Strategies and innovations for combatting diseases in animals (Review)

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Abstract. Emerging and re-emerging infectious diseases pose significant challenges to animal and public health, and are aligning with global food security concerns. Anthropogenic activities, such as changes in climate, agricultural procedures and farming practices contribute to the spread of zoonotic infections in new geographical areas. Overall diagnostic quality and treatment options have improved over the past few decades. The re-emergence of old and new lethal diseases, such as highly pathogenic avian influenza in animals and humans, along with recurring epidemics, is increasingly threatening different sectors, including the animal care industry and veterinary medicine. The rapid pace of the animal industry, environmental change and socioeconomic burdens are influencing and challenging veterinarians, farmers and epidemiologists in their capacity to survey and control the spread of diseases in animals, and signify the useful impacts on their livelihoods and environment. There is high research interest in engineering various types of drug-loaded cues with multiple functionalities to tackle several infectious and non-infectious diseases. Additionally, the issue can be resolved with international-level awareness efforts, the deployment of proper design and reliable reporting standards, precise test protocols, and acceptance of the utilization of latent class models to account for, interpret and justify imperfect reference tests. The present review discusses the challenges and strategies for preventing and combating infectious diseases in livestock. Furthermore, the ongoing challenges are summarized, and future considerations, concluding remarks and recommendations are also provided for progress in the animal care and medicine sectors.

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Contents

1. Introduction

Infection is a type of parasitism that implies an interaction between a parasite and its hosts. Parasites are typically microscopic pathogens that include viruses, bacteria, fungi, protozoans, worms and arthropods. The virulence factor of a disease-causing agent reveals the severity of the infection and is classified as infectious or non-infectious. In developing countries, emerging and re-emerging infectious diseases (IDs) among livestock pose serious challenges to animal and public health, and ultimately align with the international food

security agenda (1-6). These emerging new viral infections include diseases, such as Rift Valley fever, West Nile fever, SARS coronavirus, Hendra virus, avian influenza A (H5N1), Nipah virus, Zika virus, Ebola virus, Lassa virus, Marburg virus and swine influenza A (H1N1) virus. These diseases are not only threatening to animals, but also to humans, causing massive economic losses in the veterinary domain and public health concerns globally. The complex association between host populations and other environmental factors creates favorable conditions for the emergence of such diseases. This is mainly due to anthropogenic activities, so-called 'man-made', since the entire living system is faced with a series of devastating changes. Such devastating changes occur in the global climate, agricultural procedures and farming practices, among others, due to malpractices, imperfect design, and inefficient handling. All these are major contributors to widespread zoonotic infections in new geographical areas that are further transmissible between animals and humans, either directly or indirectly (7-17).

For instance, the spread of influenza virus A (H1N1), an emerging virus after virus gene recombination is a typical example and poses some significant threats to human health from 2009 when the first case of influenza-like infection in humans was reported in Mexico, and spread to 91 countries until July, 2009 (4,11,18,19). Similarly, in March, 2024, a young goat in Minnesota tested positive for highly pathogenic avian influenza (H5N1). Shortly thereafter, dairy cattle in Texas and Kansas were infected. The virus had likely been present since December, 2023 and had spread to 52 herds across nine states in the USA by May, 2024, causing symptoms, such as a thicker milk consistency and reduced output in affected cows, with evidence of high virus levels in raw milk (12,20-23).

Since 1997, 909 human cases of influenza A (H5N1) have been reported globally, with a 52% mortality rate. From January, 2022 to April, 2024, 26 cases were recorded in eight countries, resulting in seven deaths. In the USA, two cases were recently confirmed among dairy farm workers in Michigan and Texas, marking the first documented instance of human transmission from infected cattle. The virus, identified as Clade 2.3.4.4b, has been detected in various mammals since 2022, emphasizing the need for enhanced surveillance and preventive measures to mitigate international transmission risk (24-26).

According to one estimate, ~75% of new or emerging IDs spread from animals and >60% of IDs spread in humans (27,28). Therefore, effective control and treatment measures for IDs and non-infectious diseases (NIDs) are of high priority to safeguard and secure animals and humans, along with national and international food supplies (4,29-33).

