Andrzej Korpacki[1], Arkadiusz Szydełko[2], Daniel Strub[2], Bartosz Urbanek[2], Aleksandra Kuzan[2], Agnieszka Bronowicka-Szydełko[1]

[1]Wroclaw Medical University, Wroclaw, Poland
[2]Wroclaw University of Science and Technology, Wroclaw, Poland

Prevention and methods of mitigating transmission of FIV, FeLV and SARS-CoV-2 from cats to humans

Corresponding author:
Aleksandra Kuzan, PhD
Wrocław University of Science and Technology,
50–370, Wroclaw, Poland
e-mail: aleksandra.kuzan@pwr.edu.pl

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ABSTRACT

The Covid-19 pandemic has shown how much of a global threat animal-borne viruses pose to human health and life. Despite increased hygiene practices, interspecies transmission of viruses can still occur. Pathogens undergo mutations, which makes it difficult to develop effective vaccines and targeted therapies. The tendency of viruses to mutate, their virulence and the ease of spreading in populations make it necessary to develop methods for neutralization and drugs against these pathogens.

The paper presents an overview of substances effective in disinfecting surfaces contaminated with viruses transmitted by cats, such as feline immunodeficiency virus (FIV), feline leukaemia virus (FeLV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV -2) that may be transmitted by these animals. Ethanol, propanol, isopropanol, octenisept 4-phenoxyethanol, IV ammonium salts and mixtures of these substances effectively eliminate feline viruses. The article also discusses drugs used to treat infections and draws attention to misconceptions spread among cat owners.

Keywords: disinfection, COVID-19, FeLV, FIV, SARS-CoV-2

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Introduction

The Feline Immunodeficiency Virus (FIV) and Feline Leukaemia Virus (FeLV) are among the most common pathogens in the cat population, with prevalence ranging from a few per cent to as high as several dozen per cent depending on the region [1]. Due to the potentially life-threatening nature of infections caused by these viruses, they raise concerns among cat owners. Although FIV shares significant similarities with its human counterpart, the Human Immunodeficiency Virus (HIV), there have been no documented cases of FIV transmission from cats to humans, unlike the case of the SARS-CoV-2 virus. While there is no evidence yet to suggest that SARS-CoV-2 poses a threat to cats similar to FIV or FeLV, these animals can serve as reservoirs for the virus [2]. Some literature sources also hypothesize that SARS-CoV-2 can be transmitted from animals to humans [3]. In light of the threats posed by these feline viruses, it is necessary to develop methods to mitigate their presence in the environment through appropriate and effective disinfection. This is crucial not only for managing local infection outbreaks that may occur in shelters or veterinary clinics but also for protecting cat owners in the face of potential interspecies transmission.

The Feline Immunodeficiency Virus (FIV) causes infections that pose a threat not only to domestic cats but also to other species within the Felidae family. This pathogen belongs to the same retrovirus family as the human immunodeficiency virus (HIV). FIV attacks the host's immune system, rendering it susceptible to opportunistic infections, which are responsible for most of the observed symptoms during viral disease. The virus is mainly transmitted through direct contact between cats, typically through biting wounds inflicted by an infected carrier on a healthy animal. Transmission can also occur through the placenta or during mating. As a result of infection, a cat becomes a lifelong carrier of the virus, although this does not necessarily mean that symptoms will appear — the animal can remain asymptomatic throughout the carrier state. The most common symptoms occur in cats experiencing weight loss, dental problems, or recurrent infections. Infected FIV cats have an increased risk of developing tumours [3].

The FIV virus has a size ranging from 100 to 125 nm and exhibits a characteristic structure of retroviruses. Its lipid envelope contains two major glycoproteins: the surface glycoprotein (SU) and the transmembrane glycoprotein (TM). The surface glycoprotein (gp95 or gp120) is responsible for binding to host cell receptors, while the transmembrane glycoprotein (gp40) enables the fusion process between the virus and the host cell membranes. The capsid protein (p24) forms a protective protein shell around two single-stranded viral RNA molecules and other components. It plays a crucial role in maintaining the structural integrity of the virion. The matrix protein (p15) is located beneath the viral envelope. It assists in connecting the envelope glycoproteins to the capsid and plays a role in virus assembly and release. The FIV virus contains an enzyme called reverse transcriptase, which consists of two subunits: an RNA-dependent DNA polymerase (p65) and an RNase H (p14). This enzyme is responsible for converting viral RNA into DNA, which is then integrated into the host cell genome using integrase [5] (Fig. 1).

