CURRENT VETERINARY SCIENCE

Curr Vet Sci, 2(1): 11-18, 2025

Current Veterinary Science

Review Article

Herpesviral Infections of the Nervous System in Ruminants: BoHV-1, BoHV-5, PRV, MCFV

Fatma Nur Yüce[1,2], Hayrunnisa Bostan Yörü[3], Gülizar Acar[3], Hakan Aydın[3], Mehmet Özkan Timurkan[3*]

[1] Atatürk University, Health Science Institute, Department of Virology, Erzurum, Türkiye
[2] Veterinary Control Institute, Republic of Türkiye Ministry of Agriculture and Forestry, Erzurum, Türkiye
[3] Ataturk University, Faculty of Veterinary Medicine, Department of Virology, Erzurum, Türkiye

ABSTRACT

Bovine Herpesvirus-1 (BoHV-1), Bovine Herpesvirus-5 (BoHV-5), Pseudorabies Virus (PRV), and Malignant Catarrhal Fever Virus (MCFV) are significant viral pathogens that cause respiratory, neurological, and immunological system diseases in cattle. This review aims to provide a comparative evaluation of these viruses based on current literature regarding etiology, epidemiology, clinical manifestations, diagnostic methods, treatment options, and preventive strategies. BoHV-1 is a globally prevalent virus that can be effectively controlled through vaccination, whereas BoHV-5 primarily affects young calves by causing severe CNS infections and is associated with high mortality rates. Although originating from swine, PRV can lead to peracute and fatal neurological syndromes in cattle. It has been established that MCFVs, transmitted from various reservoir species, are the causative agents of lymphoproliferative and vasculitic disease courses in ruminants. The agents' ability to cross species barriers, establish latent infections, and induce neurological signs complicates their control. Practical diagnostic tests, strict biosecurity protocols, and the development of new-generation vaccines are the main approaches to controlling these infections.

Keywords: BoHV-1, BoHV-5, MCFV, Neurological disease, PRV, Ruminants

INTRODUCTION

Herpesvirus infections in ruminants have been demonstrated to cause significant health and economic losses in the livestock sector, primarily due to the pathologies they cause on the central nervous system (CNS) (1). The primary agents responsible for CNS involvement are bovine herpesvirus type 1 (BoHV-1), bovine herpesvirus type 5 (BoHV-5), malignant catarrhal fever viruses (MCFV) and pseudorabies virus (PRV). These viruses have been observed to induce severe neurological findings, including encephalitis, meningoencephalitis, ataxia and paralysis, often resulting in high mortality rates, particularly among juvenile animals (2).

The latent infection ability of these pathogens results in their persistence within herds for extended periods, thereby hindering effective control and eradication efforts (3). It has been demonstrated that the reactivation of BoHV-1 is exceptionally responsive to stress and immunosuppression. Furthermore, it has been observed that latently infected animals have the potential to become virus shedders. MCFV infections have the potential to induce fatal clinical manifestations when transmitted from subclinical carrier species (e.g., sheep) to susceptible species (cattle, deer) (4).

The consequences of such infections are twofold, impacting animal health and animal husbandry productivity. A plethora of indirect losses have been identified, including but not limited to: a decline in milk yield; a decline in fertility; growth retardation; an increase in labor and treatment costs; and the replacement of animals removed from the herd (1). Furthermore, in the event of outbreaks, measures such as trade restrictions, quarantine practices, and animal movement prevention can result in significant economic repercussions (5).

In this review, the etiology, epidemiology, pathogenesis, clinical findings, diagnosis and treatment approaches of BoHV-1, BoHV-5, MCFV and PRV infections were analyzed in the light of current literature.

BOVINE HERPESVIRAL MENINGOENCEPHALITIS (BOVINE ALPHAHERPESVIRUS 1 and 5)

Etiology, epidemiology and pathogenesis

Bovine herpesviral meningoencephalitis (BHM) is an infectious disease characterized by neurological signs, usually seen in young calves and rare in adult cattle. BoHV-5 and BoHV-1 mainly cause the disease, but BoHV-1 can also cause meningoencephalitis. It is impossible to distinguish these two agents using conventional laboratory tests because they are genetically and antigenically closely related (1). It has been demonstrated that both BoHV-1 and BoHV-5 manifest neurotropic effects, with BoHV-5 reaching the frontal regions of the brain and causing neurological diseases

***Corresponding Author:** motimurkan@atauni.edu.tr

Submitted: 15.05.2025, **Accepted:** 17.06.2025, **Published online:** 30.06.2025

How to cite this article: Yüce FN, Bostan Yörü H, Acar G, Aydın H, Timurkan MÖ: Herpesviral Infections of the Nervous System in Ruminants: BoHV-1, BoHV-5, MCFV, PRV. Curr Vet Sci, 2(1):11–18, 2025.

that are frequently fatal. In contrast, BoHV-1 is rarely responsible for bovine encephalitis. (6).

The order *Herpesvirales* consists of 3 families: *Alloherpesviridae* (frog and fish herpesviruses), Malacoherpesviridae (oyster herpesviruses) and *Orthoherpesviridae* (mammalian, reptile and avian herpesviruses). The *Orthoherpesviridae* family contains three subfamilies: *Alphaherpesvirinae, Betaherpesvirinae* and *Gammaherpesvirinae*. All ruminant herpesviruses are classified in the subfamilies *Alphaherpesvirinae* or *Gammaherpesvirinae*. BoHV-1 and BoHV-5 are in the subfamily *Alphaherpesvirinae*, genus *Varicellovirus* (1). According to the classification by the International Committee on Taxonomy of Viruses (ICTV), BoHV-1 and BoHV-5 share high genetic similarity (>80% amino acid identity) (2,7).

Herpesviruses are linear DNA viruses and their genomes are 120-250 nm in diameter, double-stranded, contain 135.3 kilobase pairs (kbp) and are high in guanine and cytosine (GC) content (1,3). Surrounded by an icosahedral protein capsid of 162 capsomers, viral DNA encodes approximately 200 genes. (3). The nucleocapsid is embedded in an amorphous protein tegument originating from the host cell and surrounded by an envelope consisting of a double lipid layer covered with viral glycoproteins. Herpesviruses (especially those of the *Alphaherpesvirinae* family) can cause acute or latent infection (1). The site of latency is sensory neurons in the trigeminal ganglia, but it has also been observed in lymphoid tissues (6).

