucus nigra)	Elderberry is believed to have antiviral qualities, especially against viruses that cause the common cold and influenza and is frequently used to treat respiratory infections[74].	Anthocyanins and other flavonoids found in elderberries may prevent viruses from replicating[75].
4	Licorice Root (Glycyrrhiza glabra)	Licorice root can help with immune system support, inflammation reduction and sore throats[76].	It has immune-modulating, antiviral and anti-inflammatory properties.
5	Turmeric (Curcuma longa)	Turmeric is well known for its antioxidant and anti-inflammatory qualities. It is frequently used to lessen pain and inflammation[77].	Turmeric's main ingredient, curcumin, may have anti-inflammatory and immunomodulatory effects[78].
6	Oregano Oil	The antiviral and antibacterial qualities of oregano oil are well established. It is occasionally used to treat gastrointestinal and respiratory infections[79].	It contains substances that are thought to have antiviral properties, such as thymol and carvacrol.
7	Astragalus Root (Astragalus membranaceus)	Traditional Chinese medicine frequently uses the herb astragalus to strengthen the immune system and aid in the body's defence against illnesses[80].	White blood cell production is thought to be stimulated, which can help fight off infections.
8	Garlic (Allium sativum)	Garlic's antibacterial and immune-stimulating qualities have been utilized for a long time[81].	A compound found in garlic called allicin has demonstrated modest efficacy against a range of bacteria and viruses.

11. Survey

A viral zoonotic disease, monkeypox is mainly transmitted from animals to people. Since its discovery in 1958, it has spread to countries in Central and West Africa, as well as the US, UK, Spain, Germany and Australia[82]. A significant global outbreak in 2022 prompted public health measures and the designation of a public health emergency of international concern[83]. In response, immunization campaigns have been started and health officials are keeping an eye on and separating afflicted individuals. Although m-pox was no longer considered an emergency by the end of 2023, public health officials continued to be concerned about it[84]. There were continuous efforts to raise vaccination rates, decrease transmission and keep people informed about the virus. Preventing a revival and making sure that the lessons acquired from the outbreaks in 2022 and 2023 were applied to any future difficulties would be the main priorities as the situation developed into 2024. The death rate of monkeypox is influenced by factors such as the virus strain, population health

and healthcare access. The WHO estimates the case fatality rate to be between 3% and 6%[85]. The virus comes in two primary strains: the Congo Basin strain, which is more severe with CFR estimates as high as 10% and the West African strain, which is milder with a lower CFR of 1% to 3%[86].

12. Discussion and Conclusion

With the aid of this review paper, we have investigated and determined that the virus that causes the rare viral disease known as monkeypox is the Orthopoxvirus, a member of the Poxviridae family. The monkeypox virus has an exterior membrane composed of lipoproteins and is oval in shape, similar to other poxviruses. Monkeypox viruses' genomes encode most of the proteins they require to multiply in the cytoplasm. This contagious illness affects both humans and other animals and manifests as rash, blisters, fever, lymph node enlargement and muscle aches. Pneumonia, encephalitis, sepsis and eye infections that cause blindness are other complications. a range of majors, including therapeutic majors like tecovirimat, brincidofovir, cidofivir and others and supportive therapy majors. The best approach, outside from therapeutic intervention, is prevention, which the Mpox vaccination can provide. JYNNEOS and ACAM2000 are the two FDA-approved vaccines for monkeypox that are currently on the market and exhibit a favourable response to the monkeypox virus.

13. Acknowledgement

The authors are thankful to the management and principal, Columbia Institute of Pharmacy, Raipur (C.G.) for providing necessary facilities to complete this review article.

Conflict of interest

The authors declare no conflict of interest.

Funding

We do not receive any kind of funding from any source for this review article.

Author's Contribution:

Darshana Rathi: Preparation of the content, Editing.

Laxmi Sahu: Diagram, Figures.

Anjali Minj: overall correction.

