Indian Journal of Natural Products and Resources
Vol. 15(4), December 2024, pp. 473-490
DOI: 10.56042/ijnpr.v15i4.13951

MONKEY POX (M-Pox/MPXV): Epidemiology, transmission, clinical findings, treatment and herbal treatment

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Received 25 September 2024; revised received 24 November 2024; accepted 27 November 2024

There is a serious increase in the number of viral diseases today. Monkeypox virus (M-Pox/MPXV) is defined as a viral infection caused by a virus called Orthopoxvirus in the Poxviridae family. It is frequently found in the tropical rainforests of West and Central Africa. However, it has spread to other countries over time. In this study, the Monkeypox virus, which has recently caused a significant number of deaths, was examined in detail. Based on the literature data, the health problems, symptoms, and treatment approaches caused by the disease were discussed. In addition, natural products that can be effective using traditional treatment methods were compiled. As a result, this study can be a source of treatment approaches for the Monkeypox virus.

Keywords: Monkey POX, Monkeypox virus, M-POX, MPXV, Viral infections

IPC code; Int. cl. (2021.01)−A61K 36/00, A61P 31/00, A61P 31/12

Introduction

Monkeypox is a viral zoonosis caused by an enveloped double-stranded DNA virus from the genus Orthopoxvirus within the family Poxviridae. Monkeypox was first identified in the Democratic Republic of the Congo (DRC) in 1970 and has predominantly remained localised to Central and West Africa. Recent global outbreaks have raised concerns regarding its epidemiology, transmission, and public health implications[1-3].

The World Health Organization (WHO) has declared the monkeypox virus outbreak a "public health emergency of international concern" (PHEIC) as of August 14, 2024. WHO is urging countries to take necessary precautions regarding diagnosis, surveillance, immunisation, and treatment. It has been reported that in the Democratic Republic of Congo Remove unnecessary keyword alone, 15.600 cases were recorded in 2024, with 537 deaths[4]. Monkeypox outbreaks have also been reported in at least 13 African countries, including Burundi, Kenya, Rwanda, and Uganda. The number of suspected cases is increasing across the continent; there were 7.146 cases in 2022, 14.957 cases in 2023, and as of August 2024, the number has reached 17.000. Given the limitations in diagnosis and observation, as well as the lack of medical follow-up, these numbers likely represent just the tip of the iceberg[5,6].

In its Monkeypox report dated August 12, 2024, the WHO indicated that nearly 100,000 cases and 208 fatalities were documented across 116 countries from January 1, 2022, to June 30, 2024. Ninety-six per cent of these cases transpired in the Democratic Republic of Congo[4].

While the "clade 2b" subtype of the virus was predominant in the 2022 outbreak, since September 2023, the more severe "clade 1" type has been reported to be more prevalent[7,8]. There is no effective treatment, and there are concerns that the disease

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could spread rapidly in different parts of the world, especially in Africa, due to challenges in obtaining the vaccines needed for protection. Millions of vaccine doses are required, but a vaccination program has yet to be initiated in Africa, with preparations still ongoing[4,9].

This study provides a comprehensive overview of the monkeypox virus (MPXV), including its epidemiology, transmission routes, clinical presentations, diagnostic methodologies and current treatment options. By investigating plant species with known antiviral properties against MPXV, herbal medicine was found to be an alternative treatment option. It is also expected to be a valuable resource for future research on the monkeypox virus.

Mode of transmission of monkeypox

Monkeypox (MPX) is a zoonotic virus classified under the Orthopoxvirus genus of the Poxviridae family[10]. This virus, often infecting animals, was first documented to cause sickness in humans in 1970 in the Democratic Republic of the Congo (DRC)[11]. It was later reported to be prevalent in West and Central Africa, particularly among youngsters residing in rural and rainforest areas. Nevertheless, the laboratory was unable to definitively identify the majority of cases due to factors such as insufficient local health systems and challenges in accessing patients[12]. In 2003, 71 cases were documented in the United States, with more cases reported in Europe, North America, and Asia from 2003 to 2022[13]. As of now, human MPX cases have been documented in 110 countries, including Portugal, Spain, Canada, and Belgium. Sweden, Italy, Australia, France, Germany, the United States, and the United Kingdom[14,15]. The transmission of the monkeypox virus can occur directly or indirectly between individuals, from animals to humans, and from humans to animals[16]. The transmission routes of this virus remain incompletely understood. However, several theories regarding its forms of transmission exist. Animal-to-human transmission is believed to occur by direct contact with deceased or infected animals (including bodily fluids such as saliva, respiratory secretions, and feces), hunting and ingestion of wild animals, and butchery[17,18]. Transmission is also believed to occur via bites or scratches resulting from injuries[18,19]. It can be transferred indirectly via the respiratory system. Transmission routes between individuals include direct contact with lesions on an infected person, exposure to respiratory droplets, and close-contact activities such as cohabitation, sharing a bed, or consuming food and drink from the same dish, all of which are recognised as risk factors for viral transmission[16,20]. It has also been shown that it is more prevalent among men who engage in sexual activity[21]. A study indicated that the disease is transmitted from humans to animals in France. Six days post-coitus, two men, who resided separately, presented at the hospital with symptoms including anal ulceration and a vesiculopustular rash on the face, ears, and legs; the second patient exhibited symptoms localised to the legs and back. Four days subsequent to the onset of these symptoms, a rash was accompanied by asthenia, and complaints of headaches emerged. The Monkeypox virus was validated via PCR for the first and second patients, and 12 days post-symptom onset, mucocutaneous lesions, including abdominal pustules and thin anal ulceration, were found in 4-year-old male Italian Greyhound dogs with no prior disease history. The findings from the initial patient and the viral agent identified in the canine exhibited 100% sequence homology[22].