All BoHV-1 strains belong to a single viral species but are divided into three subtypes based on antigenic and genomic analysis: BoHV-1.1, -1.2a and -1.2b. Subtype 1 virus strains, the causative agent of infectious bovine rhinotracheitis (IBR), are typically found in the respiratory tract and aborted fetuses. Strains of this type are prevalent in Europe and North and South America. Subtype 2a infections are associated with various clinical symptoms in the respiratory and genital systems. This type causes infectious pustular vulvovaginitis (IPV), infectious balanoposthitis (IPB) and abortions. Subtype 2b has been identified in Australia and Europe and is linked to respiratory diseases, IPV and IPB. However, it has been demonstrated not to be the causative agent of abortions (3).

BHM was first reported in Australia in 1963 (5). Due to its shared virion morphology, cytopathic effect in cell culture, and antigenic properties, the virus was categorized as a neuropathogenic variant of BoHV-1. This categorization resulted in the designation of bovine encephalitis herpesvirus (BEHV) or BoHV-1 subtype 3. Subsequently, based on restriction site mapping of viral DNA and cross-reaction with monoclonal antibodies, BEHV was detected as a separate strain with distinct genomic and antigenic properties. Therefore, in 1992, the ICTV recognized BEHV as a separate virus species, namely BoHV-5 (5).

BoHV-5 is the primary etiologic agent of non-suppurative, necrotic meningoencephalitis, which is usually fatal in calves (6). BoHV-5 has been shown to trigger fatal meningoencephalitis or a meningitis-like illness after intravaginal infection or intranasal vaccination. Neurological symptoms begin with severe depression, loss of appetite, jaw clenching and excessive salivation (9). Animals vaccinated by the intraconjunctival route develop hyperthermia with nasal replication of the virus but do not show any neural signs (10). BoHV-5 is divided into 5a, 5b and 5c subtypes (2). The only strain classification to subtype b was recognized as a natural recombinant between BoHV-1 and BoHV-5 (6). BoHV-5 cases are highly prevalent in South America, especially in Brazil and Argentina, but sporadic disease in some countries (11).

Although data on the factors affecting BoHV-5 transmission are limited, viral DNA and infectious viruses have been detected in the semen of subclinically infected bulls (10). For BoHV-1, viral transmission occurs directly or indirectly between animals. The virus's initial replication occurs in the epithelial cells of the oral, nasal, oropharyngeal and ocular mucosa, where the virus spreads through local invasion of nerve endings and/or viremia. Approximately 7 days after infection, the entry of viruses into the CNS occurs via retrograde axonal transport along the cranial nerves, particularly the olfactory nerves. In the CNS, a new cycle of viral replication leads to either meningoencephalitis (the primary manifestation of the disease) or lifelong latent infection (1).

The prevalence and incidence of BoHV-1 infection varies worldwide (12). During the latent period, a new reactivation, often triggered by stressful conditions, enables the virus to disseminate and infect other individuals. Several factors have been identified as causative to the propagation of viruses within a herd. These include the reduction of passive immunity, the weaning of calves during this period, large numbers of animals, transport, the introduction of cattle from outside the herd, alterations to feed, paddock changes, vaccination, ear numbering, cauterization and castration. Decreased maternal immunity is associated with an increased risk of infection and seroconversion. This condition leads to a higher prevalence of antibodies to BoHV-1 in adult cattle, where the seroconversion rate is lower due to herd immunity (1,12). Early weaning of calves has been documented in 75% of BoHV-5-induced investigations on farms with BHM cases; however, a possible failure of passive transfer of immunity has not been confirmed. The effect of passive immunity was confirmed by experimental studies showing that calf groups that did not receive colostrum developed meningoencephalitis and respiratory disease after BoHV-5 and BoHV-1 vaccinations, respectively (1).

Latent viruses can be detected by polymerase chain reaction (PCR) or in situ hybridization. Viral particles produce a latency-associated gene, but no viral proteins or infectious particles are produced. The viral DNA is localized in the nucleus of latently infected neurons. Sites of latent infection in cattle include the trigeminal nerve or sensory root ganglia, olfactory bulbs, telencephalic cortex, midbrain, pons, cerebellum and medulla oblongata (1). Reactivation of BoHV-1 after a latent period is necessary for virus transmission. During this period, immune responses are temporarily suppressed, and the integrity of mucosal surfaces is disrupted, but it does not cause serious recurrent diseases. Therefore, reactivation during the latent period may accelerate secondary bacterial infections in the lower respiratory tract and lead to pneumonia (13).

There is a strong association between BoHV-1 infection and bovine respiratory disease complex (BRDC), which causes losses of approximately US$1 billion annually. These economic losses have led to the widespread adoption of vaccination against BoHV-1. Natural or vaccine-induced immunity to BoHV-1 protects animals against BoHV-1 and BoHV-5, which may explain the lower prevalence of BHM cases in Europe and North America. In countries where vaccination against BoHV-1 is less frequent, outbreaks of neurological diseases are more common (1).

Factors affecting the survival, transmission and dispersal of BoHV-1 include temperature and humidity. BoHV-1 remains stable at 4°C for up to 1 month, but stability decreases with increasing temperature. The infectivity of the virus decreases 106-fold in 50 days at 22°C, 10 days at 37°C and 21 minutes at 56°C. High humidity is conducive to virus reproduction because it survives longer and spreads rapidly in high humidity. The virus can survive up to 30 days in a cold environment with a humidity of more than 90% and 5-13 days in a warmer environment. Aerosol dispersion has been demonstrated over short distances of up to 4 m, but transmission is estimated to occur over distances of up to 8 km. The virus can be detected in contaminated feed for up to 30 days. BoHV-1 is sensitive to many disinfectants, such as quaternary ammonium, phenol and formalin (14).

Clinical signs

Lethargy and loss of consciousness are typical clinical symptoms of BHM in endemic areas and are important indicators of the disease. Infected cattle move away from the herd and remain immobile with a low head posture. As the disease progresses, mucoid and mucopurulent serous nasal and ocular discharge is observed. Cerebrocortical symptoms include behaviors such as teeth grinding, muscle tremors, circling, blindness, incoordination, pressing the head against objects, nystagmus and seizures. Some cattle may remain lying down and unable to get up. Aggression is a rare clinical symptom. Non-specific symptoms include dehydration, weight loss, hard hair, fever, abdominal pain, anorexia, tachycardia and tachypnea. Some affected individuals may develop complications from inpatient treatment, such as bacterial bronchopneumonia (1).