Trilochan Satapathy: Supervision and Proof reading

14. Reference

1. Karagoz A, Tombuloglu H, Alsaeed M, Tombuloglu G, AlRubaish AA, Mahmoud A, Smajlović S, Ćordić S, Rabaan AA, Alsuhaimi E. Monkeypox (mpox) virus: Classification origin, transmission, genome organization, antiviral drugs and molecular diagnosis. J of infection and public health, 2023;16:531-41.
2. Parker S, Buller RM. A review of experimental and natural infections of animals with monkeypox virus between 1958 and 2012. Future virology, 2013;8:129-57.
3. Hutin YJ, Williams RJ, Malfait P, Pebody R, Loparev VN, Ropp SL, Rodriguez M, Knight JC, Tshioko FK, Khan AS, Szczeniowski MV. Outbreak of human monkeypox, Democratic Republic of Congo, 1996 to 1997. Emerging infectious disease, 2001;7:434.
4. Devaux CA, Mediannikov O, Medkour H, Raoult D. Infectious disease risk across the growing human-non human primate interface: a review of the evidence. Frontiers in public health, 2019;7:305.
5. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings, 2019.
6. Letafati A, Sakhavarz T. Monkeypox virus: A review. Microbial Pathogenesis 2023;176:106027.
7. Beer EM, Rao VB. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. PLoS neglected tropical diseases, 2019;13:0007791.
8. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: infection biology, epidemiology and evolution. Viruses, 2020;12:1257.
9. Hraib M, Jouni S, Albitar MM, Alaidi S, Alshehabi Z. The outbreak of monkeypox 2022: An overview. Annals of medicine and surgery, 2022;79:104069.
10. Reynolds MG, McCollum AM, Nguete B, Shongo Lushima R, Petersen BW. Improving the care and treatment of monkeypox patients in low-resource settings: applying evidence from contemporary biomedical and smallpox biodefense research. Viruses, 2017;9:380.
11. Karagoz A, Tombuloglu H, Alsaeed M, Tombuloglu G, AlRubaish AA, Mahmoud A, Smajlović S, Ćordić S, Rabaan AA, Alsuhaimi E. Monkeypox (mpox) virus: Classification origin, transmission, genome organization, antiviral drugs and molecular diagnosis. Journal of infection and public health, 2023;16:531-41.
12. Abdelhamid AA, El-Kenawy ES, Khodadadi N, Mirjalili S, Khafaga DS, Alharbi AH, Ibrahim A, Eid MM, Saber M. Classification of monkeypox images based on transfer learning and the Al-Biruni Earth Radius Optimization algorithm. Mathematics, 2022;10:3614.
13. Maqsood S, Damaševičius R, Shahid S, Forkert ND. MOX-NET: Multi-stage deep hybrid feature fusion and selection framework for monkeypox classification. Expert Systems with Applications, 2024;255:124584.
14. Cho CT, Wenner HA. Monkeypox virus. Bacteriological reviews, 1973;37:1-8.
15. Sklenovská N. Monkeypox virus. InAnimal-origin viral zoonoses 2020;39-68.
16. Buller RM, Palumbo GJ. Poxvirus pathogenesis. Microbiological reviews, 1991;55:80-122.
17. Liu J, Corroyer-Dulmont S, Pražák V, Khusainov I, Bahrami K, Welsch S, Vasishtan D, Obarska-Kosińska A, Thorkelsson SR, Grünewald K, Quemin ER. The palisade layer of the poxvirus core is composed of flexible A10 trimers. Nature Structural & Molecular Biology, 2024:1-9.
18. Mansfield K, King N. Viral diseases. InNonhuman primates in biomedical research 1998;1-57.
19. Alkhalil A, Hammamieh R, Hardick J, Ichou MA, Jett M, Ibrahim S. Gene expression profiling of monkeypox virus-infected cells reveals novel interfaces for host-virus interactions. Virology Journal, 2010;7:1-9.
20. Moss B. Poxvirus DNA replication. Cold Spring Harbor perspectives in biology. 2013;5:010199.
21. Saied AA, Dhawan M, Metwally AA, Fahrni ML, Choudhary P, Choudhary OP. Disease history, pathogenesis, diagnostics and therapeutics for human monkeypox disease: a comprehensive review. Vaccines. 2022;10:2091.
22. Kaler J, Hussain A, Flores G, Kheiri S, Desrosiers D. Monkeypox: a comprehensive review of transmission, pathogenesis and manifestation. Cureus, 2022;14.
23. Grant R, Nguyen LB, Breban R. Modelling human-to-human transmission of monkeypox. Bulletin of the World Health Organization, 2020;98:638.