Most used identification techniques for monkeypox

Recent population growth, heightened trade and travel, and global phenomena like climate change enhance the likelihood of new viral development and pose a greater hazard to civilization[23]. The MPXV, characterised by double-stranded DNA, is associated with the variola virus (VARV), the causative agent of smallpox, both of which are classified under the genus Orthopoxvirus. The MPXV has two separate clades. Clade I induces illnesses such as smallpox, whereas Clade II results in milder and less transmissible diseases among humans[24,25]. The World Health Organization (WHO) has proclaimed an international emergency owing to the protracted incubation period of MPXV sickness, which extends up to 21 days, the prolonged duration of the illness lasting two to four weeks, and the rise in case numbers. Consequently, swift and efficient identification of MPXV is crucial for the control and management of the disease[25].

Recently used diagnostic methods

Viral culture/isolation

Chorioallantoic membrane or other cell-based viral culture techniques are employed for diagnosis; however, these approaches necessitate live and viable viruses and often require one to two days.

Electron microscopy

The electron microscopy technique employed for phenotypic characterisation presents considerable

challenges in differentiating MPXV from other orthopoxviruses, despite the visibility of the distinctive brick-shaped viral particles of Poxviruses through negative staining[26,27].

Serology test (Anti-orthopoxvirus IgG, IgM)

The serological test ELISA (enzyme-linked immunosorbent assay)and Clustered Regularly Interspaced Short Palindromic Repeats, in conjunction with Cas proteins (CRISPR-Cas), have been documented[28-31].

Conventional PCR and real-time (RT)-PCR tests

The molecular characterisation of the MPX virus demonstrated that both Real-time and conventional Polymerase Chain Reaction (PCR) techniques effectively differentiate between poxviruses[30].

Nucleic acid amplification tests

Nucleic acid amplification tests (NAATs), including Loop-mediated isothermal amplification (LAMP)[32] and Recombinase polymerase amplification assay (RPA)[33] are applicable for diagnostic purposes[34].

Monkeypox case definitions

Suspected

A rapid onset of high fever, accompanied by a vesicular-pustular rash predominantly located on the face, palms, and soles; or the existence of a minimum of five scabs like those of smallpox.

Confirmed

A suspected case validated by laboratory analysis (Positive IgM Antibody, PCR, or virus isolation).

Probable

A suspected case lacking laboratory proof, however possessing an epidemiological connection to a confirmed case.

Possible

A vesicular, pustular, or crusted rash not recognised as chickenpox by the family or healthcare practitioner, accompanied by a history of fever and a vesicular or crusted rash. The individual fulfills one of the epidemiological requirements or exhibits elevated levels of orthopoxvirus-specific IgM, accompanied by an unexplained rash, fever, and two additional signs or symptoms from the clinical criteria[5].

MPOX Transmission

The virus can be transmitted to humans from animals like squirrels, rats, and mice, in addition to monkeys. The predominant mode of transmission during outbreaks is interpersonal (Fig. 1).

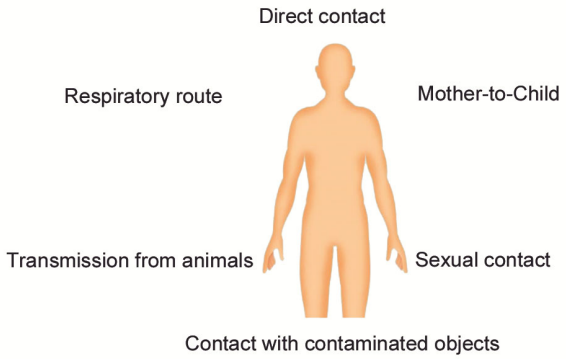

Fig. 1 — MPOX Transmission

Direct Contact

The Mpox virus can be transmitted via direct contact with the skin lesions, bodily secretions, or crusted rashes of an infected individual. This is a prevalent transmission pathway and is essential in the dissemination of the disease[5,35].

Sexual Contact

The likelihood of transmission is heightened during sexual intercourse due to exposure to bodily fluids and dermal lesions.Recent studies indicate that the principal mode of transmission occurs through close contact during personal or sexual activities, especially when an individual has lesions in the oral cavity, anorectum, or vagina. The majority of infections have been documented among men who engage in sexual activity with men (MSM)[36,37].

Respiratory Route

The virus may also be transferred through respiratory means during extended face-to-face interactions with infected persons. The risk increases when the patient has lesions in the oral cavity, nasal passages, or pharynx, as droplet transmission is more probable[38,39].

Contact with Contaminated Objects

The virus can spread by touching contaminated surfaces such as clothing, bedding, or other personal items of infected individuals. Transmission can occur when touching these surfaces and then touching the face, mouth, nose, or eyes without washing hands[38,40].

Mother-to-Child

Mpox can be spread from an infected mother to her infant during parturition. There exists a danger of transmission via the placenta during pregnancy[41,42].

Transmission from Animals

MPOX is usually transmitted to humans via direct contact with infected animals, particularly rodents and monkeys. The virus can be transmitted via bites, scratches, or direct contact with the animals' tissues. Consequently, it is imperative to prevent interaction with wild animals[38,43].

Clinical findings

Lesions linked to Mpox are typically hard or rubbery, well-defined, deeply situated, and frequently display umbilication, resembling a dot at the apex of the lesion. In the present worldwide pandemic:

- Lesions commonly manifest in the vaginal, anorectal, or oral regions.
- The rash may not be extensive and can be confined to a small number of lesions or even a solitary one.
- The rash is less frequently observed on the palms and soles.
- Rectal symptoms, including purulent or sanguineous feces, rectal discomfort, or rectal haemorrhage, have been often documented in this outbreak.
- Lesions frequently cause pain until they transition into the healing phase, during which they may become pruritic and develop crusts.
- Fever and other first symptoms (e.g., chills, lymphadenopathy, malaise, myalgia, or cephalalgia) may manifest prior to the rash, subsequent to the rash, or may be absent altogether.
- Respiratory symptoms, such as pharyngitis, nasal obstruction, or cough, may also occur.
- Lesions typically emerge concurrently and advance through four stages: macular, papular, vesicular, and pustular, before ultimately forming scabs and flaking.

