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A REVIEW ON HERBAL REMEDIES TO COUNTER THE EFFECT OF MONKEYPOX DISEASE

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ABSTRACT: Monkeypox is a zoonotic disease, which refers to its ability to be transmitted between animals and humans. The symptoms of the disease are similar to those of smallpox. However, the symptom, swollen lymph nodes, has been observed as the symptom that differentiates it from smallpox. The disease has been a cause of concern around the world due to its high rate of transmission. The most common symptoms of the disease include fever, rash, sore throat, headache, muscular aches, back discomfort, conjunctivitis, mouth sores, chills, sweating, enlarged lymph nodes, and lethargy. The current MPX outbreak has impacted countries on every continent, making it a serious global health threat. The most effective methods to prevent and cure monkeypox remain a mystery. This review outlines the epidemiology, transmission, symptoms, comorbidities, prevention, and management of monkeypox disease. It also examines the clinical therapies, immunizations, and herbal remedies used to control the infection. The condition is known to adversely affect pregnant or lactating women and immunocompromised individuals, who require additional consideration. Thus, the purpose of this review is to examine the current state of treatments available to combat the monkeypox virus and manage its symptoms. Critical emphasis is placed on drug discovery from plant sources against the monkeypox virus. When used as prescribed, herbal medications have very few, if any, negative side effects, and are nearly as effective as synthetic options.

INTRODUCTION: Monkeypox is a zoonotic illness that presents symptoms that are similar to smallpox. The symptom, swollen lymph nodes, has been observed as the symptom that differentiates it from smallpox [1]. It has a high transmission rate, which poses a global threat [2]. Swollen lymph nodes, fever, and rashes on the body are among the most common symptoms of this disease [1, 3, 4].

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The present MPX outbreak has affected the countries on every continent, turning it into a serious global health threat [5]. The most effective methods to prevent and cure monkeypox remain a mystery. The virus is part of the family *Poxviridae* and the genus *Orthopoxvirus* [6].

It features an enclosed double-stranded DNA structure and is divided into two clades: Clade I and Clade II. Clade I has subclades Ia and Ib, while Clade II includes subclades IIa and IIb [6]. The present monkeypox outbreak has escalated into a major health concern around the world, which has impacted countries across many continents [5]. Concern over the monkeypox infection is

developing due to its potential for transmission and spread around the world [2]. The best treatment to prevent and cure this deadly disease is still a mystery. Two smallpox vaccines have been found to be effective against the disease [7, 8]. However, the vaccines may be restricted to some compromised groups of individuals, including immuno-compromised people and pregnant or lactating women [7]. There may be adverse effects from the immunization. Highly infectious viruses continue to mutate and threaten global health status, which has led to extensive research into the antiviral properties of medicinal plants. The field of medicinal plant research has been making huge strides, mostly due to the improved accessibility of technological instruments [9]. A lot of plants have been utilized in clinical research as well as traditional medical practices to identify potential medications to treat the disease caused by the monkeypox virus [10]. Plants have always been known for the potential to produce secondary metabolites. The secondary metabolites produced by plants have been utilized as the starting material for drug development [11]. Evidence is found that certain naturally occurring plant metabolites - including phenolic compounds, flavonoids, terpenoids, and alkaloids exhibit inhibitory activity against the monkeypox virus [9]. A number of herbs and plant metabolites have been sorted, identified, and investigated for their antiviral qualities through a number of scientific studies [10].

These studies have included clinical trials aimed at elucidating the therapeutic effects of antiviral herbs and their utilization in controlling viral infections [9]. Comprehensive studies of newly developing and reemerging infectious diseases - including their origins, diagnosis, and treatments - have been enabled by drug design approaches [12]. Drug design approach is responsible for the rapid development of innovative drugs and vaccine candidates to control viral infections. It is one of the most extensively studied areas in the present era of herbal medicine development [12]. Especially, at present times, when different diseases are prevailing more and spreading around the world as pandemics. Almost all the modern drugs in use derive from natural sources. However, synthetic medications are heavily processed and often contain harmful substances. Although synthetic drugs and vaccines may be effective and fast in treating diseases, they come with many fatal side effects and cannot be granted to every individual.

This paper lists potential herbal remedies that can be proven effective in treating monkeypox infections.