From the world population hike prospects, according to the United Nations (UN), Department of Economic and Social Affairs, the current world population of 7.8 billion is expected to reach 8.6 billion by 2030, 9.8 billion by 2050 and 11.2 billion by 2100 (34). Such a rapid pace in the world population growth rate also poses significant challenges, such as an increasing food demand, with a massive burden on the livestock industry to fulfill the increasing food demand for meat or other dairy products (35-37).

In addition, statistics on livestock populations, growth rates, and quality vary considerably from source to source and from place to place. To equalize this fast-paced demand and production ratio, methods or strategies in farm production are extremely varied and pose risks related to the transmission of IDs owing to malpractice. This type of known or unknown vulnerability demonstrates the importance of infectious livestock diseases in global food security (38-43). More specifically, and as aforementioned, the emergence of new pathogenic variants or the re-emergence of old infections and NIDs in the animal industry has devastated national flocks, as has occurred with strains of highly pathogenic avian influenza and others (7,44-49).

Historically, both domestic and commercially raised animals have been affected by IDs and NIDs. According to the World Organization for Animal Health (OIE) report, for the year 2024, the list included 173 animal diseases, infections and infestations (50). With advancements being made in scientific understanding and increased societal awareness, consumers are becoming increasingly concerned about issues related to previous epidemics and current outbreaks (48,49). These concerns have intensified as outbreaks, such as foot-and-mouth disease (FMD), Query fever (Q fever), hemorrhagic septicemia, avian influenza, Newcastle disease, Bluetongue, bovine virus diarrhea, African swine fever, classical swine fever, brucellosis, Peste des petits ruminants, contagious bovine pleuropneumonia, contagious caprine pleuropneumonia, East Coast fever, heartwater, African horse sickness, Aujeszky's disease, tuberculosis, sylvatic rabies, and trichinellosis have become more severe, as shown in Table I (26,49,51-66).

Efforts have been made from a scientific standpoint to prevent and combat the further invasion of highly infectious diseases. The objective of the present review was to illustrate and discuss certain drug-loaded cues and their smart exploitation for IDs and NIDs in animals. The present review focuses on various IDs and NIDs, along with the detection measures, forecasting and control of infectious disease epidemics.

2. Detective measures and epidemiological modeling

The implementation of epidemiological modeling is not new and has a long progressive history (67-74). The use of real-time epidemiological modeling to design robust policies during serious outbreaks has increased over the past 20 years (75-78).

For instance, there are recent examples of the real-time epidemiological modeling of animal diseases, such as FMD epidemics (75,76,78-80). Among the various deployed modeling systems, compartmental modeling is the most commonly used and has been further categorized as deterministic or stochastic (81). Various parameters, such as infection type, symptoms and status, are considered critical when implementing compartmental modeling (82-84). Protective measures are typically considered before a pathogen enters a new population, using modeling analytics to guide targeted surveillance. Comprehensive surveillance systems integrating livestock, wildlife and human components are crucial, and have been recommended in several reports (29,85-88).

Despite the usefulness of modeling, several challenges remain. Numerous articles have highlighted issues in modeling infectious disease dynamics, including applications in public health policy and livestock diseases (89,90). From the public health policy perspective (90), six main challenges have

Table I. Some examples of infectious and/or non-infectious diseases in the animal industry along with their characteristic features.