The incubation period ranges from 3 to 17 days, during which an individual may remain asymptomatic and feel healthy. The ailment often endures for a duration of 2 to 4 weeks[44-46].

Dermatological course of rash

Pitted scars and/or regions of brighter or darker pigmentation may persist after the scabs have detached. Once all scabs have detached and a new epidermal layer has developed, the individual is no longer infectious[47,48] (Table 1).

General symptoms

The distribution of symptoms (in 36.506 patients) is shown as follows. In this context, "systemic rash" refers to rashes on the body, excluding mucosal and genital rashes. "Any rash" encompasses one or more types of rashes (systemic, oral, genital, or unknown location). "Any lymphadenopathy" includes both general and local lymphadenopathy. Symptom data are presented for all cases with available information from January 2022 onward, intravascular thrombogenicity rd[49] (Table 2).

Differential diagnosis

Potential differential diagnoses encompass varicella, measles, bacterial dermatoses, scabies, syphilis, and pharmacological hypersensitivities. Lymphadenopathy prior to the rash can serve as a clinical indicator to differentiate M-pox from varicella, measles, and smallpox. Possible differential diagnoses are shown in Table 3.

Diagnosis

The differential diagnosis for M-pox includes varicella, measles, bacterial skin diseases, scabies, syphilis, and medication allergies, all of which may induce rashes. Lymphadenopathy preceding the rash may aid in differentiating M-pox from these illnesses.

The diagnosis of M-pox is validated using Polymerase Chain Reaction (PCR) examination of samples obtained from skin lesions encompassing crusts and exudates. Sample accuracy is contingent upon appropriate packaging and compliance with standards[2,50].

Table 1 — Enanthem to Scab Stage Progression[44]

Stages	Time Period	Attributes
Enanthem	-	Lesions may initially develop on the tongue and within the oral cavity.
Macules	1−2 days	Flat, macular lesions form on the integument.
Papules	1−2 days	Lesions evolve from flat macules to elevated papules.
Vesicles	1−2 days	Lesions become vesicular, indicating they are elevated and contain clear fluid.
Pustules	5−7 days	Lesions accumulate opaque fluid, transforming into pustules. They are prominently elevated, generally round, solid, and deeply embedded. A central depression (umbilication) may ultimately arise. Pustules persist for approximately 5 to 7 days prior to commencing crust formation.
Scabs	7−14 days	By the conclusion of the second week, pustules desiccate and develop scabs. The scabs generally persist for around one week before detaching.

Note: This timeline is typical but can vary

Table 2 — Symptom Distribution by Gender (Summary as of 31 July 2024)[49]

Symptom	Total	Male	Female
Any rash	32,397 (88.5%)	31,097 (89.0%)	1,129 (82.0%)
Fever	21,177 (57.9%)	20,278 (58.1%)	724 (52.6%)
Systemic rash	20,030 (54.7%)	19,064 (54.6%)	932 (67.7%)
Genital rash	18,105 (49.5%)	17,574 (50.3%)	392 (28.5%)
Any lymphadenopathy	10,955 (29.9%)	10,664 (30.5%)	230 (16.7%)
Headache	10,536 (28.8%)	9,971 (28.5%)	513 (37.3%)
Muscle ache	9,474 (25.9%)	9,062 (25.9%)	399 (29.0%)
General lymphadenopathy	8,455 (23.1%)	8,246 (23.6%)	149 (10.8%)
Fatigue	6,555 (17.9%)	6,397 (18.3%)	152 (11.0%)
Local lymphadenopathy	5,813 (15.9%)	5,680 (16.3%)	132 (9.6%)
Sore throat	5,544 (15.2%)	5,265 (15.1%)	227 (16.6%)
Rash, unknown location	3,491 (9.5%)	3,466 (9.9%)	22 (1.7%)
Oral rash	2,924 (8.0%)	2,829 (8.1%)	83 (6.0%)
Chills	2,689 (7.3%)	2,534 (7.3%)	121 (8.8%)
Cough	864 (2.4%)	791 (2.3%)	56 (4.1%)
Vomiting	776 (2.1%)	721 (2.1%)	52 (3.8%)
Lymphadenopathy, location unknown	472 (1.3%)	458 (1.3%)	14 (1.0%)
Anogenital pain and/or bleeding	382 (1.0%)	376 (1.1%)	6 (0.4%)
Asymptomatic	284 (0.8%)	259 (0.7%)	18 (1.3%)
Other	254 (0.7%)	249 (0.7%)	5 (0.4%)
Conjunctivitis	205 (0.6%)	189 (0.5%)	14 (1.0%)
Diarrhoea	128 (0.3%)	106 (0.3%)	2 (0.1%)
Genital oedema	45 (0.1%)	44 (0.1%)	0

Table 3 — Differential Diagnosis Considerations

Disease	Description
Varicella (Chickenpox)	A common viral infection characterised by an itchy rash and flu-like symptoms.
Herpes Simplex Virus (HSV)	A virus causing oral or genital herpes, presenting with sores or blisters.
Smallpox	An eradicated virus that caused a severe disease with characteristic pustular rash.
Tanapox	A poxvirus infection causing lesions similar to smallpox but with distinct features.
Orf	A viral infection typically causing lesions on the skin of sheep and goats, transmissible to humans.
Cowpox	A poxvirus infection related to smallpox, presenting with pustules, primarily in cows and sometimes in humans.

PCR is preferred due to its accuracy. Other tests like virus isolation, electron microscopy, ELISA, and immunofluorescent antibody tests may provide useful information but are not definitive. Due to serological cross-reactivity among orthopoxviruses, specific confirmation for M-pox cannot be achieved with antigen or antibody tests alone. Serology is not recommended for individuals vaccinated before smallpox eradication[50].