24. Peter OJ, Kumar S, Kumari N, Oguntolu FA, Oshinubi K, Musa R. Transmission dynamics of Monkeypox virus: a mathematical modelling approach. Modeling Earth Systems and Environment, 2022:1-2.
25. Ophinni Y, Frediansyah A, Sirinam S, Megawati D, Stoian AM, Enitan SS, Akele RY, Sah R, Pongpirul K, Abdeen Z, Aghayeva S. Monkeypox: Immune response, vaccination and preventive efforts. Narra J. 2022;2.
26. Di Giulio DB, Eckburg PB. Human monkeypox: an emerging zoonosis. The Lancet infectious diseases, 2004;4:15-25.
27. Lum FM, Torres-Ruesta A, Tay MZ, Lin RT, Lye DC, Rénia L, Ng LF. Monkeypox: disease epidemiology, host immunity and clinical interventions. Nature Reviews Immunology, 2022;22:597-613.
28. Rimoin AW, Mulembakani PM, Johnston SC, Lloyd Smith JO, Kisalu NK, Kinkela TL, Blumberg S, Thomassen HA, Pike BL, Fair JN, Wolfe ND. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. Proceedings of the National Academy of Sciences, 2010;107:16262-16267.
29. Gruber MF. Current status of monkeypox vaccines. npj Vaccines, 2022;7:94.
30. Hammarlund E, Lewis MW, Carter SV, Amanna I, Hansen SG, Strelow LI, Wong SW, Yoshihara P, Hanifin JM, Slifka MK. Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox. Nature medicine, 2005;11:1005-1011.
31. Saadh MJ, Ghadimkhani T, Soltani N, Abbassioun A, Pecho RD, Kazem TJ, Yasamineh S, Gholizadeh O. Progress and prospects on vaccine development against monkeypox infection. Microbial Pathogenesis, 2023;180:106156.
32. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of autoimmunity, 2020;109:102433.
33. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, Palich R, Nori A, Reeves I, Habibi MS, Apea V. Monkeypox virus infection in humans across 16 countries-April–June 2022. New England Journal of Medicine, 2022;387:679-691.
34. Russo AT, Grosenbach DW, Chinsangaram J, Honeychurch KM, Long PG, Lovejoy C, Maiti B, Meara I, Hruby DE. An overview of tecovirimat for smallpox treatment and expanded anti-orthopoxvirus applications. Expert review of anti-infective therapy, 2021;19:331-344.
35. Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y. Prevention and treatment of monkeypox. Drugs, 2022;82:957-963.
36. Shamim MA, Padhi BK, Satapathy P, Veeramachaneni SD, Chatterjee C, Tripathy S, Akhtar N, Pradhan A, Dwivedi P, Mohanty A, Rodriguez-Morales AJ. The use of antivirals in the treatment of human monkeypox outbreaks: a systematic review. International J of Infectious Diseases, 2023; 127:150-161.
37. Mucker EM, Goff AJ, Shamblin JD, Grosenbach DW, Damon IK, Mehal JM, Holman RC, Carroll D, Gallardo N, Olson VA, Clemmons CJ. Efficacy of tecovirimat (ST-246) in nonhuman primates infected with variola virus (Smallpox). Antimicrobial agents and chemotherapy, 2013; 57:6246-6253.
38. Grajales DB, Kar S. Exploring Monkeypox: Prospects for therapeutics through computational-aided drug discovery. Molecular Diversity, 2023:1-25.
39. Jordan R, Leeds JM, Tyavanagimatt S, Hruby DE. Development of ST-246® for treatment of poxvirus infections. Viruses, 2010; 2:2409.
40. Sattentau Q. Avoiding the void: cell-to-cell spread of human viruses. Nature Reviews Microbiology, 2008; 6:815-826.
41. Petersen I, Eastman R, Lanzer M. Drug-resistant malaria: molecular mechanisms and implications for public health. FEBS letters, 2011;585:1551-1562.