Disease name	Animals affected	Signs/symptoms	Transmission source
Foot-and-mouth disease (FMD)	All cloven-hoofed animals	Sore feet; thus, they lie down or kneel, saliva dripping from the mouth, blisters in the mouth, ulcers around the feet	Ingestion of contaminated forage and water; all infective body excretions, including urine, milk, feces, and semen
Highly pathogenic avian Influenza (HPAI)	Chicken, ducks	Swollen wattles, blue/purple comb, red streaks on legs, bleeding under the skin, accumulation of fluid/blood	Feces or saliva
Newcastle disease (ND)	Numerous species of birds	Swelling and redness of the eyelids, diarrhea, crooked neck, paralyzed, speckled spleen, hemorrhage in some parts of the intestine	Feces and saliva, infected cages, footwear, or equipment
African swine fever (ASF)	All kinds of swine	High fever, red skin on ears and tail, ulcer, enlarged spleen	Feces, saliva, and blood
Classical swine fever (CSF)	Pigs	High fever, weight loss, convulsions, crusty bloody fluids around the eyes	Feces and saliva, infected equipment
Peste des petits ruminants (PPR)	Sheep and goats	Foul-smelling diarrhea, crusting around the mouth and nose, ulcers in the mouth, reddened lungs	Feces and saliva, infected food or equipment
Contagious bovine pleuropneumonia (CBPP)	All breeds of cattle	Runny nose, extended neck, yellow covering around the lungs	Saliva or mucus
Contagious caprine pleuropneumonia (CCPP)	Goats	Fever, breathing difficulty, coughing, weight loss, frothy nasal discharges, enlarged and bloody lungs	Saliva or mucus
East Coast fever (ECF)	Cattle and buffalo	High fever, breathing difficulty, swelling/enlarged lymph nodes	Tick-transmission
Heartwater	Cattle, sheep, and goats	High fever, convulsions, crooked necks, excess fluid around the heart/ lungs, engorged Amblyomma ticks on the skin,	Bitten by an infected tick (vector)
African horse sickness (AHS)	Horses	High fever, excess sweating, coughing, swollen around the eye area, Accumulation of fluid in the lungs	AHS virus is transmitted by small biting insects
Hemorrhagic septicemia (HS)	Buffalos and cattle; other goats, camels, horses, and donkeys, while dogs and fowls are not susceptible	Rapid onset, high fever, dullness, lacrimation, dyspnea, swelling in the head-throat-brisket region	Ingestion or inhalation of causative agents by contaminated feed and water that occurs during wet condition
Bovine viral diarrhea	Cattle	Bloody diarrhea, high fever, mouth ulcer, off-feed, ataxia	Ingestion of contaminated fomites or either through congenital infection
Trichinellosis	Pigs, horses, carnivores and other animals (zoonotic disease)	Eye swelling, cough, itching, diarrhea or constipation, achy joints, fever, nausea, vomiting	Ingestion of contaminated meat or meat products because infected animals or humans have nematode larvae lodged in their muscles

been described: i) Communicating the limits of modeling; ii) maintaining the value of models in the face of long time horizons; iii) usefully deploying modeling in the context of 'black swans'; iv) integrating modelers and model-building into the policy process; v) economic analysis and decision support; and vi) creating a cycle where results inform decisions and vice versa. Similarly, another study (89), presented eight challenges: i) Linking models to transmission experiments; ii) disease control by selective breeding; iii) applying models to data/resource-poor settings; iv) how best to exploit rich livestock data; v) improving spatial models; vi) unifying multiple scales of transmission; vii) linking livestock populations to other species; and viii) modeling livestock with political and economic constraints in modeling infectious livestock diseases (91).

3. Forecasting and control of infectious disease epidemics

Once the initial phase of an outbreak is identified, the effective management and control of the causative agent are often required to minimize its overall impact on animal and human health. Upon this initial detection in the host population, a considerable challenge which is often encountered is forecasting whether this initial phase will dissipate or will progress to a major epidemic concern (83,92,93). For the effective control of IDs or epidemics or to help manage diseases, the implementation of surveillance programs is of utmost importance. The most advanced countries/jurisdictions have executed routine surveillance programs in direct response to major disease outbreaks that have caused catastrophic losses. The implementation of surveillance programs or surveys combined with a range of biosafety and biosecurity measures have allowed these jurisdictions to effectively eradicate certain diseases of concern (94). In this context, lessons for underdeveloped countries lie in these directions. Herein, six key drivers are proposed, which should be taken into consideration: i) The notifiable reporting of major disease outbreaks; ii) the protection of wild and native species; iii) the control of trade, border biosecurity and biosafety to prevent undesirable disease epidemics; iv) the implementation of legislative measures; v) socioeconomic contribution and public pressure; and vi) routine-based inspections of in-practice surveillance programs (95,96). Routine-based inspections of in-practice surveillance programs have been further subcategorized into six categories: i) The reporting notifiable diseases and elevated mortality; ii) routine testing for pathogens; iii) regular inspections of farm areas; iv) reliable quality tests before trade; v) the maintenance of a proper hygienic environment; and vi) onsite reporting requirements (97).