Semen obtained during the initial stages of infection (day 6 post-symptom start) may contain a replication-competent virus capable of transmitting mpox[51].

Treatment

At present, there is no officially sanctioned therapy for monkeypox virus (MPXV) infections. For the majority of patients with mpox possessing a strong immune system and absent skin problems, supportive care and pain control will facilitate healing without necessitating medical intervention.

Paracetamol and NSAIDs are advised for the management of pain in patients with mpox. Topical steroids and lidocaine may also be regarded as local anaesthetics. Disposable gloves are advisable due to the potential of autoinoculation. Opioids and gabapentin may be utilised for the management of severe pain[52]. Tecovirimat (also known as TPOXX, ST-246): Tecovirimat is generally the primary therapeutic option contemplated for mpox patients needing more than supportive care. It received approval from the European Medicines Agency (EMA) and the US FDA in 2022 following animal and human tests; nonetheless, it is not extensively accessible globally.

The CDC has an Expanded Access-Investigational New Drug (EA-IND) policy that allows the utilisation

of stockpiled tecovirimat for the treatment of mpox patients who satisfy the EA-IND eligibility requirements. Tecovirimat may be administered orally or intravenously to specific individuals who are at high risk of severe or life-threatening illness, including those who are significantly immune compromised, have atopic dermatitis or other conditions that compromise skin integrity, as well as children and pregnant or breastfeeding individuals.

- Brincidofovir (CMX001 or Tembexa): Brincidofovir, a prodrug of cidofovir, is licensed by the FDA for the treatment of human smallpox in both adult and pediatric populations, including neonates. Utilise for individuals with severe disease or those with an elevated risk of acquiring severe disease[53].
- Vaccinia Immün Globulin Intravenöz (VIGIV): There is no evidence about the efficacy of VIGIV in treating MPXV virus infections in people. VIGIV has not been demonstrated to be advantageous for mpox treatment, and it remains questionable if an individual with severe mpox infection would derive any benefit from VIGIV. Nonetheless, healthcare providers may contemplate its application in severe instances where the formation of a strong antibody response can be hindered[53].
- Cidofovir: It is an antiviral drug licensed by the FDA. Cidofovir, utilised for the treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS) and commercially accessible as an injection, lacks data regarding its efficacy in treating MPXV infections in humans[54].
- Trifluridine: It is an antiviral ocular drug recognised for its ability to impede the replication of many viruses, including the vaccinia virus. It has demonstrated efficacy against ocular vaccinia infections in both animal models and people. It is crucial to refrain from prolonging treatment beyond the advised 4-week period to mitigate the danger of corneal epithelial toxicity[55,56].

Monkey-pox Complications

Local consequences of mpox encompass pain and subsequent bacterial infections. Timely detection of mucosal or vaginal lesions can mitigate severe discomfort in sensitive regions and avert consequences, such as proctitis, which induces acute rectal pain. Patients must be advised to report any indications of a bacterial infection or abscess development related to mpox lesions, including heightened erythema, warmth, or purulent discharge, as these may result in considerable morbidity and necessitate hospitalization[57,58].

Instances of myopericarditis have been documented in immunocompetent individuals. The pathogenic mechanism remains ambiguous but may involve direct viral invasion of the heart or pericardium, lymphocyte infiltration, sequelae such as myonecrosis or cardiac fibrosis, or an immunological response[59,60].

Pathophysiology of Monkey-pox virus and cardiovascular involvement

The pathophysiology of cardiovascular symptoms linked to MPXV infection remains incompletely elucidated; however, numerous mechanisms can be identified. The initial occurrence transpires via direct viral invasion. MPXV is a virus that specifically targets the skin and mucous membranes[61]. In addition to this invasion, it can directly invade the endothelial cells covering the entire cardiovascular system. With this invasion, endothelial cells lose their function. This causes the cardiovascular symptoms of the virus[62]. Endothelial cells have many functional properties. These can be listed as inhibition of platelet aggregation, inhibition of coagulation activation, formation of a clotting surface with fibrinolysis functions, exchange of substances between tissue and circulation, regulation of vascular tone, regulation of leukocyte and platelet adhesion, and the loss of these functions causes serious cardiovascular diseases. In addition, an inflammatory response occurs against the virus. In this response, which occurs by the immune system to control and eliminate the virus, cytokine release occurs[63]. As a result of cytokine release, there is a loss of function in endothelial cells, and with this mechanism, cardiovascular system findings occur. In addition, as in every infection, the virus can indirectly affect the cardiovascular system. These effects occur with factors such as fever, dehydration and electrolyte imbalances. The clinical manifestation of cardiovascular system involvement results in diverse symptoms, with varying degrees of illness severity. It may lead to myocarditis, pericarditis, congestive heart failure, arrhythmia, and vascular problems.

Myocarditis refers to the inflammation of the cardiac muscle tissue. The pathophysiology involves direct invasion of cardiac cells or immunological-mediated injury by the immune system[64]. The engagement may be minimal; however, it can potentially lead to significant harm. Symptoms including chest discomfort, palpitations, dyspnea, and

fatigue may be noted. The clinical presentation of viral myocarditis may vary from mild influenza-like symptoms to severe cardiac failure and lethal arrhythmias[65]. The diagnosis of viral myocarditis can be established using clinical assessment, laboratory tests including inflammatory and cardiac biomarkers, echocardiography, cardiac MRI imaging techniques, and cardiac biopsies[66]. The management of the condition differs based on its severity. In moderate cases, rest and symptomatic management may suffice, whereas severe cases may necessitate anti-inflammatory therapy, immunosuppressive therapy, and treatment for heart failure. Although treatment may result in a complete cure in certain instances, chronic heart failure and persistent arrhythmias can manifest in other individuals[67]. Pericarditis is characterised by inflammation of the membrane encasing the heart. The pathophysiology of viral pericarditis includes direct viral invasion and immune-mediated processes. Patients may experience chest discomfort, fever, dyspnea, and palpitations with the symptoms and findings. Clinical assessment, laboratory examinations, and imaging studies are essential for diagnosis. A physical examination is essential following the symptomatic assessment of the patient. The characteristic friction sound of pericarditis is audible during cardiac auscultation. ECG findings, such as extensive ST-segment elevation or PR segment depression, may indicate pericarditis, thus aiding in diagnosis; hence, fluid monitoring via echocardiography is essential. Inflammatory indicators ought to be assessed through laboratory testing. The primary objective in patient treatment is to mitigate symptoms and reduce inflammation[66,68].