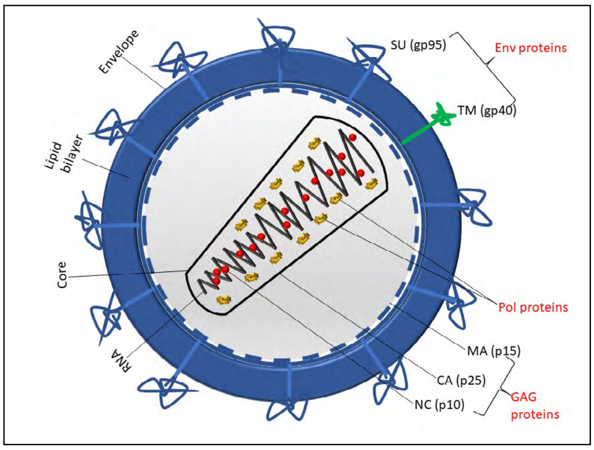

Figure 1. FIV structure consists of an envelope, lipid bilayer, core and RNA. To major proteins belong: gags — (p15), (p25), (p10) — a group of specific antigens; pol — (p14), (p65), (p51) — proteinase; env — (gp95), (gp40) — envelope proteins [5]; SU — surface glycoprotein; TM — transmembrane glycoprotein

The Feline Leukaemia Virus (FeLV) belongs to the gamma retroviruses and causes an infection that can lead to serious health consequences in cats. FeLV is primarily transmitted through direct contact of a cat with the infected saliva, urine, faeces, or nasal secretions of infected cats. It can also be transmitted from an infected mother to her kittens during pregnancy or lactation. Upon infection, the virus enters the bloodstream, attacking cells of the haematopoietic system, including lymphocytes, which are crucial in fighting various viruses. FeLV weakens the immune system, making cats more susceptible to various infections.

FeLV infection can lead to different outcomes. In some cats, the virus is completely cleared, resulting in a regressive infection. Other cats may become persistent carriers, periodically shedding the virus and potentially infecting other cats. Unfortunately, in some cats, FeLV infection leads to the development of serious haematologic and/or immunologic diseases, such as anaemia, immunosuppression accompanied by secondary infections, as well as blood cancers [3].

The FeLV virion consists of several key components that are essential for its structure and function. The FeLV virus has a lipid envelope that contains two major glycoproteins. The surface glycoprotein (gp70) is responsible for the virus binding to receptors on host cells, while the transmembrane glycoprotein (TM) plays a role in the fusion process between the virus and the host cell. The envelope protein p15E is involved in the interaction with cell receptors. The FeLV also contains a capsid, which protects the viral genome. The capsid is formed by the capsid protein (p27) and surrounds the viral genome. The FeLV genome consists of two single-stranded RNA molecules that contain the genetic information necessary for the replication and assembly of new viruses. The virion also contains reverse transcriptase.

All these components of the FeLV virus act together in the processes of infection, replication, and spread of the virus within the cat's body. Their proper functioning is crucial for the pathogenesis and outcome of FeLV infection [6] (Fig. 2).