Epidemiological Featuresl: The monkeypox virus was first identified in 1958 in the country of Denmark while conducting experiments on monkeys at a laboratory [13].

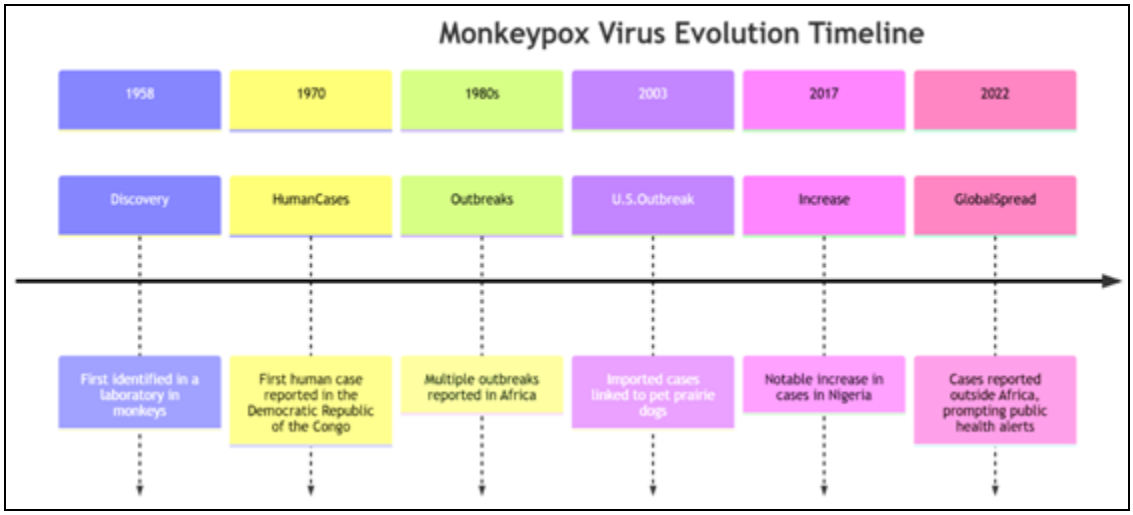

FIG. 1: TIMELINE SHOWING THE EVOLUTION OF MONKEYPOX VIRUS

The first infection in humans was recorded in the year 1970 in a baby aged 9-month-old in the Democratic Republic of the Congo [13]. The virus gradually spread across Central, East, and West Africa during the 1980s when smallpox immunization was discontinued globally [14].

Since then, there have been reports of Mpox in different parts of Africa. In 2003, there was an outbreak of the monkeypox virus in the USA, which was an imported case from Ghana, West Africa, through MPXV-infected prairie dogs [15, 16]. The country that is most affected by the virus to date is the Democratic Republic of the Congo, which has been reporting thousands of cases annually since 2005 [17]. In 2017, the African country Nigeria saw a notable increase in monkeypox cases, which re-emerged after 39 years of remaining dormant [18]. Clade IIb started to spread around the world in 2022 and is still going strong, even in certain African nations. The timeline of the evolution of the monkeypox virus as a disease is illustrated in **Fig. 1.**

The Democratic Republic of the Congo and other African nations are also experiencing an increase in clade Ia and Ib epidemics [19]. Clade Ib has also been identified outside of Africa as of August 2024 [20]. Clade I - related Mpox epidemics occurred in the Republic of the Sudanese refugee camps in 2022 [21]. The Democratic Republic of the Congo has also seen a rise in Mpox infections and fatalities since 2022 [22]. Clade Ib is a recent variant of Clade I that has been spreading from person to person in various parts of the world [23]. Between January 2022 and August 2024, more than 100,000 laboratory-confirmed monkeypox infections in over 120 nations were reported. There are over 220 fatalities among those confirmed cases [23]. The first case of monkeypox to be reported in India was in Kerala on July 14, 2022. It was estimated that the patient was an imported case [24]. In September 2024, the fast-spreading clade Ib strain of Mpox was first detected in a Keralan managed 38-year-old, who returned from Dubai [25].