The course of the disease caused by BoHV-1 is influenced by factors such as virus-specific virulence properties, infected tissue type, presence of secondary bacterial infections, host age and resistance factors. Clinical signs of BoHV-1 in cattle usually include fever, apathy, cough, persistently increased respiratory rate and anorexia. In adult dairy cows, there is a severe decline in milk yield. Primary infection occurs in the turbinates of the nose and trachea, while mucopurulent discharge from the nostrils and eyes is associated with pustular lesions of the nasal mucosa and conjunctivitis (3). BoHV-5 meningoencephalitis usually affects cattle as young as 18 months, but older animals can also be affected. Clinical symptoms of the disease include tremors, rotation, incoordination, depression, loss of visual, hearing or skin reflexes, blindness, mandibular trismus, bruxism, nystagmus, opisthotonos, paresis, permanent recumbency, pedaling movements, tetany, convulsions. BoHV-5 meningoencephalitis is characterized by low morbidity and high mortality. Death can occur in 4-15 days, along with clinical symptoms. (15).

Diagnosis

Current diagnostic methods for BoHV-1 infection include virus neutralization test (VNT), serological tests such as enzyme-linked immunosorbent assay (ELISA), virus isolation, detection of viral DNA and antigens. Madin Darby Bovine Kidney (MDBK) cell line has been successfully used for virus isolation (9).

Purification, amplification and detection of DNA is expensive and time-consuming. PCR testing is a rapid method for the diagnosis and/or typing. However, viral DNA detection techniques such as PCR and real-time PCR require specialized instruments and trained personnel. Therefore, they are not suitable for searching for viruses in large numbers of samples.

BoHV-1 or BoHV-5-specific herpesviral differentiation can be done with a PCR test directed against the glycoprotein C (gC) region. PCR detection of the glycoprotein B (gB) gene region confirms herpesviral infection but does not distinguish between species. In cases of neurological disease, serological methods are of little use as cattle are often dead or lethargic at the time of sample selection. Furthermore, this serological method is expensive and requires high-quality antisera as it is severely affected by improper sampling and autolysis. Immunohistochemistry (IHC) can be used to diagnose BoHV infection routinely. However, IHC is unreliable for diagnostic confirmation as immunolabelling is often inconsistent in diagnostic cases. These methods cannot perform rapid detection of clinical samples. Immunochromatography assays (ICAs) are sensitive, specific, rapid, easy to perform, and accurate diagnostics, which are next-generation detection technologies for detecting and controlling bovine diseases. ICAs have been widely applied in clinical diagnosis, food chemistry and environmental monitoring (1,16,17). Clinical signs and necropsy findings are important for the diagnosis of BHM. As a differential diagnosis, diseases such as polioencephalomalacia and rabies, which affect the CNS of cattle with neurological, should be considered. The hallmark of BHM that distinguishes it from other non-viral cerebral cortical diseases, such as polyencephalomalacia, lead poisoning, salt toxicity and vitamin A deficiency, is the absence of blindness in BHM. (14,15).

Treatment

Better identification of infectious disease prevention and effective treatment strategies is based on a thorough understanding of the replicative cycle of the pathogen. As BoHV-1 is a latent virus that remains in organisms for life, it is important to understand the entry route and develop ways to intervene. There is no specific or effective treatment for cattle in cases of BHM. Treatments for BHM are supportive (1,18). Antiviral research is continuous, and its efficacy is being investigated. Although it is known that non-toxic antiviral agents are not available for BoHV-1 infection, the use of non-toxic zinc oxide (ZnONPs), silver nanoparticles (AgNPs) and flavonoid derivatives are also being investigated (19,20). Plant and fungal extracts are of great interest for developing new antiviral drugs. More specifically, peptides derived from a strain of *Scytalidium sp*., macrolides derived from an unidentified fungus belonging to the Pleosporales, and lactones derived from a strain of *Aspergillus terreus* have shown inhibitory activity against herpesviruses (21). To date, a potential antiviral effect against BoHV-1 is due to traditional synthetic drugs (acyclovir, fenbendazole, famciclovir, ivermectin) administered alone or in combination with natural agents. Few medicinal compounds without toxicity have been identified to treat BoHV-1 infection. Examples include polyphenols, which are known to have anti-herpesvirus activity. Polyphenols and flavonoids have been shown to have in vitro antiviral activity in MDBK cells, and *Thymus capitata*, a plant rich in these substances, provides antiviral activity by interfering with the early stages of viral adsorption and replication and inhibiting viral replication. Another substance that shows a strong antiviral effect against virus replication is kaempferol. Genistein, a soy isoflavone, inhibits BoHV-1 replication; curcumin, a component of the spice turmeric, inhibits the entry of BoHV-1 into MDBK cells. (19).

Although antiviral studies on BoHV-5 are minimal, the activity of three antiherpes drugs (acyclovir, ganciclovir and foscarnet) was tested in vitro using plaque reduction assay and it was revealed that foscarnet might be effective against herpesviral infections. (22).

In conclusion, various antiviral agents are being investigated to treat BoHV-1 infections in BHM cases. Investigation of the efficacy of these agents against BoHV-5 and the development of new treatment approaches may provide new literature on specific antiviral treatment options for BoHV-5 because there is limited literature on the treatment of BoHV-5.

Prevention

In endemic areas, control and prophylactic measures are implemented to reduce economic losses caused by respiratory, reproductive and neurological diseases. These are determined using serology to determine whether infection is present in the herd or in individuals to be included in the herd. Potentially stressful situations should be minimized and affected individuals should be isolated in cases of clinical illness to detect the disease early, prevent its spread and develop control strategies. In endemically infected herds, high immunity levels also provide adequate protection against disease. In particular, genetically modified vaccines produce antibodies that can be distinguished from those produced by natural infection, giving them an advantage over conventional vaccines (1).

Commercial BoHV-1 vaccines can be classified as modified

live (MLV) or inactivated. MLV was developed on cell cultures and evokes a high humoral and cellular immune response due to attenuated virus replication. Existing MLVs establish latency and can periodically reactivate from latency, allowing the virus to spread and infect pregnant cows and cause abortions. MLV vaccines have been reported to be pathologic in calves whose immune systems are not fully developed because they are immunosuppressive. Inactivated vaccines, which consist of viruses inactivated by chemical processes, usually contain all viral particles. The effectiveness of these vaccines depends on establishing a protective neutralizing antibody titer, which requires multiple vaccinations.