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus responsible for the COVID-19 (Coronavirus disease 2019) pandemic. The transmission of the virus primarily occurs among humans, but there is evidence suggesting that cats may also be susceptible to this virus. Cats can become infected with SAR S-CoV-2 through close contact with infected humans or other infected cats. Studies have shown that the virus can replicate in the respiratory system of cats, causing mild respiratory symptoms. Although cats can become infected with this virus, the risk of transmission from cats to humans appears to be low and is still a subject of debate. There

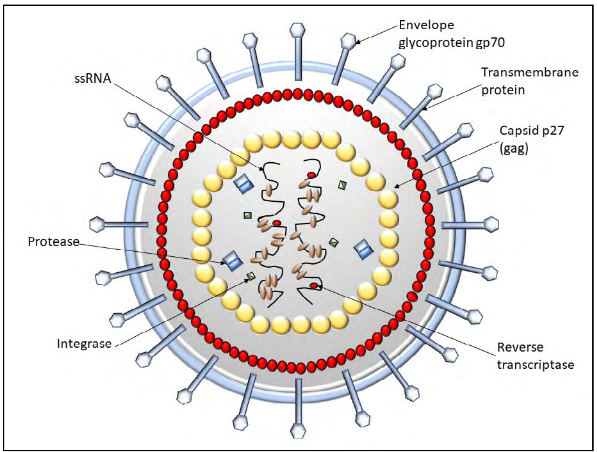

Figure 2. FeLV structure. Virus molecule consists of membranes including envelope glycoprotein gp70, transmembrane protein and capsid including capsid p27 (gag) protease integrase, reverse transcriptase and ss RNA [7]

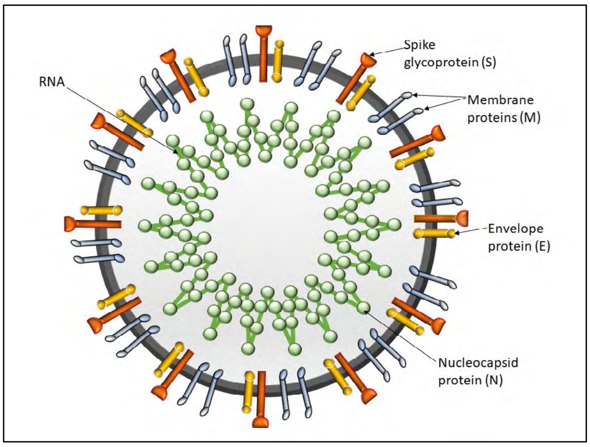

Figure 3. General SARS-CoV-2 structure: The virus contains a membrane with Membrane (M) proteins, Spike (S) proteins and Envelope (E) proteins. Inside there is an RNA molecule with nucleocapsid (N) proteins [10]

have been a few reported cases of transmission from humans to cats, usually from owners infected with the SARS-CoV-2 virus [8].

SARS-CoV-2 belongs to the coronavirus family, and its characteristic feature is the longest single-stranded RNA molecule among viruses. The virion consists of four main structural proteins visible in the diagram: the spike (surface) fusion glycoprotein S, which is responsible for interaction with cell receptors, the envelope protein E involved in virion formation, the membrane protein M, and the nucleocapsid protein N, which serves a protective function for the large RNA molecule [9]. The structure of SARS-CoV-2 is shown in Figure 3.

FIV, FeLV and SARS-CoV-2

According to available knowledge, feline RNA viruses such as FIV or FeLV are capable of surviving on dry surfaces for a short period, probably only a few minutes, although there is not enough precise data confirming this hypothesis. This information contradicts the prevailing belief that a home where an FIV or FeLV carrier resided is not suitable for introducing another cat, even after a long time has passed since the infected animal's presence. Guidelines from the American Association of Feline Practitioners (AAFP) indicate that to inactivate the virus and prevent indirect transmission (through bowls, litter boxes), it is sufficient to follow basic hygiene principles and clean surfaces with detergent or another active agent [1, 11, 12]. In contrast to FIV and FeLV, the SARS-CoV-2 virus demonstrates a greater ability to remain active on various surfaces despite the passage of time. The characteristics of active substances against FIV, FeLV, and SARS-CoV-2 viruses are presented in Table 1.

Based on the conducted analysis of active substances effectively eliminating RNA viruses such as FIV, FeLV, and SARS-CoV-2, it can be concluded that the highest efficacy was observed for ethanol, quaternary ammonium compounds (QACs), propanol, and isopropanol.