Congestive heart failure resulting from MPXV infection arises from myocardial damage induced by the infection. It is marked by dyspnea, tiredness, and oedema, particularly in the lower extremities, which are the hallmark signs of heart failure. The management of heart failure entails a holistic strategy focused on enhancing cardiac function, alleviating symptoms, and averting additional problems[69].

The virus can also cause cardiac arrhythmias by causing conduction disturbances in the electrical system of the heart. MPXV can cause dysfunction in endothelial cells, leading to impaired vascular blood flow. Vasoconstriction and increased peripheral resistance may occur due to decreased release of vasodilating mediators, such as NO, from endothelial cells[62]. In addition, intravascular thrombogenicity increases due to endothelial dysfunction, and vascular occlusions may occur. As a result, MPXV infection may cause direct or immune system-mediated pericarditis, myocarditis, congestive heart failure, various cardiac arrhythmias and thrombosis due to endothelial dysfunction as cardiovascular diseases. The treatment of these clinical conditions affects the mortality and morbidity of the patients, and the clinical course may range from mild to serious and even fatal[70,71].

Additional studies are needed due to individual differences in the course of cardiovascular involvement of the infection.

Preventive measures and protection

Handwashing is essential for upholding personal hygiene and averting the spread of the illness. It is crucial to meticulously cleanse hands with soap and water following contact with infected persons or contaminated surfaces. Individuals at elevated risk exhibiting symptoms indicative of mpox should promptly seek medical care and refrain from sexual or other close-contact activities until the infection has resolved. Individuals suspected of having mpox should be isolated, tested, and promptly notified of the results. Contact tracing must be executed for confirmed cases[36,72,73]. Primary prevention entails evading direct touch with dermal lesions or objects utilised by infected persons. Healthcare providers, including nurse practitioners and other caregivers, must don personal protective equipment (PPE) such as gowns, gloves, eye protection, and fitting N95 masks when attending to patients with lesions. The sufferer must be confined to a solitary room. Gloves, gowns, and masks must be utilised when managing contaminated clothing to avert contact with lesion material[36,40,74].

Vaccines

Two vaccines are available for mpox prevention:

- JYNNEOS (Imvamune® or Imvanex®): It is a live vaccine derived from the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) strain, which is an attenuated, non-replicating orthopoxvirus. Authorised for smallpox and mpox, it is advised for anyone at risk of orthopoxvirus exposure and has been the principal vaccine employed during the ongoing outbreak. The JYNNEOS vaccination is given in two doses, spaced 28 days apart. The typical dosage is 0.5 mL administered subcutaneously. An

alternate regimen of 0.1 mL injected intradermally (ID) is available for individuals aged 18 and older, especially in situations with low vaccination supply. The CDC does not endorse routine mpox vaccine for the general populace or healthcare professionals unless sexual risk factors are evident. The vaccine must be provided promptly following exposure, preferably within four days; however, it can still provide some protection if administered between 4 to 14 days post-exposure. Historical studies indicate that the smallpox vaccination, utilising the vaccinia virus, is around 85% effective against mpox[75].

- ACAM2000: It is used for active immunisation to prevent smallpox and mpox disease in individuals determined to be at high risk for smallpox or mpox infection. Authorised for smallpox prophylaxis and advised for anyone at risk; however, it has not been utilised in the current mpox outbreak. The potential adverse effects and consequences are more pronounced. Most people who get the vaccine experience only mild reactions. Reactions include arm pain, fever and body aches. People with chronic conditions may experience more serious side effects, including life-threatening effects[36,75].

Herbal treatment approaches

From primitive people to the present day, many communities have used plants against different diseases[76]. Many plant species that stand out with their nutritional properties are widely used as medicines against diseases[77]. Various researchers have documented that plants exhibit diverse biological activities, including antioxidant, anticancer, antiviral, antibacterial, antiproliferative, antiaging, and DNA-protecting properties[78-83]. In this context, investigating the biological activities of plants can play an important role in the treatment of different diseases[84]. There are many different approaches to the MPXV virus. Today, vaccines are important in combating the disease. In addition, many studies have predicted that different plant species will be effective. In our study, plant species that are effective on the MPXV virus in the literature were compiled. It is shown in Table 4.

Jatropha curcas

J. curcas (Euphorbiaceae) is referred to as the "castor oil plant" or "hedge castor oil plant". It is particularly prevalent in tropical and subtropical areas. It attains a height of approximately 6 meters. It is a perennial shrub or little tree. The leaves are arranged alternately or sub oppositely, featuring three to five lobes and exhibiting spiral phyllotaxy. Both male and female flowers are present inside the same inflorescence. Their fruits appear in winter. The seeds mature as they transition from green to yellow[85-88]. Literature research indicates that *J. curcas* exhibits antioxidant, anti-inflammatory, anticancer, antibacterial, and cytotoxic properties[89-92]. A study in the Democratic Republic of the Congo indicated that oil derived from