According to 'Business Today' of India, 32 confirmed cases have been recorded in India as of September 24, 2024, since the WHO declared Mpox a public health emergency. A pie chart showing the approximate number of laboratory-confirmed cases of monkeypox is provided in **Fig. 2.**

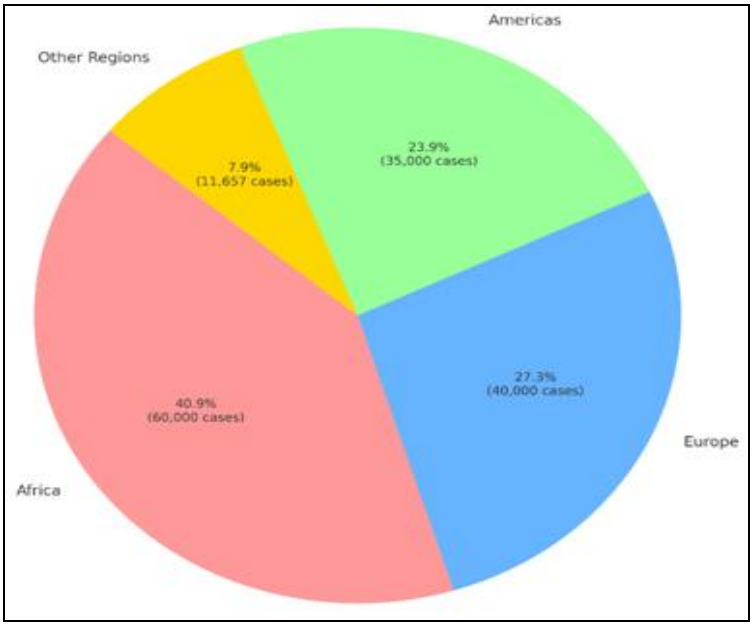

FIG. 2: A PIE CHART SHOWING THE APPROXIMATE NUMBER OF CONFIRMED MPX CASES GLOBALLY

Transmission Mode: The primary method by which Mpox is transmitted from person to person is through close contact with an infected individual, especially family members [26]. The virus spreads through close contact, such as mouth-to-mouth or mouth-to-skin, or skin-to-skin contact [27]. Close contact can also involve being in close proximity to someone who has Mpox. Additionally, those who have multiple sexual partners or men who have sex with other men are more likely to have Mpox [28]. Furthermore, Mpox can be acquired through injuries like needle puncture in medical facilities, establishments like tattoo parlours, and salons, or through equipment which are infected, like clothing or linen [29]. The virus may be transmitted to the unborn child from the mother during pregnancy or delivery [30]. In addition to being harmful to the foetus or baby, Mpox during pregnancy can cause

issues for the parent, including stillbirth, pregnancy loss, or neonatal mortality [31]. Infected animals can spread Mpox to people through contact, like scratches or bites, or practices, like hunting, trapping, skinning, handling carcasses, cooking, or eating animals [32]. More research is being conducted to determine the monkeypox virus's animal reservoir.

Symptoms: Signs and symptoms of Mpox often appear a week after exposure, although they might appear as early as one to twenty-one days later. The symptoms usually last for two to four weeks [33]. However, symptoms might linger longer in people with compromised immune systems [34]. Typical signs of Mpox include fever, rash, sore throat, headache, muscular pain, back discomfort, conjunctivitis, mouth sores, chills and sweating, enlarged lymph nodes, and poor energy [35]. Some people notice a rash on their body as their first Mpox symptom, while others may experience fever, sore throat, or muscular pain. The Mpox rash starts on the face and spreads to the palms of the hands and soles of the feet. Additionally, the rash may start on other areas of the body, such as the genitalia, where contact occurred [36]. It begins as a flat sore and progresses into a blister that is filled with pus, which causes discomfort or itching. The lesions dry up, crust over, and fall off as the rash cures [37]. Those who have Mpox can infect others if all the wounds have not healed and a new layer of skin has not grown. There is also the possibility of some individuals getting infected without showing any symptoms [38]. There have been reports of Mpox being contracted from an asymptomatic person. Pregnant women, children, and those with compromised immune systems, such as HIV patients, are at a greater risk of developing serious complications and dying as a result of the complications caused by monkeypox [39]. Monkeypox can make some individuals severely ill. Bacterial infections of the skin, for instance, can result in abscesses or severe skin damage. There are a number of additional complications that can arise, including pneumonia, an infection of the cornea that can result in blindness, difficulty swallowing, vomiting, and diarrhoea that can lead to malnutrition or dehydration, and infections of the blood, brain, heart, rectum, genital organs, or urinary tract [40]. Most of the common symptoms of monkeypox have been illustrated in **Fig. 3.**