Furthermore, inactivated vaccines do not consistently induce cellular immune responses. Marker vaccines are vaccines prepared by removing virulence-related genes from the virus genome. These vaccines can distinguish between vaccinated animals and animals infected with the field strain. Two types of commercial marker vaccines are currently available. The first involves the deletion of the glycoprotein E (gE) gene. The second type involves deleting the gE and the viral thymidine kinase (TK) gene. The gE gene encodes a protein required for anterograde transport from the TG to the ocular surfaces and nasal cavities. Therefore, if a gE marker virus establishes latency, reactivation from latency should not occur easily. The viral TK gene encodes a protein that phosphorylates thymidine and plays an important role in viral replication in non-dividing cells. Although deleting TK in the context of the gE gene further reduces the chance of reactivation from the latent stage, a thymidine kinase BoHV-1 mutant has been reported to reactivate from the latent stage and cause abortions. Therefore, mutating the viral TK gene alone is insufficient to produce a safe and effective BoHV-1 MLV (23).

Current vaccines used in BoHV-1 or BoHV-5 infections can reduce the clinical symptoms of the disease but cannot routinely prevent its latency. Another study reported that calves fed colostrum were protected against BoHV-1 and BoHV-5 encephalitis (14).

PSEUDORABIES VIRUS-PRV (AUJESZKY DISEASE)

Etiology, epidemiology and pathogenesis

PRV is also named Aujeszky disease virus or Suid alphaherpesvirus 1 (SuHV-1). PRV belongs to the *Orthoherpesviridae* family, subfamily *Alphaherpesvirinae*, genus *Varicellovirus*. It contains 143 kb of double-stranded, enveloped linear DNA. PRV can encode more than 70 proteins and has an approximately 74% GC content (24-26). Tegument proteins between the capsid and envelope provide various functions during virus entry, replication and exit. Glycoproteins enable the virus to attach to host cells, fuse to cell membranes, and enter the cell (27). Like other members of the Varicellovirus genus, PRV is neurotropic and can cause latent infection in the peripheral nervous system (28). Genetically, the PRV strains prevalent worldwide are divided into two genotypes, and the majority of PRV strains in China belong to genotype II (29). This genotype can be further divided into classical and variant strains (30).

A Hungarian veterinarian first documented PRV as the causative agent of Aujeszky's disease in 1902. Wild boars and pigs are the primary natural hosts of PRV (31). Neurological disorders in newborn piglets and reproductive problems in sows can be observed after infection (28). Firstly, respiratory symptoms, fetal death, abortion in pregnant sows, or both may occur in older pigs. In piglets and more susceptible species, PRV infection is usually fatal due to CNS disorders (25). Although pigs are known to be the only reservoir of PRV, they can infect many animal species, including sheep, cattle, dogs, foxes, tigers, bears, rats, raccoons, panthers, mink, Iberian lynx, wolves, bats, and cats. In addition, the zoonotic potential of PRV infection is also a threat to public health (31). PRV infection can cause retinal vasculitis, endophthalmitis and encephalitis in humans (25,26).

PRV infection was first described as 'mad itch' in cattle in America in 1813 (28). PRV infection is enzootic and widespread in Eurasian wild boars. As wild boar populations expand their range, the risk of disease transmission increases, which may affect the health of humans, domestic pigs, and wildlife conservation. Characterization of PRV from wild boars helps understand population diversity and can trace back the infection pathway. In Europe, phylogenetic analysis of partial sequences of the gC gene shows that wild boar isolates can be differentiated into A and B clades. Clade A isolates originate from Austria, France, Germany, Hungary, Italy and Slovakia, while clade B isolates originate from south-western Europe, including Germany, France and Spain. Thus, clades A and B isolates geographically overlap in Central Europe, Germany and France. PRV isolated from the USA was distinct from European isolates and closely related to domestic swine isolates. It may represent a transmission from domestic to feral pigs (31).

PRV infection usually begins with viral replication in epithelial cells of the nasal and oropharyngeal mucosa. It then spreads to the neurons of the peripheral nervous system that innervate the infected epithelium. Viral particles are carried by retrograde transport to the sensory and autonomic peripheral ganglia. It causes a latent infection in this region and infects the host for life. When reactivation occurs, PRV particles multiply by replication. It returns to the mucosal surfaces, where infection begins in an anterograde direction along the sensory nerves. In addition, PRV infection can spread from the primary replication site to other organs of the pregnant host, such as the uterus, by viremia associated with peripheral blood mononuclear cells. Then, secondary replication can occur in the endothelial cells of these organs. As a result of this replication, vasculitis and multifocal thrombosis may occur, leading to pregnancy loss (26).

Although the disease was initially controlled worldwide in 1961 with the gE-negative vaccine Bartha-K61 from Hungary, PRV reemerged. The mutated variant of PRV spread rapidly and the conventional vaccine provided only partial protection against this new variant. It has been highlighted that PRV variant strains may be more virulent to animals and humans than classical strains. In addition, due to the latent persistent infection pattern of PRV, infected animals can become lifelong carriers and latent shedders of the virus (26).

Cattle are more resistant to PRV than other domestic species and can be infected by direct or indirect contact with pigs. Transmission is mainly airborne but can also occur through skin or mucous membrane injuries. In rare cases, rodents or biting flies can also cause infection. Due to the neurotropic properties of the virus, a small amount of virus production occurs in the fascia at the bite site and reaches the brain via the peripheral nerves. PRV replicates intensively in the brain and causes encephalomyelitis. This situation leads to death within a short time. Although the gastrointestinal tract does not usually play a significant role, infection can occur after ingesting contaminated feed. In cases of close contact, severe itching and death in the hindquarters of cattle due to sniffing and biting by pigs, especially in the perineum, are also significant. Experimental infection of cattle is possible through intranasal, intramuscular, subcutaneous, intravenous, and intradermal routes. Since transmission from cattle to cattle does not occur, they appear to be the final host (32,33).

Sheep and goats infected with PRV usually do not shed. Infection usually results in CNS disease, often severe itching and death. Although the natural incidence of infection in sheep is low, mortality rates due to PRV can be as high as 60% and cause

significant losses to sheep flocks. The source of infection in sheep is always infected pigs. Sheep and goats are most commonly infected by aerosol but are also highly susceptible to percutaneous infection. Small ruminants shed very little virus and are not transmitted between each other as in cattle. However, lambs can shed as much virus as piglets through nasal secretions just before and during the onset of clinical signs. Horizontal transmission of PRV from lambs to pigs has been demonstrated. Generally, goats are more susceptible than sheep and clinical signs are more pronounced (30,32).

Clinical signs

The disease is always fatal in all hosts except pigs. Excessive itching is characterized by a mortality rate approaching 100% and severe clinical signs in the CNS (32).