To date, various treatment strategies have been developed and exploited to control various diseases and disease-causing agents. Comprehensive guidelines for the judicious therapeutic use of antimicrobials in poultry have been reported by the American Veterinary Medical Association (AVMA) (for further details, please visit AVMA online: www.avma.org). A range of antibacterial drugs, such as amoxicillin, metronidazole, clindamycin, doxycycline, spectinomycin, bacitracin, chlortetracycline, cephalexin, ciprofloxacin, sulfamethoxazole and trimethoprim, and antiviral therapeutics, such as oseltamivir and zanamivir, are currently being used. However, direct and excessive drug use has raised concerns regarding drug resistance (98,99). Of note, the effectiveness of treatment with antiviral drugs, such as oseltamivir and zanamivir, is becoming increasingly reduced due to the development of resistance. Oseltamivir is a selective antiviral prodrug that is used in the treatment of influenza. Zanamivir is another drug which is used as an inhibitor of neuraminidase; this drug is used in the treatment of the common flu and to protect against viruses A and B (100). The development of antiviral drugs which are highly effective and which can protect against a wide range of viral pathogens is an arduous task; this is due to the fact that viruses use host cells for replication. For this reason, the global research community is aiming to expand the range of currently available antiviral drugs to other pathogen families (99). Drug resistance is continually becoming more of a challenge; thus, the development of novel drugs which are able to combat a wide variety of viral infections, is of utmost importance. Another key issue is the fact that the genetic composition of viruses may change and this may subsequently render the virus resistant to several therapeutics (101). Viruses may become resistant to antiviral drugs primarily due to spontaneous and intermittent mechanisms. A previous study isolated three types of influenza A viruses; each of these types was found to have a distinct neuraminidase genetic mutation and all types were found to be resistant to the neuraminidase inhibitor, oseltamivir (102). Due to viral evolution, viruses are becoming more resistant to antiviral drugs; thus, continuous monitoring is required. (103).

In this context, materials-based cues/constructs with antimicrobial 'non-drugs' e.g., nanoparticles or effective drug-loaded composite materials have found widespread biomedical applications (104,105). The importance of such drug-loaded interventions (also known as Trojan horse strategies of drug delivery) has been established through various reports, expanding the efficacy of conventional drugs, helping to reduce the dosage and frequency of drug usage, and preventing antimicrobial resistance against drugs (106). Specific strategies, such as antibiotic stewardship programs and alternatives to antibiotics have improved animal husbandry practices, legislation and regulatory measures, surveillance and monitoring, public awareness and education, and research and development are being used to combat antimicrobial resistance.

Material-based cues with or without loaded drugs provide additional advantages, such as targeted drug delivery, slow and controlled drug release, low or no toxicity, internal/external stimuli-responsive behavior and controlled degradation or effective release rate in a sophisticated manner. With these added values, substantial research efforts have been made to engineer material-based cues/constructs with or without loaded drugs with antibacterial and/or antiviral activity (107).

4. Quest for materials-based cues

With key scientific advances being made in the field of materials science and the added value of nanotechnology, the quest for material-based cues/constructs in numerous geometries with multifunctional activities (Fig. 1), such as antibacterial, antifungal and antiviral activities, has increased over the past several years (99,104,108-112). In addition, material-based cues possess exceptional biocompatibility, biodegradability,