Ethanol is recommended by the World Health Organization (WHO) at a very high concentration of at least 70%. Although this alcohol shows significant virus reduction (4log10) already at concentrations of 27%, it requires a contact time of up to 3 minutes [21]. Ethanol at a concentration of 40% is sufficient to achieve a > 4log10 reduction of the virus in just 5 seconds [18]. Higher concentrations of ethanol result in satisfactory (> 4log10) reduction [19, 22].

Quaternary ammonium compounds (QACs) are very effective active substances, especially when combined with alcohol. The best results among the tested active substances were achieved with benzalkonium chloride, which showed virus reduction ranging from >2log10 to >4log10 at concentrations ranging from 0.025% to 0.2%. Cetylpyridinium chloride showed comparable, albeit slightly weaker, activity (> 97% reduction in 20 seconds at concentrations from 0.05% to 0.3%). Decylamine chloride, on the other hand, did not achieve satisfactory results [14, 16, 18, 20, 22]. Some ammonium salts may have cytotoxic effects, as demonstrated by in vitro studies.

Propan-1-ol and propan-2-ol, although mainly studied in combination with other compounds where they exhibit excellent activity against RNA viruses, also show satisfactory efficacy in virus elimination (> 4log10 reduction at a concentration as low as 15% in 20 seconds) when used as a single active substance [16].

Table 1. Characteristics of activity of various active substances against FIV, FeLV, SARS-CoV-2

Type of virus	Active agent	Additional information
FIV	Isopropyl alcohol — good viral reduction [12]	FIV, once adequately dried, can survive on surfaces for up to one week
	Quaternary ammonium compounds (QAC) [12]	–
FeLV	FIV and FeLV can be easily inactivated using detergents, isopropyl alcohol, and quaternary ammonium compounds [5]	–
SARS-CoV-2	Ethanol–virus inactivation at a concentration of 42.6% [13], and a concentration of 53% ethanol for one minute, the value is > 4.2log10 [14]. The disinfectant properties of ethanol are significantly enhanced when it is combined with another active substance, such as QAC or phenoxyethanol	SARS-CoV-2 can persist on various smooth surfaces for several days, and even up to 7 days on a surgical mask! [15]
	A 20% or 80% solution prepared with 0.26% QAC in isopropanol or a mixture of isopropanol/ethanol (m/m 17.4 g/ 12.6 g) achieves a > 4log10 reduction in 20% solution within 15 seconds [15]. With a 2-minute contact time, a > 3log10 reduction is observed on stainless steel, porcelain, and wood surfaces using a 0.25% QAC concentration in 50% ethanol [17]	QAC reduces the survival time of the SARS-CoV-2 virus from 665 minutes to 5 minutes [18]. Alcohols (ethanol/isopropanol or both) and their solutions with surfactants exhibit synergistic effects. For example, a 70% isopropanol solution combined with 3% hand soap achieves a > 7.8log10 reduction [19]
	A 20% or 80% solution of octenisept (octenidine with phenoxyethanol) achieves a > 4 log10 reduction within 15 seconds [16]	–
	Cetylpyridinium chloride	A reduction of > 97% was achieved at concentrations of 0.05%, 0.1%, and 0.3% with exposure times of 20 s, 60 s, and 300 s (only the shortest time and concentration reached 91.9%) [20]

Furthermore, mixtures containing alcohols with quaternary ammonium compounds and alcohols combined with surfactants are extremely effective [14, 16, 17, 19, 23].

The effectiveness of disinfection is also influenced by other factors, such as preliminary cleaning of surfaces with which the infected animal was in contact, ventilation of the room, and time and frequency of contact of the animal with the environment. Although the preparations eliminate SARS-CoV-2, FeLV and FIV as well as some bacteria and fungi, due to frequent superinfections with other pathogens as a result of the progression of the underlying disease and the dose of the virus released during the disease, it is important to maintain the principles of basic hygiene.

Safety and potential health hazards of disinfectants

Disinfection is a key aspect of controlling and preventing the spread of viruses carried by cats. Eliminating pathogens from surfaces with which cats come into contact prevents the virus from entering the body of one cat into another cat, the body of another animal, or even humans. This prevents further virulence and, consequently, the viruses from mutating and becoming infected with mutated forms of viruses. Disinfection is the first step in eliminating viruses, so it is considered a key step in preventing infectious diseases.