PRV in cattle begins with a fluctuating fever with a temperature of up to 42°C until shortly before death. Characteristic signs of PRV are behavioral disturbances and CNS signs (severe itching, convulsive restlessness followed by paralysis). Other symptoms include incoordination, unsteady gait, circling, howling, drooling, jaw paralysis, grunting, self-mutilation (auto-mutilation), head banging against the wall, and floppy ears with friction at the base of the ear. Initially, there were only jerky twitches of individual muscle groups in the head, neck, and back. The animals lick or gnaw at various body parts, most commonly the knee joint area, the inside of the hind legs, the udder or the base of the tail and the perineum. Death occurs 6-48 hours after the onset of clinical signs due to paralysis (32,33).

Infection with the PRV has been demonstrated to affect sheep of all age groups, with the resultant clinical signs including degeneration and paralysis of the CNS. This form of CNS paralysis is characterized by paresis, recumbency, pharyngeal paralysis, dyspnoea and rumen atony. The main clinical signs are fever, restlessness and movement disorders. Excessive pruritus, characteristic of cattle, is also seen in sheep. Lambs become recumbent and die acutely. Fever is not always high, may occur early in the disease and is not severe (32). Pathological examination revealed hemorrhagic pneumonia, hemorrhagic lymphadenopathy syndrome, cerebral hyperemia and hemorrhages in dead goats (29).

Diagnosis

For definitive diagnosis, anamnesis, clinical findings, and hematologic and biochemical parameters should be evaluated and supported by laboratory diagnosis. Various direct and indirect tests are used for laboratory diagnosis (immunofluorescence, immunoperoxidase, IHC, PCR, VNT, latex agglutination, or ELISA). The most commonly used diagnostic methods are immunofluorescence and immunoperoxidase. Virus isolation is difficult and time-consuming and requires experienced personnel and equipment. The immunoperoxidase test is the most preferred method (33).

Clinical diagnosis in cattle, sheep and goats is based on clinical signs and history of direct contact with pigs. In cases where pruritus is not prominent, it is difficult to differentiate from other causes of viral encephalitis. Severe neurological lesions are not usually seen. Microscopically, diffuse non-suppurative inflammation with perivascular congestion and focal neuronal necrosis observed in the brain and spinal cord. Intranuclear inclusion bodies are rarely seen. Serological diagnosis in cattle, sheep, or goats is ineffective because most infected animals die before antibodies can be detected in serum. In surviving and latently infected adult animals, diagnosis can be made by VN or antibody ELISA tests. Serological tests form the basis of most testing and culling programs for pseudorabies eradication. False-positive results are rare (14).

Treatment

No effective treatment for PRV in cattle, sheep and goats has been reported. In latently persistently infected animals, reactivation and shedding of the virus often occur after a stressor. Stress factors include micro-infection, transport, poor husbandry, parturition and treatment with immunosuppressive agents (e.g., corticosteroids) (34). There are currently no drugs available for PRV infection, and vaccination remains the main method of disease prevention. The combination of acyclovir and ribavirin has been shown to inhibit PRV replication in vitro. In addition, several synthetic diaminopurine-based acyclic nucleoside phosphonate analogs have been reported to have anti-PRV activity. Natural plant extracts, including kumazasa extract, *Duabanga grandiflora* leaf extract and *Houttuynia cordata,* can suppress PRV replication in vitro at high concentrations of isobavachalcone and resveratrol (35).

Prevention

Vaccines against PRV have been developed primarily to prevent disease caused by wild-type virus infection. The vaccine is intended to activate the body's natural defense mechanisms and develop immunity against disease or infection caused by field viruses. The use of inactivated and attenuated live vaccines to control PRV is widespread. Simultaneously, more effective and safer recombinant vaccines are being developed (36,37).

Although vaccines can effectively control the spread of PRV, they do not protect against the latency of the wild-type virus. Since 2011, outbreaks of new PRV variants have been reported in pigs vaccinated with the Bartha-K61 strain. The variability of viral strains and the inability to safely use attenuated vaccines pose a serious threat to the pig industry (37).

This disease causes significant economic losses to the pig industry each year, and vaccination with classical live attenuated PRV or inactivated PRV vaccines has been one of the main methods used to prevent and control the disease. Many European countries, such as New Zealand and the United States of America, have implemented strict national eradication programs based on compulsory vaccination, culling positive pigs, and establishing PRV-free pig herds (25).

MALIGNANT CATARRHAL FEVER-MCF (CORIZA GANGRENOZA BOVUM-CGB)

Etiology, epidemiology, and pathogenesis

MCF or Coriza Gangrenoza Bovum (CGB) affects a wide range of susceptible hosts, including hoofed animals from the order *Artiodactyla*, such as cattle, water buffalo, bison, deer, antelope, elk, and reindeer. It is a sporadic but often fatal disease in ruminants (4,38). Rarely pigs may also be affected, and experimental infections have been demonstrated in rabbits, guinea pigs, and hamsters. The causative agents of MCF are herpesviruses from the genus *Macavirus*, within the subfamily *Gammaherpesvirinae*, of which at least six are known to be pathogenic under natural conditions. Ovine gammaherpesvirus 2 (OvHV-2) is the most widespread globally. MCF is endemic in sheep and can cause sheep-associated MCF in various ruminant and pig species. Alcelaphine gammaherpesvirus 1 (AlHV-1) is endemic in antelope and is responsible for antelope-associated MCF outbreaks in domestic cattle in sub-Saharan Africa. Caprine gammaherpesvirus 2 (CpHV-2) is endemic in domestic goats and has been reported to cause MCF in particular deer species and water buffalo. White-tailed deer and red deer are susceptible to Malignant Catarrhal Fever Virus (MCFV-WTD - malignant catarrhal fever virus–white-tailed deer), which domestic goats carry. Ibex MCF virus (Ibex-

MCFV) has been identified in the bongo antelope and anoa, a buffalo species. The virus is known to be carried by the Nubian ibex. Alcelaphine herpesvirus 2 (AlHV-2), carried by the hartebeest and topi antelopes, has been reported to cause MCF in Barbary red deer and, experimentally, in bison (4).

MCFVs are both antigenically and genetically related. The presence of the 15-A antigenic peptide of gB and a high degree of homology in the DNA polymerase gene sequence characterize them. Simultaneous infections with multiple MCFV strains in a single host are possible (39). While these viruses typically cause subclinical infections in their natural hosts, they can lead to clinical disease in susceptible species such as cattle, deer, bison, and pigs (38).