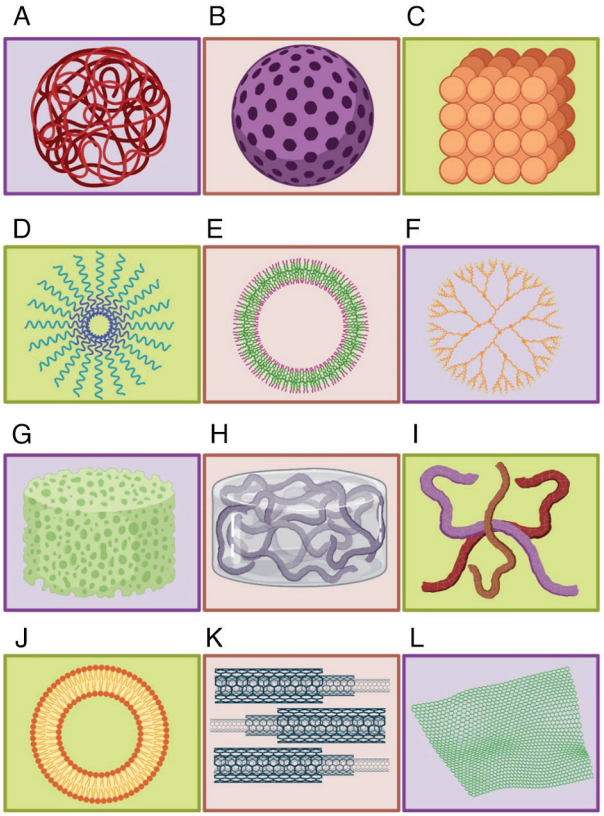

Figure 1. Schematic illustration of a range of materials used in different geometries, i.e., (A) polymeric nanoparticle, (B) mesoporous nanoparticle, (C) nanocrystal (cubic arrangement), (D) polymeric micelle, (E) polymersome, (F) dendrimer, (G) microporous scaffold, (H) hydrogel, (I) nanofiber, (J) liposome, (K) carbon nanotube (multi-walled), and (L) nanosheet. The image was created using BioRender.com.

and internal and external stimuli-responsive modes; thus, they are broadly used in various sectors of the modern world, such as clinical, pharmaceutical, cosmeceutical, nutraceutical, biomedical engineering, tissue engineering and veterinary medicine (109,112-115). Biocompatible and stimuli-responsive materials can lead to the development of more effective treatments by ensuring that they positively interact with animal tissues and adapt to changing physiological conditions. Biocompatibility minimizes the risk of adverse immune responses and other complications, thereby making treatment safer for a wide range of animal species. Stimuli-responsive materials enable precise control over the release and action of therapeutic agents, enhance treatment efficiency, and reduce the need for frequent interventions. These materials can be tailored to the specific needs of different veterinary applications, allowing for customized treatments that cater to the unique requirements of various animal species and conditions. The majority of infectious or non-infectious diseases in humans and animals are mainly caused by viruses, bacteria, fungi, protozoans, worms and arthropods. Thus, materials science has provided a new wave of pristine or drug-loaded cues/constructs with antibacterial, antifungal, and/or antiviral potentials.

Currently, there is an increasing demand for antibiotic alternatives for the treatment of infections, and advances in drug delivery can play a crucial role in enhancing the efficacy of herbal-derived active principles, such as curcumin and flavonoids. It has been reported that curcumin encapsulated in nanocapsules can effectively reduce the extent of listeriosis in gerbils experimentally infected with *Listeria monocytogenes* (116). Another study reported the improved bactericidal and biofilm formation inhibitory effects of flavonoids against *Escherichia coli* upon nanoencapsulation (117). In another study, the nano-delivery of *Origanum majorana* essential oil required lower doses of therapeutic oil to treat fish infected with *Aeromonas hydrophila* (118).

Another potential application of this drug delivery system is in biofilms, which are a public health hazard. Nano-encapsulated glycerol monolaurate has been reported to reduce viable bacteria within the biofilm of *Pseudomonas aeruginosa*, providing a positive response to nano-drug delivery against biofilms (119,120). Nano-loaded antibiotics have also been reported to be more efficient against *Pseudomonas aeruginosa* (121). However, findings obtained *in vitro* must also be able to be produced *in vivo*; some *in vitro* findings have not been observed in *in vivo* biofilm therapeutic studies (122).