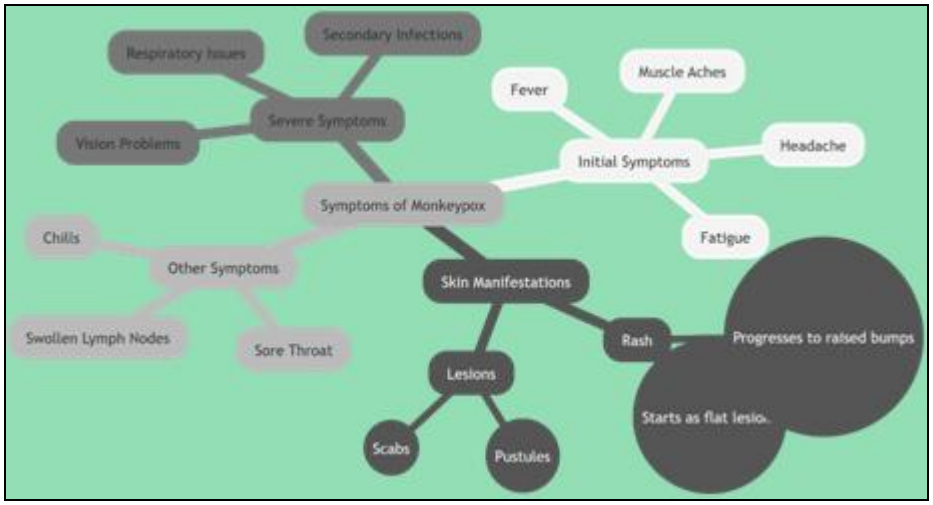

FIG. 3: A FLOWCHART SHOWING THE COMMON SYMPTOMS OF MONKEYPOX DISEASE

Monkeypox and Associated Disorders: A number of comorbidities, including compromised immune systems or underlying medical conditions, have been linked with monkeypox. Most infections of monkeypox are minor and resolve on their own. However, some sensitive groups of people may experience more serious consequences. The risk of developing a serious illness is raised by the presence of health disorders or comorbidities [41]. Patients suffering from HIV/AIDS have weakened immune systems and are prone to severe cases of monkeypox [42]. A compromised immune system may cause the duration and impact of the infection to worsen, which increases viral replication. Studies have shown that pregnant women are more prone to monkeypox complications, and the developing foetus is at risk of resulting in stillbirth or having congenital diseases [43].

Patients on drugs that are immunosuppressive, cancer patients undergoing chemotherapy, or recipients of organ transplants are at high risk of developing severe conditions of monkeypox and may experience a longer duration of illness, worse skin lesions, and bacterial infections [39, 44]. Severe respiratory diseases like asthma, chronic obstructive pulmonary disease (COPD), or other lung diseases may worsen the respiratory symptoms associated with monkeypox [44].

Chronic skin conditions like psoriasis or eczema may disrupt the skin barrier, which can result in secondary infections or more extensive lesions [45]. The severity of a viral infection may increase multiple times in people with cardiovascular diseases [46]. Diabetes can weaken the immune system, raise the risk of complications, delay wound healing, and complicate the healing of lesions [47]. Malnutrition can impair the immune system, and malnourished people may experience more severe diseases and take longer to recover [48]. Older adults and very young children have weaker body defence mechanisms and, even in the absence of comorbidities, they are more vulnerable to infections [49]. The presence of other viral infections, such as herpes simplex virus (HSV), varicella-zoster virus (VZV), or other poxviruses, may affect the course of a monkeypox infection [50, 51].

Prevention and Management: The best way to prevent monkeypox infection is to avoid being in contact with a person or animal infected with the disease. People should avoid visiting areas where people are affected by monkeypox infections. Infected animals and patients should be handled with personal protective equipment (PPE), such as gloves, masks, and other protective gear [52]. Infected patients should be quarantined to prevent human-to-human transmission. Smallpox vaccination or the currently available JYNNEOS vaccine may provide protection to individuals who are at high risk or may have been exposed to the virus [52, 53, 54, 55, 56]. Maintenance of proper hygiene habits, like washing hands often and disinfecting surfaces, is necessary to lower the risk of infection.