MCFVs are present wherever clinically susceptible hosts are close to their wildlife reservoirs. The earliest described forms of MCF are the European and African forms. The African form (associated with AlHV-2) has been primarily reported from sub-Saharan African countries such as Kenya, Tanzania, and South Africa, where antelopes represent a significant component of the native wildlife. Blue and black wildebeests (Connochaetes spp.) serve as carriers and reservoir hosts for AlHV-1. The annual migration of these antelopes through the Maasai Mara and Serengeti regions threatens cattle populations in these areas. Approximately 10% of cattle herds in Kenya are lost annually due to the African form of MCF. Outside of Africa, OvHV-2 is the primary causative agent of MCF in domesticated animals, with domestic sheep acting as the primary reservoir hosts. The European form, or sheep-associated MCF caused by OvHV-2, is most commonly observed in domestic livestock, captive ruminants, and wildlife populations outside Africa. The disease occurs sporadically but is widely distributed across Europe, North and South America, the Middle East, Asia, Africa, and New Zealand. The American bison (Bison bison) is approximately 1,000 times more susceptible to clinical disease caused by OvHV-2 than domestic cattle (Bos taurus and Bos indicus), which show a high degree of resistance. Water buffalo are also more susceptible to OvHV-2 than cattle. Diseases associated with CpHV-2 have been reported not only in cervids but also in buffalo (38).

MCFV is a lymphoproliferative disease characterized by lymphoid cell accumulation in non-lymphoid organs, vasculitis, and T-lymphocyte hyperplasia in lymphoid tissues. Histological examination reveals necrosis in the respiratory, digestive, and urinary epithelial tissues. This necrosis is considered to be a consequence of systemic vasculitis affecting the brain and blood vessels. Vasculitis is a prominent pathological feature of MCF across all affected species. It is believed to result from immune dysregulation, leading to the accumulation of lymphocytes (4). The complex epidemiology and pathogenesis of MCF contribute to the challenges in fully understanding the disease. Like most gammaherpesviruses, MCFVs can establish latent, persistent infections in lymphoid tissues during the early stages of infection. The incubation period varies across species: approximately 14 days in rabbits, 21–90 days in rodents, and 16–29 days in cattle. Among affected cattle, approximately 95–100% succumb to the disease within 4–7 days after the onset of clinical signs (38).

OvHV-2 is primarily transmitted through direct contact or aerosol from lambs under one year of age. Lambs typically acquire the virus via aerosol exposure from other flock members between 3 and 6 months of age and begin actively shedding the virus between 6 and 9 months. Viral shedding decreases around 10 months and occurs at significantly lower levels in adults than in adolescents. Adult sheep can also become infected with OvHV-2 through natural contact and may intermittently shed large quantities of the virus. Clinically susceptible species usually acquire the virus via inhalation; however, ingesting virus-contaminated secretions through contaminated feed or water may also represent a transmission route. Colostrum and milk samples from infected sheep have tested strongly positive for OvHV-2 DNA, suggesting that mammary secretions may serve as an important source of infection for newborn lambs. High levels of OvHV-2 DNA have also been detected in ram semen, raising the possibility that vertical transmission may play a significant role in disease spread (40).

Clinical signs

MCF is a progressive, lymphoproliferative, and typically fatal disease. The main clinical signs include fever, profuse nasal discharge, ophthalmia, corneal opacity, generalized lymphadenopathy, upper respiratory tract erosions, and gastrointestinal tract leukopenia. Affected animals typically die within days or weeks following the onset of clinical signs. The clinical outcome can vary depending on the species and their level of susceptibility, and symptoms may also be species-specific (39). The disease may manifest in several clinical forms, including peracute, head and eye, alimentary, neurologic, and cutaneous forms. In susceptible Cervidae species, the clinical course is shorter than in cattle, and sudden death can occur. Highly susceptible species often present with the peracute form of the disease. In cattle, MCF generally follows an acute course, with the head and eye form being the most commonly observed. Affected animals may exhibit swelling of limb joints and a significant decrease in milk production. Some animals show neurological symptoms such as hyperesthesia, incoordination, and nystagmus. Approximately 25% of infected cattle may develop the chronic form of the disease, and mortality can reach up to 95%. Severe ocular lesions such as panophthalmitis and hypopyon are commonly observed in deer and bison. Infected animals may also display aggressive and violent behavior. The average time from onset to death is approximately 48 hours in deer, 3 days in bison, and 1 week in cattle (38).

Diagnosis

The diagnosis of MCF is based on clinical signs, histopathological features, and the detection of viral DNA via PCR. Histopathological confirmation includes evidence of vasculitis, lymphoid tissue hyperplasia, and the accumulation of lymphoid cells in non-lymphoid organs such as the brain, kidneys, and liver. A history of exposure to pastures recently grazed by sheep or antelopes often supports the diagnosis. However, the extended incubation period can complicate the clinical presentation. In cattle, the disease manifests sporadically and disseminates slowly within the herd. In conjunction with a history of contact with sheep or antelopes, the characteristic lesions and signs observed frequently serve as sufficient evidence for a presumptive diagnosis.

Nevertheless, the wide range of clinical manifestations may make differential diagnosis challenging, particularly for diseases such as Bovine Viral Diarrhea, Foot-and-Mouth Disease, Lumpy Skin Disease, and Infectious Bovine Rhinotracheitis. Given the prevalence of MCF in regions such as Southern Africa and Northern Europe, differentiation from Bluetongue virus infection is also critical. Both diseases can present with similar clinical signs, including lachrymation, stomatitis, coronitis, sloughing of the skin on the udder and mouth, and diarrhea. Therefore, laboratory confirmation through diagnostic testing is essential for a definitive diagnosis (38).

Treatment

Although no specific treatment for MCF exists, symptomatic therapies are commonly applied. These include using anti-inflammatory steroids, antibiotics to prevent secondary infections, and supportive fluid therapy. Oxytetracycline, sulfadimidine, procaine penicillin, and ceftiofur sodium can be administered

parenterally to prevent secondary bacterial infections. Supportive treatment may also include the administration of flunixin meglumine and vitamin A (38,40). Although recovery has been observed in some animals following treatment, it remains unclear whether these recoveries can be directly attributed to therapeutic intervention. Despite ongoing research over the past six decades, no effective commercial vaccine is available for AlHV-1. However, a field study using an attenuated AlHV-1 virus vaccine demonstrated a 56% reduction in infection rates in cattle exposed to antelope contact (38).

Prevention

The primary control strategy for MCF is to prevent interaction between susceptible and non-susceptible host species. This situation minimizes the risk of virus transmission from reservoirs and carrier animals to susceptible species (39). There is currently no commercially available effective vaccine. In addition to maintaining species separately, control programs may include preventing lambs from contacting infected sheep before they reach two months of age to produce OvHV-2-free flocks. Only seronegative animals should be introduced into herds. Maintaining the maximum possible separation between sheep and susceptible species is crucial; even in confined environments, a minimum distance of 1,000 meters should be maintained between them (40).