Table 4 — Plant species effective against monkeypox virus

Plant species	Family	Used parts	Effect
Jatropha curcas	Euphorbiaceae	Seed	DNA replication inhibitory
Zingiber officinale	Zingiberaceae	Aerial	Inhibitory, body's healing
Curcuma longa	Zingiberaceae	Aerial	Binding affinity
Prunella vulgaris	Lamiaceae	Aerial	Inhibitory
Piper nigrum	Piperaceae	Aerial	Binding affinity
Salvia rosmarinus	Lamiaceae	Aerial	Inhibitory
Tapinanthus bangwensis	Loranthaceae	Leaves	Immune-modulating
Origanum vulgare	Lamiaceae	Aerial	Inhibitory
Annona muricata	Annonaceae	Leaves, fruit	Immune system enhancement and fever relief
Quercus infectoria	Fagaceae	Aerial	Inhibitory
Azadirachta indica	Meliaceae	Leaves, Bark	Immune-boosting
Rhus chinensis	Anacardiaceae	Aerial	Inhibitory
Aloe vera	Asphodelaceae	Leaves	Healing skin lesions
Solanum macrocarpon	Solanaceae	Leaves, fruit	Immunomodulatory
Phyllanthus acidus	Phyllanthaceae	Leaves	Protein binding affinity
Vernonia amygdalina	Asteraceae	Leaves	Binding affinity to receptors
Capsicum annuum	Solanaceae	Fruit	Binding affinity to RNA polymerase
Moringa oleifera	Moringaceae	Leaves	DNA Polymerase inhibitor
Cupressus sempervirens	Cupressaceae	seed, globose cones	Inhibitory
Sarracenia purpurea	Sarraceniaceae	Whole	Replication inhibitory

J. curcas seeds inhibited two molecular targets associated with the DNA replication of the Monkeypox virus[93].

Aloe vera

A. vera (Asphodelaceae) is a succulent plant species. It is prevalent in numerous places globally. It is a perennial evergreen plant. It attains a height of 60-100 cm and possesses either no stem or a very short stem. The foliage is robust and succulent, with hues ranging from green to gray-green. The leaf's margin is serrated and features little white dentations[94-96]. Literature indicates that *A. vera* exhibits properties including wound healing, antifungal activity, hypoglycemia effects, antidiabetic capabilities, anti-inflammatory actions, anticancer potential, immunomodulatory effects, and gastroprotective qualities[97]. A study in Pakistan indicated that the gel derived from *A. vera* leaves contributed to reducing symptoms of skin lesions caused by monkeypox and promoted healing through its therapeutic qualities in relaxing and mending tissue damage[98].

Zingiber officinale

Z. officinale (Zingiberaceae) is commonly referred to as ginger. It is disseminated over the Southeast Asia region[99]. Literature research indicate that *Z. officinale* exhibits numerous biological properties, including antioxidant, anti-inflammatory, antibacterial, cytotoxic, neuroprotective, cardiovascular protective, anti-obesity, antidiabetic, anti-nausea, and anti-vomiting actions[100,101]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *Z. officinale*, exhibit an inhibitory impact on the MPox virus[102]. A study in India indicated that the anti-inflammatory and antioxidant characteristics of *Z. officinale* may enhance inflammation reduction and support the body's healing processes during monkeypox infections[103].

Phyllanthus acidus

P. acidus (Phyllanthaceae) is a plant species that attains a height of 2 to 9 meters. The leaves are pointy, oval, or lanceolate. The flowers are little and pinkish. The blooms develop in the upper section of the tree, on the leafless portions of the primary branches[104,105]. Literature indicates that *P. acidus* exhibits anti-inflammatory, antinociceptive, antioxidant, cytotoxic, antibacterial, and anticancer properties[106-108]. A study in India validated the efficacy of phytocomposites derived from *P. acidus* leaves against monkeypox (MPV) using PASS prediction and network pharmacology analysis, indicating strong binding affinity with specific viral proteins[109].

Solanum macrocarpon

S. macrocarpon (Solanaceae) is referred to as "African eggplant." It is prevalent in Africa, the Caribbean, South America, and certain regions of Southeast Asia. It attains a height of 1 to 1.5 meters. The leaves are ovate and lobed with undulating margins. The leaves possess hairs, and certain ones exhibit spines. The fruit exhibits hues of green, ivory, or dark-striped purple and white. Upon ripening, the fruit attains a golden or yellow-brown hue. The fruit possesses several seeds and is partially enveloped by calyx lobes[110-112]. Literature indicates that *S. macrocarpon* has antioxidant, antibacterial, anticancer, and anti-inflammatory properties[113-115]. A study in Pakistan revealed that several components of *S. macrocarpon*, including leaves and fruits, are abundant in alkaloids, flavonoids, and saponins. African eggplant has been documented as beneficial against monkeypox due to its potent antiviral and immunomodulatory effects[98].

Curcuma longa

C. longa (Zingiberaceae) is referred to as "turmeric." It is prevalent in numerous Asian countries, including Pakistan, India, China, and Bangladesh. The primary roots of the plant have an egg or pear form. The lateral roots exhibit a digitiform morphology. The exterior of the rhizomes is yellowish, while the interior is yellow. It possesses a bitter flavor[116-118]. Literature indicates that *C. longa* exhibits actions including anti-inflammatory, cytotoxic, oxidative, anticancer, antibacterial, antiviral, antifibrinogen, antidiabetic, and antimutagenic properties[119,120]. A study in Bangladesh examined the efficacy of various bioactive compounds derived from *C. longa* against the monkeypox virus by molecular docking techniques. The study indicated that curcumin exhibited the highest binding affinity among the metabolites, with a value of -37.43 kcal/mol, followed by gedunin (-34.89 kcal/mol), piperine (-34.58 kcal/mol), and coumadin (-34.14 kcal/mol)[121].