The disinfectants used that eliminate any pathogens should be safe at the so-called "three levels": 1) for the people who produce, store, transport and use them, 2) for animals that come into contact with the washed surfaces, and 3) for the disinfected surface. Their production, transport, storage and use must not pose fire, explosion or health hazards. The entire process of production, transport and storage of flammable disinfectants, especially those containing alcohol, must be safe, which is achieved by introducing specific production and storage standards: the use of personal protective equipment, adequate ventilation of rooms to prevent the accumulation of alcohol vapours, which may create explosive mixtures (rooms must be equipped with appropriate sensors), building rooms from non-flammable materials, separating storage zones while maintaining a distance from flammable substances and materials, constant technical monitoring. The production line should be equipped with devices to prevent explosions and fires by using electrical devices adapted to work in an explosive environment and with appropriate grounding. Disinfectants must be safe for health, in particular, they must be safe for tissues and organs that may come into contact with them, i.e. skin, eyes, epithelia, mouth, throat, oesophagus, lungs, liver, hair, and fur. When using disinfectants containing high-percentage alcohols, e.g. ethanol, propanol, isopropanol [13] or chlorine compounds [22] undesirable side effects may occur: irritation, dryness, cracking and peeling of the skin, allergic reactions. Prolonged contact with alcohol may lead to the development of dermatoses such as dermatitis (redness, itching, rash). Alcohols may also irritate the eyes (burning, redness, and even damage to the conjunctiva and cornea), the respiratory system (irritation of the nasal mucosa, cough, shortness of breath, sore throat, and in extreme cases acute respiratory distress syndrome), lead to neurological disorders - long-term exposure to high concentrations of alcohol vapours may lead to dizziness, headache, nausea and impaired concentration. Quaternary ammonium salts may lead to much less severe side effects, which is due to their much lower concentration than the concentration of alcohol contained in disinfectants. In rare cases, irritation may occur, manifesting as redness, rash, eye irritation (watering, burning), respiratory irritation or allergic reactions. Disinfectants may lead to similar side effects in humans and animals depending on the dose of active substance used (different toxicity thresholds). However, it should be remembered that in disinfectants containing quaternary ammonium salts, the concentration of the active substance is very low (usually about 1%), so the probability of side effects is low. In the case of alcoholic substances in which the concentration of e.g. ethanol is 70% or more, or substances containing chlorine compounds, side effects may occur much more often and be very severe.

Spraying disinfectants containing quaternary ammonium salts does not affect the treated surfaces, unlike disinfectants containing concentrated alcohols or chlorine compounds, which may damage surfaces, e.g. furniture polish, floors, and countertops. Alcohols soften and deform some plastics and rubbers, leading to a loss of structural integrity of these materials as well as surface dullness and colour change. Alcohol and chlorine compounds can cause the wood to dry out, crack, shrink and weaken the structure, and destroy the protective layers of oil or wax on wooden surfaces. Alcohol and chlorine compounds also damage metal objects, causing them to corrode. They can also discolour fabrics and cause fibres to weaken. Alcohols cannot be used on the surface of electronic devices because they lead to cracking of the paint and dulling of the protective coatings.

Quaternary ammonium salts, only at high concentrations (i.e. not in the case of disinfectants), can lead to similar surface damage. Moreover, their high concentrations may lead to stains and discolouration on some ceramic surfaces and tiles, as well as to the formation of deposits on glass surfaces.

Prevention and treatment

Cats infected with FIV and/or FeLV undergo a similar therapeutic process, which mainly focuses on providing comfort to the patient and preventing and combating secondary symptoms and diseases associated with the infection.