CONCLUSION

Herpesvirus infections pose significant threats to the cattle industry, leading to substantial health issues and economic losses due to their complex etiologies, wide host ranges, and variable clinical outcomes. This review focuses on BoHV-1, BoHV-5, PRV and MCFV as major pathogens affecting the respiratory, nervous and immune systems. The review examines the acute and subacute courses of the pathogens in particular species and the potential progression to peracute and fatal forms. Critically, these viruses can establish latent, persistent infections in ruminants, allowing them to persist for life and transform their hosts into long-term carriers. Their widespread distribution, capacity for latency, the high mutation potential of PRV, and their ability to cross species barriers collectively make control and eradication particularly challenging. Despite considerable progress in diagnostic methods, particularly through the utilization of PCR, serological analyses, virus isolation and histopathology, there is an urgent requirement to develop rapid, reliable and portable diagnostic tools suitable for field conditions. Treatment remains supportive mainly, as the availability of virus-specific antiviral agents is still limited. As a result, preventive veterinary practices remain paramount in managing these diseases. Vaccination is currently an effective control strategy for BoHV-1; however, the lack of effective and commercially available vaccines for BoHV-5, PRV, and MCFVs remains a significant concern. This underscores the importance of strict herd isolation, minimizing contact with reservoir hosts, and implementing comprehensive biosecurity measures. Future studies should focus on understanding virus-host interactions, preventing interspecies transmission, and developing next-generation vaccines, particularly for MCFVs and BoHV-5. In this regard, interdisciplinary approaches are promising for enabling more sustainable livestock health management under field and laboratory conditions.

DECLARATIONS

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Funding Support: There is no any funding support.

Competing Interests: The authors declare that there is no competing of interest regarding the publication of this article.

Declaration of Generative Artificial Intelligence: The authors of the current study declare that the article and/or tables and figures were not written/created by AI and AI-assisted technologies.

Authors' Contributions: All authors contributed to this present work: FMY, HBY, GA, HA and MÖT designed, drafted, read and approved the final manuscript.

REFERENCES

1. Santos BS, Lemos RAA, Rech RR, Barros CSL, Rissi DR: Bovine herpesviral meningoencephalitis: Large case study and literature review. J Vet Diagn Invest, 37(3), 417–428, 2025. DOI: 10.1177/10406387251319804
2. Can-Sahna K, Abayli H, Ilgin M, Aksoy M: Investigation of some neuroinfectious viral agents in Turkish cattle: First detection and molecular characterization of bovine herpesvirus type 5 (BoHV5). Pak Vet J, 44(3), 896–902, 2024. DOI: 10.29261/pakvetj/2024.211
3. Ostler JB, Jones C: The bovine herpesvirus 1 latency-reactivation cycle, a chronic problem in the cattle industry. Viruses, 15(2), 552, 2023. DOI: 10.3390/v15020552
4. Saura-Martinez H, Al-Saadi M, Stewart JP, Kipar A: Sheep-associated malignant catarrhal fever: Role of latent virus and macrophages in vasculitis. Vet Pathol, 58(2), 332–345, 2020. DOI: 10.1177/0300985820978310
5. Kumar N, Chander Y, Riyesh T, Khandelwal N, Kumar R, Kumar H, Tripathi BN, Barua S: Isolation and characterization of bovine herpes virus 5 (BoHV5) from cattle in India. PloS One, 15(4), e0232093, 2020. DOI: 10.1371/journal.pone.0232093
6. Marin M, Burucúa M, Rensetti D, Rosales JJ, Odeón A, Pérez S: Distinctive features of bovine alphaherpesvirus types 1 and 5 and the virus-host interactions that might influence clinical outcomes. Arch Virol, 165, 285–301,2020. DOI: 10.1007/s00705-019-04494-5
7. International Committee on Taxonomy of Viruses. 2025. ICTV. https://ictv.global/
8. Johnson LAY, McGavin MD, Simmons GC: Diseases of the bovine central nervous system in south east Queensland. Aust Vet J, 38(10), 397–403, 1962. DOI: 10.1111/j.1751-0813.1962.tb04013.x
9. Oberto F, Carella E, Caruso C, Acutis PL, Lelli D, Bertolotti L, Masoero L, Peletto S: A qualitative PCR assay for the discrimination of bubaline herpesvirus 1, bovine herpesvirus 1 and bovine herpesvirus 5. Microorganisms, 11(3), 577, 2023. DOI: 10.3390/microorganisms11030577
10. Del Médico Zajac MP, Ladelfa MF, Kotsias F, Muylkens B, Thiry J, Thiry E, Romera SA: Biology of bovine herpesvirus 5. Vet J, 184(2), 138–145, 2010. DOI: 10.1016/j.tvjl.2009.03.035
11. Verma A, Kamboç H, Handelwal N, Kumar R, Riyeş T, Kumar N: Genome sequencing of bovine herpesvirus 5 (BoHV-5) isolated from India. Microbiol Resour Announc, 14, e00950-24, 2024. DOI: 10.1128/mra.00950-24
12. Raaperi K, Orro T, Viltrop A: Epidemiology and control of bovine herpesvirus 1 infection in Europe. Vet J, 201(3), 249–256, 2014. DOI: 10.1016/j.tvjl.2014.05.040
13. El-Mayet F, Jones C: Stress can induce bovine alpha-herpesvirus 1 (BoHV-1) reactivation from latency. Viruses, 16(11), 1675, 2024. DOI: 10.3390/v16111675
14. Callan RJ, Van Metre DC: Viral diseases of the ruminant nervous system. Vet Clin North Am Food Anim Pract, 20(2), 327–vii, 2004. DOI: 10.1016/j.cvfa.2004.02.001
15. Pinheiro IAB, Dias BP, Ferreira JM, Dos Santos AJF, Moron SE, Silva GMDL, de Lima LBD, de Cordova FM: Bovine herpesvirus meningoencephalitis in the State of Tocantins, Brazil. Braz J Vet Med, 46, e004023, 2024. DOI: 10.29374/2527-2179.bjvm004023
16. Jiang L, Zhang G, Wang P, Niu X, Liu Q, Zhang S, Gao W, Li Y: Simultaneous detection of bovine viral diarrhea virus (BVDV) and bovine herpesvirus 1 (BoHV-1) using recombinase polymerase amplification. Sci Rep, 14, 10169, 2024. DOI: 10.1038/s41598-024-56869-7
17. Liu W, Zhang K, Cheng J, Yu S, Cheng C, Jiang B, Zhou L, Li Y: Development and evaluation of a time-resolved fluorescence labelled immunochromatographic strip assay for rapid and quantitative detection of bovine herpesvirus 1. Front Microbiol, 15, 1371849, 2024. DOI: 10.3389/fmicb.2024.1371849
18. Pastenkos G, Lee B, Pritchard SM, Nicola AV: Bovine herpesvirus 1 entry by a low-pH endosomal pathway. Virol J, 92, e00839-18, 2018. DOI: 10.1128/jvi.00839-18
19. Cerracchio C, Amoroso MG, Piccolo M, Ferraro MG, Nocera FP, De