Prunella vulgaris

P. vulgaris (Lamiaceae) is commonly referred to as "self-heal, heal-all, woundwort, heart-of-the-earth, carpenter's herb, brownwort, blue curls." It is a perennial species. It is scattered in Europe, Asia, Africa, North America, Australia, New Zealand, Hawaii, and the Pacific Islands. The leaves are

lanceolate, serrated, and have a scarlet tip. The flowers exhibit a bilabiate and tubular morphology. The upper lip is characterised by a purple hue, whereas the bottom lip is often white[122-125]. Literature indicates that *P. vulgaris* has antioxidant, antibacterial, anti-inflammatory, anticancer, anthelmintic, antiviral, antiulcer, and antihypertensive properties[126-128]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *P. vulgaris*, exhibited an inhibitory impact on the MPox virus[102].

Salvia rosmarinus

S. rosmarinus (Lamiaceae) is commonly referred to as "rosemary." It is predominantly found in the Mediterranean regions. It is a shrub characterised by evergreen, needle-like foliage with blooms that are white, pink, purple, or blue[129,130]. Literature indicates that *S. rosmarinus* has antioxidant, anti-inflammatory, anti-cancer, antibacterial, cytotoxic, and antiviral properties[131-135]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *S. rosmarinus*, exhibited an inhibitory impact on the MPox virus[102].

Origanum vulgare

O. vulgare (Lamiaceae) is an aromatic, perennial plant of 30-50 cm in height, characterised by white or purple flowers and lanceolate, serrated leaves, indigenous to the Mediterranean region and Western Eurasia[135,136]. Literature indicates that *O. vulgare* has antioxidant, anti-inflammatory, antibacterial, hepatoprotective, antiviral, anticancer, and cytotoxic properties[137-141]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *O. vulgare*, exhibited an inhibitory impact on the MPox virus[102].

Annona muricata

A. muricata (Annonaceae) is commonly referred to as "Soursop, graviola, guyabano, guanábana." It is sometimes referred to as soursop because of its mildly acidic flavour when mature. It is extensively cultivated in tropical and subtropical climes[142,143]. Literature indicates that *A. muricata* exhibits anti-arthritic, anticancer, anticonvulsant, antidiabetic, hypolipidemic, anti-inflammatory, antinociceptive, antioxidant, antiparasitic, antihypertensive, hepatoprotective, and insecticidal properties[144]. A study in Pakistan indicated that the leaves and fruits of *A. muricata* enhance the immune system and alleviate fever in monkeypox cases owing to acetogenins[98].

Quercus infectoria

Q. infectoria (Fagaceae) is referred to as "Aleppo oak." It is a little tree that attains a height of 1 to 2 meters. The trunks are gnarled and dense. The leaves are obtuse, round, glabrous, asymmetrical at the base, and lustrous on the adaxial surface[145,146]. Literature indicates that *Q. infectoria* has antibacterial, anticancer, anti-inflammatory, antileishmanial, antioxidant, cytotoxic, and antiparasitic actions[147-151]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *Q. infectoria*, exhibited an inhibitory impact on the MPox virus[102].

Azadirachta indica

A. indica (Meliaceae) is referred to as "neem, margosa, nimtree, Indian lilac." It is prevalent in tropical and subtropical areas. It is a perennial tree species. The leaves are hairy. It possesses white and aromatic flowers[152-154]. Literature indicates that *A. indica* possesses anti-inflammatory, antipyretic, analgesic, hypoglycemic, antiulcer, antibacterial, antioxidant, antimalarial, antiviral, and hepatoprotective properties[155,156]. A study in Pakistan indicated that nimbin and nimbidin present in the leaves and bark of *A. indica* contributed to the treatment of monkeypox due to their immune-enhancing effects[98].

Piper nigrum

P. nigrum (Piperaceae) is referred to as "Black pepper." Its native land is India. It is prevalent in tropical climates. Black pepper is derived from the green, unripe drupe of the plant[157-159]. Literature indicates that *P. nigrum* has anticancer, antibacterial, antioxidant, anti-inflammatory, antidepressant, hepatoprotective, antidiarrheal, anticonvulsant, and antiviral properties[159-161]. A study in Bangladesh examined the efficacy of various bioactive compounds derived from *P. nigrum* against the monkeypox virus by molecular docking techniques. The investigation indicated that curcumin had the highest binding affinity among the metabolites, measuring -37.43 kcal/mol, succeeded by gedunin (-34.89 kcal/mol), piperine (-34.58 kcal/mol), and coumadin (-34.14 kcal/mol)[121].

Rhus chinensis

R. chinensis (Anacardiaceae) is referred to as "Chinese sumac" or "nutgall tree." It is a deciduous shrub or little tree. It attains a height of up to 6 meters, featuring hairy stems and compound leaves composed of several leaflets. It is geographically dispersed across East and South Asia[162,163]. Literature indicates that

R. chinensis exhibits hepatoprotective, anti-obesity, intestinal protective, gastroprotective, antidiabetic, antioxidative, cytotoxic, anti-inflammatory, antibacterial, antiviral, anticancer, anticarious, antiosteoporotic, and anticancer activities[164,165]. A study in Iran indicated that vitamins K and B17, along with gallotannin derived from *R. chinensis*, exhibited an inhibitory impact on the MPox virus[102].

Tapinanthus bangwensis

T. bangwensis (Loranthaceae) is a hemiparasitic plant species indigenous to the tropical areas of Western Sub-Saharan Africa[166-168]. Literature indicates that *T. bangwensis* has antioxidant, antibacterial, anticancer, anti-angiogenic, cytotoxic, and hepatocurative properties[169-173]. A study in Pakistan indicated that the pectins and polysaccharides present in *T. bangwensis* demonstrated antiviral and immunomodulatory properties against the MPox virus[98].