Studies have shown that staying in a stress-free environment, characterized by low density, and proper diet (limiting raw meat, which can be a source of pathogens) significantly reduces the frequency of symptoms [1]. There are also many vaccines available against FeLV on the market. Studies indicate that the risk of infection decreases 7.5-fold when bitten. However, there is not a large amount of research on this topic, and the results vary, so the vaccine should not be used as the sole method of prevention. The AAFP recommends vaccinating all kittens with two doses and administering a booster dose annually. As for the FIV, there is only one vaccine (Fel-o-Vax FIV; Boehringer Ingelheim) which is not available in most of the western countries. Its use is limited by the paucity of research and discouraging results. According to the AAFP guidelines, appropriate veterinary care is also crucial, including regular check-ups of infected animals, with special attention to the oral cavity, lymph node size, and possible changes in the eyes. Regular blood tests (annually for FIV-positive cats and every 6 months for FeLV-positive cats), as well as urine tests and cultures to exclude opportunistic infections characteristic of both viruses, are essential. Additionally, more frequent preventive use of antiparasitic therapy is recommended. Antiretroviral therapy is relatively rare due to its high costs, lower effectiveness compared to therapy administered to humans, impractically long duration of treatment, or its toxicity. The most popular drug is Zidovudine (3'-azido-2',3'-dideoxythymidine, AZT), which is a thymidine analogue, reverse transcriptase inhibitor, used since the second half of the 1980s for HIV-infected patients. Shortly thereafter, it was found that FIV sensitivity to zidovudine is similar to that of HIV [24]. Unfortunately, FIV can develop resistance to nucleoside analogues, just like HIV. Zidovudine-resistant FIV mutants can emerge after as little as six months of treatment, and a single point mutation in the FIV gene causes this resistance [24, 25]. The drug given orally is digested by animals [24].

Another pharmacological treatment option is the use of human and feline interferons, efficacious in in vitro therapies, but new well-designed studies question the effectiveness of this therapy. It is reported that human IFN-α (recombinant, available in many countries in Europe for veterinary purposes) becomes ineffective after three to seven weeks of parenteral use in cats because of the production of neutralizing antibodies [26]. Recombinant feline interferon-ω (rFeIFN-ω) does not have this effect, nevertheless, it has been shown that parenteral administration of rFeIFN-ω against FIV infection showed no difference in the survival of treated cats [24]. Treatment with oral rFeIFN-ω resulted in a significant improvement in clinical scores (e.g., oral lesions, coat appearance, body condition score, and ocular discharge) after treatment, but the virus load remained unchanged which suggests that rFeIFN-ω has an effect on secondary infections rather than on FIV itself [24, 27].

Unfortunately, the authors did not find any developed protocols or recommendations in the literature regarding the therapeutic management of cats infected with the SARS-CoV-2 virus. This may be due to the short time since the discovery of SARS-CoV-2, the mild nature of the infection, and the focus of researchers on developing therapies for human patients [28]. However, the discussion on the use of vaccines against SARS-CoV-2 in animals, including cats, is still ongoing, as well as the development of new vaccines.

Conclusions

In summary, there is a need for more intensive research in the area of chemical inactivation of FIV and FeLV viruses. Despite ongoing preventive measures, the percentage of infected cats remains high, emphasizing the importance of studies on effective disinfection methods to limit the spread of these viruses. It is also crucial to emphasize the importance of educational efforts aimed at dispelling misconceptions regarding the survival capabilities of these viruses among shelter workers and veterinary professionals.

Disinfection plays a crucial role in combating the FIV, FeLV and SARS-CoV-2 viruses. Existing studies suggest that certain methods have shown good efficacy in eliminating the virus. Chemical disinfection, including the use of isopropyl alcohol at concentrations above 70%, ethanol at concentrations above 40%, and quaternary ammonium compounds at appropriate concentrations (usually above 0.1%), have demonstrated virus-inactivating effects. It is important to note that each disinfection method has specific requirements and limitations. The effectiveness of disinfection depends on various factors such as surface type, concentration and contact time of the disinfectant, and proper application of disinfection protocols. Disinfection plays a crucial role in combating the SARS-CoV-2 virus. Despite the numerous studies conducted during the pandemic, further research and evaluation of the presented methods are still necessary, particularly regarding cytotoxicity and effective contact times on different surfaces.

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