Martino L, Serra F, Irace C, Tenore GC, Novellino E, Santamaria R, Fiorito F: Antiviral activity of Taurisolo® during bovine alphaherpesvirus 1 infection. Virus Res, 336, 199217, 2023. DOI: 10.1016/j.virusres.2023.199217
20. Zeedan GS, El-Razik KA, Allam AM, Abdalhamed AM, Zeina HA: Evaluations of potential antiviral effects of green zinc oxide and silver nanoparticles against bovine herpesvirus-1. Am J Anim Vet Sci, 8(4), 433–443, 2020. DOI: 10.17582/journal.aavs/2020/8.4.433.443
21. Fiorito F, Cerracchio C, Salvatore MM, Serra F, Pucciarelli A, Amoroso MG, Nicoletti R, Andolfi A: Antiviral property of the fungal metabolite 3-O-Methylfunicone in bovine herpesvirus 1 infection. Microorganisms, 10(1), 188, 2022. DOI: 10.3390/microorganisms10010188
22. Dezengrini R, da Silva SC, Weiss M, Kreutz LC, Weiblen R, Flores EF: Activity of three antiviral drugs against bovine herpesviruses 1, 2 and 5 in cell culture. Pesq Vet Bras, 29(1), 19–24, 2009. DOI: 10.1590/S0100-736X2009000100004
23. Righi C, Franzoni G, Feliziani F, Jones C, Petrini S: The cell-mediated immune response against bovine alphaherpesvirus 1 (BoHV-1) infection and vaccination. Vaccines, 11(4), 785, 2023. DOI: 10.3390/vaccines11040785
24. Bo Z, Li X: A review of pseudorabies virus variants: Genomics, vaccination, transmission, and zoonotic potential. Viruses, 14(5), 1003, 2022. DOI: 10.3390/v14051003
25. Ye N, Feng W, Fu T, Tang D, Zeng Z, Wang B: Membrane fusion, potential threats, and natural antiviral drugs of pseudorabies virus. Vet Res, 54, 39, 2023. DOI: 10.1186/s13567-023-01171-z
26. Zheng HH, Fu PF, Chen HY, Wang ZY: Pseudorabies virus: From pathogenesis to prevention strategies. Viruses, 14(8), 1638, 2022. DOI: 10.3390/v14081638
27. Chen X, Yu Z: Insight into the interaction mechanism of pseudorabies virus infection. Biology, 13(12), 1013, 2024. DOI: 10.3390/biology13121013
28. Liu Q, Kuang Y, Li Y, Guo H, Zhou C, Guo S, Tan C, Wu B, Chen H, Wang X: The epidemiology and variation in pseudorabies virus: A continuing challenge to pigs and humans. Viruses, 14(7), 1463, 2022. DOI: 10.3390/v14071463
29. Tan Lei, Xu K, Yang S, Wang W, Lin G, Yang L, Yao J, Wang A: First report of variant pseudorabies virus infection in goats in China: a neglected infectious disease to ruminants. Authorea. 2024. DOI: 10.22541/au.170664805.56815073/v1
30. Duan Y, Liu N, Tan L, Gao L, Zhu G, Tao Z, Liu B, Wang A, Yao J: Isolation and biological characterization of a variant pseudorabies virus strain from goats in Yunnan Province, China. Vet Res Commun 49, 149, 2025. DOI: 10.1007/s11259-025-10703-1
31. Liu A, Xue T, Zhao X, Zou J, Pu H, Hu X, Tian Z: Pseudorabies virus associations in wild animals: Review of potential reservoirs for cross-host transmission. Viruses, 14(10), 2254, 2022. DOI: 10.3390/v14102254
32. Sehl J, Teifke JP: Comparative pathology of pseudorabies in different naturally and experimentally infected species—A review. Pathogens, 9(8), 633, 2020. DOI: 10.3390/pathogens9080633
33. Yıldırım S, Özkan C, Yener Z, Cetin M, Kozat S: Immunohistochemical Diagnosis of Pseudorabies (Aujeszky's Disease) in a Cow in Van, Turkey. Kafkas Univ Vet Fak Derg, 23(1), 173-176, 2017. DOI: 10.9775/kvfd.2016.16071
34. Pomeranz LE, Reynolds AE, Hengartner CJ: Molecular Biology of Pseudorabies Virus: Impact on Neurovirology and Veterinary Medicine. Microbiol Mol Biol Rev69, 2005. DOI: 10.1128/mmbr.69.3.462-500.2005
35. Wang G, Chen R, Huang P, Hong J, Cao J, Wu Q, Zheng W, Lin L, Han Q, Chen Y, Xia N: Adefovir dipivoxil efficiently inhibits the proliferation of pseudorabies virus in vitro and in vivo. Antiviral Res, 186, 105014, 2021. DOI: 10.1016/j.antiviral.2021.105014
36. Freuling CM, Müller TF, Mettenleiter TC: Vaccines against pseudorabies virus (PrV). Vet Mic, 206, 3–9, 2017. DOI: 10.1016/j.vetmic.2016.11.019
37. Li L, Wang R, Hu H, Chen X, Yin Z, Liang X, He C, Yin L, Ye G, Zou Y, Yue G, Tang H, Jia R, Song X: The antiviral activity of kaempferol against pseudorabies virus in mice. BMC Vet Res, 17, 247, 2021. DOI: 10.1186/s12917-021-02953-3
38. Sharma B, Parul S, Basak G, Mishra R: Malignant catarrhal fever (MCF): An emerging threat. J Entomol Zool Stud, 7(3), 26–32, 2019.
39. Bianchessi L, Rocchi MS, Maley M, Piccinini R, Turin L: Molecular tools to identify and characterize malignant catarrhal fever viruses (MCFV) of ruminants and captive Artiodactyla. Viruses, 14(12), 2697, 2022. DOI: 10.3390/v14122697
40. Meravi P, Tiwari A, Singh B, Mourya A, Baghel PRS: Emerging threats of sheep-associated malignant catarrhal fever in India: A review. J Pharmacogn Phytochem, 8(5), 844–848, 2019.