In the most severe cases of infection, therapy for patients - including pain management, wound care, and hydration - is introduced. Antiviral drugs such as tecovirimat, brincidofovir, cidofovir, and other potent antiviral drugs should be prescribed to the patient [57, 58, 59, 60]. Vaccinia Immune Globulin (VIG) therapy can be administered to provide passive immunity in severe or complicated cases [61]. Antibiotics and antihistamines should also be prescribed in order to prevent bacterial infections and ease itching in the patients [62]. Diagnosis in the early stage and supportive treatment are necessary to prevent complications. Regular monitoring should be conducted in order to speed recovery, especially for those with weakened immune systems. Efficient drugs and treatments that indicate opposing effects against MPX infection are listed in **Table 1.**

TABLE 1: EFFICIENT DRUGS AGAINST MPX INFECTION

Drugs	Category	Treatment	Mechanism of Action	Remark
Tecovirimat (TPOXX)	Antiviral	Severe monkeypox infections or high-risk cases	Inhibits the viral protein involved in the replication of the orthopoxvirus.	FDA-approved for use in smallpox and monkeypox
Cidofovir	Antiviral	Severe monkeypox infections, especially in people with weakened immunity	Inhibits viral DNA polymerase which prevents viral replication.	Not FDA-approved for monkeypox. But used for investigational use.
Brincidofovir	Antiviral	Severe monkeypox cases, particularly in immunocompromised patients	Inhibits viral DNA polymerase like cidofovir and is less toxic to the kidneys.	Used as an alternative to cidofovir for those with kidney issues.
Vaccinia Immune Globulin (VIG)	Immune Therapy	Severe or complicated monkeypox cases	Provides passive immunity by administering antibodies that may inhibit the virus.	Typically used in cases of severe infection or complications.
Smallpox Vaccine (e.g., JYNNEOS)	Preventative Vaccine	Pre- or post-exposure prophylaxis to prevent monkeypox infection	Induces immunity against orthopoxviruses. Post-exposure vaccination may prevent or ease the severity of illness.	A preventive measure, especially in high-risk populations.

Potent Herbs as a Cure for Monkeypox: Traditional medicines, from time immemorial, have been one of the most extensively used practices in India, even after the discovery of new branches like homeopathy and allopathy. The main source of most of the artificial medicines in modern times is from nature [63]. Plants produce secondary metabolites to complete their life processes [64]. The secondary metabolites obtained from the plants have been the starting material for drug discovery [65]. They are known for their potential antiviral, antibacterial, anti-inflammatory, and immune-boosting qualities [66, 67, 68]. These secondary metabolites could enhance the body's defence mechanisms against infections in general. Different alkaloids, terpenoids, flavonoids, phenolic compounds, and other such compounds that occur naturally in plants have evidence of exhibiting pharmacological activities against Mpox [69].

Studies revealed that fig, moringa, black cumin, and green chirettamay be potential remedies for monkeypox infection [70, 71, 72, 73]. Immunity-boosting herbs, such as echinacea, garlic, and elderberries, may assist the body in fighting infections [74, 75, 76]. Plants with antiviral and anti-inflammatory properties, like turmeric and liquorice root, may soothe inflammation and reduce the symptoms of infection [77, 78]. Skin rash healing and immunity boosting can be provided by lemon balm and oregano oil [79, 80]. Lesser-known herbs like astragal us and popular remedies like ginger may also have the potential to combat the fatal monkeypox virus [81, 82]. Leaf extracts from plants like basil and olive have been known to exhibit antiviral effects [83, 84]. There are numerous other herbal remedies that may have the properties to inhibit the effects of monkeypox infection and its symptoms [85]. Some of the effective herbal remedies are listed in **Table 2.**