Vernonia amygdalina

V. amygdalina (Asteraceae) is referred to as "bitter leaf." It is a botanical specimen characterised by dark green foliage and coarse bark. It is geographically dispersed over multiple regions of West Africa. It is a perennial plant that attains a height of one to six meters[174,175]. In literary research, *V. amygdalina* exhibits properties including antimicrobial, anticancer, antidiabetic, antimalarial, anti-inflammatory, hepatoprotective, antioxidant, cytotoxic, analgesic, anthelmintic, antipyretic, hypolipidaemic, antimutagenic, and anti-leishmanial[176,177]. A study in India tested the phytocompounds Luteolin, Luteolin-7-o-β-glucoside, Vernodalol, Vernolepin, and Vernodalin, derived from *V. amygdalina* leaves, with the antiviral medication Tecovirimat (TPOXX). The study's docking results with PDB Id (6LUT) receptor indicate that various phytoconstituents derived from medicinal plants, including Luteolin (-3.244), Luteolin-7-o-β-glucoside (-2.357), Vernodalol (-2.089), Vernolepin (-1.757), and Vernodalin (-1.534), were evaluated against the antiviral drug Tecovirimat, which has a docking score of (-0.162). These findings suggest that these compounds may be effective in inhibiting Monkeypox infection[178].

Capsicum annuum

C. annuum (Solanaceae) is commonly referred to as "paprika, chilli pepper, or red pepper." It is prevalent in both South and North America. It resembles little shrubs with numerous branches and slender trunks. The leaves are typically round and green. The flowers are star- or bell-shaped and exhibit a range of colours, including purple, white, and green[179-181]. Literature indicates that *C. annuum* has hypolipidemic, antioxidant, anti-inflammatory, antidiabetic, antiulcer, anticancer, and antibacterial properties[182,183]. A study in Turkey indicated that structurally analogous triterpenes, including α-amirin, β-amirin, and β-sitosterol derived from *C. annuum*, exhibit a strong binding affinity to DNA-directed RNA polymerase in the monkeypox virus, potentially inhibiting this crucial viral enzyme[184].

Moringa oleifera

M. oleifera (Moringaceae) is commonly referred to as "moringa" or "drumstick tree." It proliferates extensively in numerous tropical and subtropical nations. It is cultivated commercially in India, Africa, South and Central America, Mexico, Hawaii, and across Asia and Southeast Asia[185,186]. Literature indicates that *M. oleifera* exhibits antioxidant, anticancer, anti-inflammatory, antiulcer, hepatoprotective, analgesic, antidiabetic, anti-obesity, antiasthmatic, anti-urolithiatic, anti-allergic, anthelmintic, antidiarrheal, antimicrobial, and antipyretic properties[186,187]. A study in Italy evaluated substances derived from *M. oleifera* as effective and safe inhibitors of DNA Polymerase (DNA Pol) in the monkeypox virus. The study revealed that Gossypetin exhibited the highest binding affinity (-7.8 kcal/mol), followed by Riboflavin and Ellagic acid, both at -7.6 kcal/mol. In contrast, the control drugs Cidofovir and Brincidofovir demonstrated lower binding affinities, with binding energies of -6.0 kcal/mol and -5.1 kcal/mol, respectively[188].

Cupressus sempervirens

C. sempervirens (Cupressaceae) is referred to as "Mediterranean cypress." It is prevalent in the Mediterranean regions and Iran. It attains a height of roughly 35 meters. *C. sempervirens* is a coniferous evergreen tree. Seed cones are round or rectangular, initially green and subsequently brown[189-191]. Literature indicates that *C. sempervirens* exhibits various activities, including antimicrobial, antiseptic, anti-inflammatory, antispasmodic, antiviral, antiparasitic, insecticidal, antioxidant, anticancer, antidiabetic, antiosteoporotic, hypolipidemic, anticoagulant, and hepatoprotective properties[189,190]. A study in Algeria assessed the inhibitory effects on three monkeypox targets: axania virus thymidylate kinase (VTK), viral profilin-like protein (VPP), and viral RNA polymerase (VRP) by in silico methods utilising the seed and globose cones of *C. sempervirens*. The study indicated that flavonoids, including vitamin C, vanillic acid (Pol), Flav1

(Catechin), Flav2 (Epicatechin), Flav3 (Hyperoside), Flav4 (Luteolin), Flav5 (Taxifolin), and Flav6 (Quercetin), exhibited significant potency against VTK and VPP, effectively obstructing the VRP channel with energy values between -7.0 and -9.3 kcal/mol[192].

Sarracenia purpurea

S. purpurea (Sarraceniaceae) is referred to as the "pitcher plant." It is a carnivorous pitcher plant characterised by conical leaves. In order to thrive in nutrient-deficient environments, *S. purpurea* lures, captures, and metabolises its prey to assimilate soluble nutrients essential for growth and reproduction[193,194]. In literary research, *S. purpurea* has been documented to exhibit anticancer, antioxidant, antibacterial, and antiviral properties[193,195,196]. A study in the United States involved the extraction of *S. purpurea* using a mixture of 190-degree grain ethanol, distilled water, and vegetable glycerin (63%/32%/5%), which was subsequently placed in a glass container, securely sealed and kept at room temperature for 48 days. The study reported that this herbal extract exhibited anti poxvirus activity against the vaccinia virus, monkeypox virus, and variola virus, the pathogens responsible for smallpox, and demonstrated *in vitro* efficacy as the first effective inhibitor of poxvirus replication at the early stage of viral transcription[197].

Conclusion and future perspective

This study delineates the general characteristics, symptoms, applicable treatments, and herbal treatment recommendations for MPXV, which is escalating its impact and resulting in increased morbidity in humans. The literature review revealed that symptoms of MPXV, including rash, fever, systemic rash, genital rash, and lymphadenopathy, are prevalent. Transmission occurs by direct touch, respiratory routes, mother-to-child, zoonotic transmission, sexual contact, and contact with contaminated objects. Additionally, different vaccine applications have been found to have different levels of effectiveness. Numerous plant species documented in the literature demonstrated considerable efficacy against MPXV or its consequences. Herbal medications are believed to mitigate the effects of the virus in pharmacological design investigations.

Conflict of interest

The authors declare no conflict of interest.

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