42. Siegrist EA, Sassine J. Antivirals with activity against mpox: a clinically oriented review. Clinical infectious diseases, 2023;76:155-164.
43. Ghosh N, Chacko L, Vallamkondu J, Banerjee T, Sarkar C, Singh B, Kalra RS, Bhatti JS, Kandimalla R, Dewanjee S. Clinical strategies and therapeutics for human monkeypox virus: a revised perspective on recent outbreaks. Viruses, 2023;15:1533.
44. Biron KK. Antiviral drugs for cytomegalovirus diseases. Antiviral research, 2006;71:154-163.
45. De Clercq E. Cidofovir in the treatment of poxvirus infections. Antiviral research, 2002;55:1-3.
46. Deville-Bonne D, El Amri C, Meyer P, Chen Y, Agrofoglio LA, Janin J. Human and viral nucleoside/nucleotide kinases involved in antiviral drug activation: structural and catalytic properties. Antiviral research, 2010;86:101-120.
47. Engelman A, Englund G orenstein JM, Martin MA, Craigie R. Multiple effects of mutations in human immunodeficiency virus type 1 integrase on viral replication. J of virology. 1995; 69:2729-2736.
48. Mogensen SC. Role of macrophages in natural resistance to virus infections. Microbiological Reviews, 1979; 43:1-26.
49. Clercq ED. Antivirals and antiviral strategies. Nature Reviews Microbiology, 2004;2:704.
50. Andrei G, Topalis D, De Schutter T, Snoeck R. Insights into the mechanism of action of cidofovir and other acyclic nucleoside phosphonates against polyoma-and papillomaviruses and non-viral induced neoplasia. Antiviral research, 2015;114:21-46.
51. De Clercq E. Clinical potential of the acyclic nucleoside phosphonates cidofovir, adefovir and tenofovir in treatment of DNA virus and retrovirus infections. Clinical microbiology reviews, 2003; 16:569-596.
52. You DM, Johnson MD. Cytomegalovirus infection and the gastrointestinal tract. Current gastroenterology reports, 2012; 14:334-342.
53. Huston J, Curtis S, Egelund EF. Brincidofovir: a novel agent for the treatment of smallpox. Annals of Pharmacotherapy, 2023; 57:1198-206.
54. Cundy KC. Clinical pharmacokinetics of the antiviral nucleotide analogues cidofovir and adefovir. Clinical pharmacokinetics, 1999; 36:127-143.
55. Qi H, Lu J, Li J, et al. Enhanced antitumor activity of monophosphate ester prodrugs of gemcitabine: In vitro and in vivo evaluation. Journal of Pharmaceutical Sciences, 2016; 105:2966-2973.
56. Goyal L, Ajmera K, Pandit R, Pandit T. Prevention and treatment of monkeypox: a step-by-step guide for healthcare professionals and general population. Cure us, 2022; 14:28230.
57. Prasad M, Ranjan K, Brar B, et al. Virus-host interactions: new insights and advances in drug development against viral pathogens. Current Drug Metabolism, 2017; 18:942-970.
58. Iqbal J, Ahmad J, Rehman MM, et al. Phytonanotechnology: a greener approach for bioengineering of nanomaterials and their wound healing, antimicrobial and biofilm inhibitory activities. InBioengineered Nanomaterials for Wound Healing and Infection Control, 2023; 407-441.
59. Bishop BM. Potential and emerging treatment options for Ebola virus disease. Annals of Pharmacotherapy, 2015; 49: 196-206.
60. Hraib M, Jouni S, et al. The outbreak of monkeypox 2022: An overview. Annals of medicine and surgery, 2022; 79:104069.