For this purpose, an array of novel materials, such as chitosan, alginate, cellulose and graphene, has been engineered to exhibit potent bioactivity towards different pathogens on contact without releasing any toxic biocides for healthy cells. A facile *in situ* procedure for fabricating hydrogel-silver nanocomposites involves the formation of silver nanoparticles within swollen poly (acrylamide-*co*-acrylic acid) hydrogels (123). Apart from antibiotic-nanoparticle combinations, therapeutic interventions using antimicrobial peptide-nanoparticle combinations against infectious agents are also being investigated, and a number of these have exhibited promising outcomes (124). A recent study reported thermo-magnetically responsive drug-eluting grippers as a convenient means of drug delivery with minimal invasiveness and for biomedical engineering, as they can be moved using magnetic fields after doping with magnetic nanoparticles (125). The effective targeted delivery of drugs can also reduce the dose requirement, particularly as regards the treatment of resistant bacterial forms, such as mycobacteria. A previous study reported that the nano-delivery of an antibiotic combination against *Mycobacterium avium* in mice elicited sustained and effective drug release compared to free drugs (126). This opens a promising platform for the further advanced research on drugs against bovine tuberculosis. Novel interventions, such as ultrasmall tungsten disulfide quantum dots with catalytic as well as photoluminescence properties, have been tested in biomedicine for their application as drug delivery nanoparticles against infection and biofilms, and ultimately provide a promising platform for checking infections (57,127).

Based on the antibacterial activity analysis results, the developed hydrogel-silver nanocomposites have demonstrated excellent antibacterial effects against *Escherichia coli*. A previous study prepared a polyelectrolyte complex (PEC) hydrogel using chitosan as the cationic polyelectrolyte and γ-poly (glutamic acid) (γ-PGA) as the anionic polyelectrolyte. The chitosan-based PEC gel exhibited antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* (128). Additionally, the PEC hydrogel was effective in promoting

cell proliferation when tested in an *in vitro* culture of 3T3 fibroblasts. According to that study (128), based on the results, the PEC hydrogel appears to have potential as a new material for biomedical applications and has been exploited as a wound-dressing material (129).

The development of silver nanoparticles loaded with chitosan-alginate constructs has been reported with antibacterial activities against six bacterial strains, i.e., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Morganella morganii* and *Haemophilus influenza* (130,131). In 2019, Bilal *et al* (132) developed and characterized the biogenic nanoparticle-chitosan conjugates with antimicrobial (against Gram +ve and Gram -ve bacterial isolates, i.e., *Staphylococcus aureus*, and *Escherichia coli*), antibiofilm (against *Pseudomonas aeruginosa*) and anticancer (against the MCF-7 breast cancer cell line) potential. In another study, a nanocomposite containing ceftriaxone loaded into bioactive chitosan (obtained from the fungus *Cunninghamella elegans*) sustained the antibacterial effects of ceftriaxone against several drug-resistant bacterial strains (133). Sepsis due to severe bacterial infections is at the forefront of livestock mortality. The management of systemic sepsis through the strategic management of the infectious microenvironment using bioresponsive nanoparticles in murine models has shown promise for the future development of nanomedicine for sepsis (134). In the case of antimicrobial peptide-loaded topical antibacterial therapy, it has been found that a peptide applied through poloxamer gel can effectively reduce the *Staphylococcus aureus* count, whereas application as a lipid nanocarrier was not found to be very effective (135).

As regards antiviral drugs, a previous study reported that the antiviral activity of monocaprin solutions containing 5% propylene glycol was markedly suppressed by 5% polysorbate 20 (136). The same study demonstrated that the antiviral activity of solutions containing 7.5% propylene glycol and polysorbate 20 (0.75 to 1.5% concentration) was comparable to that of pure monocaprin (136). Monocaprin is a monoglyceride that has antiviral activity. It has been demonstrated that monocaprin is effective against enveloped viruses, such as vesicular stomatitis virus, herpes simplex virus (HSV), visna virus and human immunodeficiency virus (HIV) *in vitro* (137,138).