TABLE 2: EFFECTIVE HERBAL REMEDIES AGAINST MPXINFECTION

Herbs	Efficiency	Common uses	Remarks
Fig leaves *(Ficus religiosa)*	May inhibit viral attachment to host cells and interfere with viral replication.	May be used to treat various viral infections due to its antiviral properties.	Researches indicate antiviral potential, but more studies are necessary.
Drumstick *(Moringa oleifera)*	May inhibit viral replication and interfere with viral entry into cells.	May be used to treat conditions, like liver disease, cancer, inflammation, wounds, ulcers, pain, and heart disease	Studies demonstrate that *Moringa* has antiviral properties.
Black cumin (*Nigella sativa*)	May inhibit apoptosis, which is induced by viruses, and inhibit viral replication.	May boost the immune system, fight cancer, reduce swelling, and soothe allergic reactions.	Studies have proven that *Nigella sativa* is effective against viral infections.
Echinacea *(Echinacea spp.)*	May help boost the immune system and reduce inflammation.	Used to prevent or treat colds and infections.	Some studies suggest it may stimulate immune function.
Andrographis *(Andrographis paniculata)*	May support immune function and reduce viral replication.	Traditionally used for respiratory and viral infections.	Some studies show it may assist with immune response.
Elderberry (*Sambucus nigra*)	May possess antiviral properties.	Used to treat colds, flu, and respiratory infections.	Some studies suggest it may reduce the severity of viral infections.
Garlic *(Allium sativum)*	May have antimicrobial and immunity-boosting properties.	Used as a tonic for different types of infections.	Research supports its antimicrobial properties.
Astragalus *(Astragalus membranaceus)*	May help strengthen the immune system and fight infections.	Used to improve overall immune function.	Some studies suggest immunity-boosting properties, especially for viral infections.
Ginger *(Zingiber officinale)*	May possess anti-inflammatory and immunity-supporting properties.	Used to treat digestive issues and nausea.	Contains compounds that may support immune function.
Turmeric *(Curcuma longa)*	May consist of anti-inflammatory and immunity-boosting properties.	Used to treat inflammation and prevent infection.	Contains curcumin, which has anti-inflammatory properties.
Olive Leaf Extract (*Olea europaea)*	May help fight against viruses and strengthen immunity.	Used as an antiviral and immunity-boosting tonic.	Some studies show antiviral effects.
Licorice Root	May help ease symptoms	Used to treat cold sores and	Studies reveal it contains antiviral

(*Glycyrrhiza glabra*)	associated with viral infections.	other viral infections.	compounds.
Basil (*Ocimum sanctum*, Holy Basil)	May possess antiviral, immunity-boosting, and anti-inflammatory effects.	Used to relieve stress, boost immune health, and treat infections.	Some studies support its antiviral and immunity-boosting effects.
Lemon Balm (*Melissa officinalis*)	May help to reduce symptoms of viral infections.	Used to treat cold sores and infections.	Studies suggest it possesses compounds with antiviral activity.

Remedies for Management of Symptoms: The fatal monkeypox illness comes with symptoms that can affect the well-being of the infected individual. The symptoms of Mpox are similar to the symptoms of smallpox, but the symptom that distinguishes it from smallpox is swollen lymph nodes [1]. Typically, the signs and symptoms of Mpox start to appear a week after exposure, although they may appear as early as one to twenty-one days later. The symptoms usually last for two to four weeks [33]. The symptoms that most commonly occur during the infection include fever, rash, sore throat, headache, muscular pain, back discomfort, conjunctivitis, mouth sores, chills and sweating, enlarged lymph nodes, and lethargy [35]. These symptoms cause a lot of discomfort and strain on the physical and mental health of an individual. Usually, these symptoms subside on their own as the incubation period of the monkeypox infection comes to an end. However, some symptoms may last long. There are different methods or treatments that may relieve these symptoms. Drugs like acetaminophen or ibuprofen help to reduce fever and relieve pain [86]. Rashes and itching on the body may be controlled with calamine lotion or antihistamines [62]. Antiviral drugs like tecovirimat or brincidofovir may be used for severe rashes [57, 60]. All these treatments may reduce the intensity of the symptoms of the infection. However, there are several herbal or natural remedies to ease the symptoms of monkeypox as well. Herbs like elderflower and yarrow may assist in limiting the effects of fever[87]. Aloe veramay be used to treat mouth sores and rashes [88, 89]. Chamomile may also be applied to rashes to soothe them [90]. Commonly found herbs like peppermint and lavender may assist in relieving headaches [91, 92]. Turmeric, ginger, and willow bark may act as pain relievers in the body [93, 94, 95, 96]. Turmeric may also be applied to ulcers to treat mouth sores [97]. The golden herbs ginseng and ashwagandha are known to rejuvenate the body and reduce fatigue [98, 99]. Swollen lymph nodes may be reduced by providing echinacea and licorice root to the patient [100, 101]. An infected patient may experience chills and sweating as symptoms. Ginger and cinnamon may be consumed to reduce both chills and sweating [102, 103]. A person suffering from monkeypox may also experience a sore throat. Slippery elm and honey may assist in soothing a sore throat [104, 105]. The symptoms of monkeypox, along with their potential treatments and remedies, are displayed in **Table 3.**