61. Brainard J, Hunter PR. Misinformation making a disease outbreak worse: outcomes compared for influenza, monkeypox and norovirus. Simulation, 2020; 96:365-374.

62. Earl PL, Americo JL, Wyatt LS, et al. Immunogenicity of a highly attenuated MVA smallpox vaccine and protection against monkeypox. Nature, 2004; 428:182-185.

63. Abdelaal A, Reda A, Lashin BI, et al. Preventing the next pandemic: is live vaccine efficacious against monkeypox or is there a need for killed virus and mRNA vaccines? Vaccines, 2022; 10:1419.

64. Hung YP, Lee CC, Lee JC, et al. A brief on new waves of monkeypox and vaccines and antiviral drugs for monkeypox. Journal of Microbiology, Immunology and Infection, 2022; 55:795-802.

65. Khattak S, Rauf MA, Ali Y, et al. The monkeypox diagnosis, treatments and prevention: A review. Frontiers in cellular and infection microbiology, 2023; 12:1088471.

66. Hatch GJ, Graham VA, Bewley KR, et al. Assessment of the protective effect of Imvamune and Acam2000 vaccines against aerosolized monkeypox virus in cynomolgus macaques. Journal of virology, 2013; 87:7805-15.

67. Chakraborty S, Mohapatra RK, Chandran D, et al. Monkeypox vaccines and vaccination strategies: Current knowledge and advances. An update–Correspondence. International Journal of Surgery, 2022; 105:106869.

68. Hans GH, Wildemeersch D, Meeus I. Integrated analgesic care in the current human monkeypox outbreak: perspectives on an integrated and holistic approach combining old allies with innovative technologies. Medicina, 2022; 58:1454.

69. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clinical Infectious Diseases, 2005; 41:1373-1406.

70. Goel V, Lovlin R, Chang C, et al. A proprietary extract from the Echinacea plant (Echinacea purpurea) enhances systemic immune response during a common cold. Phytotherapy Research, 2005; 19:689-694.

71. Hudson J, Vimalanathan S. Echinacea—A source of potent antivirals for respiratory virus infections. Pharmaceuticals, 2011; 4:1019-1031.

72. Saxena RC, Singh R, Kumar P, et al. A randomized double blind placebo controlled clinical evaluation of extract of Andrographis paniculata (KalmCold™) in patients with uncomplicated upper respiratory tract infection. Phytomedicine, 2010; 17:178-185.

73. Parham S, Kharazi AZ, Bakhsheshi-Rad HR, et al. Antioxidant, antimicrobial and antiviral properties of herbal materials. Antioxidants, 2020; 9:1309.

74. Torabian G, Valtchev P, Adil Q, Dehghani F. Anti-influenza activity of elderberry (Sambucus nigra). Journal of functional foods, 2019; 54:353-360.

75. Wieland LS, Piechotta V, Feinberg T, et al. Elderberry for prevention and treatment of viral respiratory illnesses: A systematic review. BMC complementary medicine and therapies, 2021; 21:1-5.

76. AlDehlawi H, Jazzar A. The Power of Licorice (Radix glycyrrhizae) to Improve Oral Health: A Comprehensive Review of Its Pharmacological Properties and Clinical Implications. Healthcare, 2023; 11:2887.

77. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. The molecular targets and therapeutic uses of curcumin in health and disease, 2007; 105-125.

78. Boroumand N, Samarghandian S, Hashemy SI. Immunomodulatory, anti-inflammatory and antioxidant effects of curcumin. Journal of Herbmed Pharmacology, 2018; 7:211-219.

79. Tariq S, Wani S, Rasool W, et al. A comprehensive review of the antibacterial, antifungal and antiviral potential of essential oils and their chemical constituents against drug-resistant microbial pathogens. Microbial pathogenesis, 2019; 134:103580.

80. Liu P, Zhao H, Luo Y. Anti-aging implications of Astragalus membranaceus (Huangqi): a well-known Chinese tonic. Aging and disease 2017; 868:886.

81. Lawson LD. Garlic: a review of its medicinal effects and indicated active compounds. Blood, 1998; 179:62.

82. Parker S, Nuara A, Buller RM, Schultz DA. Human monkeypox: an emerging zoonotic disease. Future microbiology, 2007; 2:17-34.

83. Wilder-Smith A, Osman S. Public health emergencies of international concern: a historic overview. Journal of travel medicine, 2020; 27:227.

84. Mansoor A, Mansoor E, Waheed Y, et al. Update on the M-pox virus and safety measures taken against it globally. Journal of the Formosan Medical Association, 2023; 123: 1030-1036.

85. Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLOS neglected tropical diseases, 2022; 16:0010141.

86. Huang Y, Mu L, Wang W. Monkeypox: epidemiology, pathogenesis, treatment and prevention. Signal Transduction and Targeted Therapy, 2022; 7:1-22.