TABLE 3: MONKEYPOX SYMPTOMS WITH THEIR POTENTIAL TREATMENTS AND REMEDIES

Symptom	Treatment	Herbal remedy
Fever	Hydration: Drinking fluids helps prevent dehydration. Antipyretics: Over-the-counter fever relievers like acetaminophen (Tylenol) or ibuprofen (Advil).	Elderflower (*Sambucus nigra*), Yarrow (*Achillea millefolium*)
Rash	Symptomatic treatment: Calamine lotion or antihistamines may ease itching. Antiviral treatment: In severe cases, drugs like Tecovirimat (TPOXX) or Brincidofovir may be used.	Aloe Vera (*Aloe barbadensis*), Chamomile (*Matricaria chamomilla*)
Headache	Pain reliever drugs, such as acetaminophen or ibuprofen, may relieve headaches.	Peppermint (*Mentha piperita*), Lavender (*Lavandula angustifolia*)
Muscle Aches	Pain reliever drugs, like ibuprofen or acetaminophen, may help reduce muscle pain.	Turmeric (*Curcuma longa*), Ginger (*Zingiber officinale*)
Fatigue	Plenty of rest is necessary to help the body fight the infection.	Ginseng (*Panax ginseng*), Ashwagandha (*Withaniasomnifera*)
Swollen Lymph Nodes	Swelling-related pain can be relieved by ibuprofen or acetaminophen.	Echinacea (*Echinacea spp.),* Licorice Root *(Glycyrrhiza glabra)*
Chills and	Proper hydration of the body helpsin regulating	Ginger (*Zingiber officinale*), Cinnamon

Sweating	temperature.	(*Cinnamomum verum*)
Sore Throat	Lozenges or gargles with lukewarm salt water help to soothe the throat.	Slippery Elm (*Ulmus rubra*), Honey
Back Pain	Pain relievers, such as ibuprofen or acetaminophen, assist in relieving pain.	Turmeric (*Curcuma longa*), Willow Bark (*Salix spp.*)
Conjunctivitis	Warm compresses can help soothe irritated eyes.	Eyebright (*Euphrasia officinalis*), Chamomile (*Matricaria chamomilla*)
Mouth Sores	Topical gels, such as lidocaine or benzocaine gels, may be used to numb pain.	Aloe Vera (*Aloe barbadensis*), Turmeric (*Curcuma longa*)

CONCLUSION: Monkeypox is a life-threatening disease that requires immediate medical attention. The disease has symptoms similar to those of smallpox. Proper treatment and care can help a person recover within a certain duration of time. However, complications may arise in sensitive groups of people, such as patients with weakened immunity, pregnant and lactating women, and young children. Two smallpox vaccines and antiviral drugs such as Tecovirimat, Cidofovir, and Brincidofovir are used as supplements for the control and prevention of the disease. Traditional medicines with potent antiviral, anti-inflammatory, and immunity-boosting properties have long been used to cure or treat fatal diseases.

Herbal medicines may provide supportive care by relieving the symptoms, such as fever, swollen lymph nodes, headaches, muscular aches, and rashes. Researchers have revealed that the phytocompounds in several traditionally used herbal medicines possess properties that make them potent candidates for drug design against the deadly monkeypox disease. Plants like fig, moringa, black cumin, and green chiretta contain potential phytochemicals that may inhibit the action of the monkeypox virus. Immunity-boosting herbs, such as echinacea, garlic, and elderberries, may assist the body in fighting the infection. Plants with antiviral and anti-inflammatory properties, like turmeric and liquorice root, may also soothe inflammation and reduce the symptoms of infection. Skin rashes can heal, and immunity can be boosted by providing lemon balm and oregano oil. There are numerous other herbal remedies that may have the potential to combat the fatal monkeypox virus.

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CONFLICT OF INTEREST: Regarding the publication of this article, the author affirms that there is no conflict of interest.

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