Similarly, previous studies have demonstrated that hydrophilic gels containing monocaprin at a concentration of 20 mM were able to inactivate HSV-2 and HSV-1 by >100,000-fold (137,138). In their study, Rokhade *et al* (139) developed semi-interpenetrating polymer network microspheres of acrylamide-grafted dextran and chitosan-based hydrogels for the controlled release of the antiviral drug, acyclovir. Among the antiviral therapeutics, antiretroviral drug research is the most critical, particularly for combating HIV infections. Progress has been made in the development of effective nanoparticle-based technologies for the delivery of drugs to the central nervous system to combat retroviral progression (140). For instance, an antiretroviral peptide drug (enfuvirtide), loaded through an iron oxide nanoparticle coated with an amphiphilic polymer, has been shown to be successful in crossing the blood-brain barrier for effective drug delivery to the central nervous system (141,142).

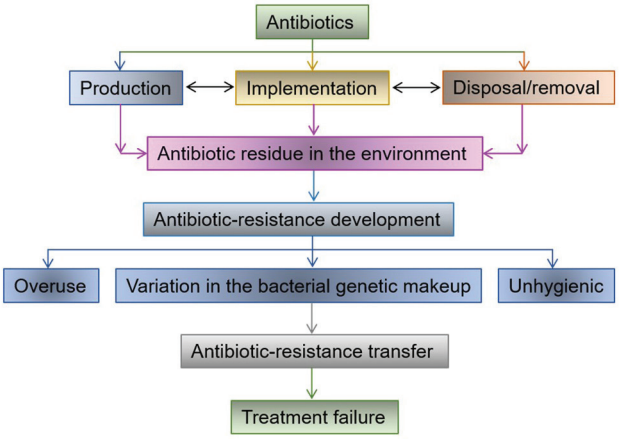

Figure 2. Conceptual framework of antibiotic resistance development associated with antibiotic residues in the environment that lead to the treatment failure.

Other examples of the smart exploitation of various drug-loaded cue formulations against infectious pathogens and diseases with considerable potential in veterinary medicine are summarized in Table II.

The therapeutic targeting of immune cells using drug-loaded constructs is gaining increasing attention, particularly for combating cancerous, inflammatory and autoimmune conditions. A previous study reported a novel nanocapsule based on silica that can be loaded with a large dose of drugs targeting immune cells, such as macrophages, which can be used in tumor therapy without systemic toxicity (143).

5. Future perspectives

Literature with suitable examples encourages veterinarians toward material-based cues to combat diseases in the animal sector. The current advancements in materials science, along with the involvement of nanotechnology in numerous clinical applications, have significantly improved the detection, diagnosis and therapy of diseases that have been difficult to manage in the past (144-146). Furthermore, with ever-increasing scientific knowledge and common awareness, consumers and producers are on common ground and are highly concerned about the overuse/overdosing/misuse of antibiotics. Such a heavy consumption of antibiotics has also resulted in the emergence of multidrug-resistant pathogens. In this context, the absence of highly effective and 100% reliable treatment against various concerning and resistant diseases makes material-based cues, with or without loaded drugs in their active form, a promising option for veterinarians. The conceptual framework of antibiotic resistance development associated with antibiotic residues in the environment that lead to treatment failure is illustrated in Fig. 2.

Studies developed at a laboratory scale using animal models for different disease-causing agents have stimulated employment in routine practice and can certainly be extrapolated for veterinary medicine in the future. For instance, skin-related infections and NIDs can be efficiently diagnosed in infected animals or companion animals. Thus, material-based drug-loaded hydrogels could be a straightforward solution for improving Veterinary Dermatology.

Table II. Smart exploitation of various drug-loaded cues/constructs formulations against infectious pathogens with considerable potentialities for veterinary medicine.

Infectious pathogen or disease	Loaded drug	Co-material used	Animal model	Bioactivity or proposed applications	(Refs.)
Cutaneous leishmaniasis (*L. amazonensis* and *L. braziliensis*)	Amphotericin B	Poly(vinyl alcohol) (PVA) hydrogels	-	Antifungal and leishmanicidal activity, functional wound dressing	(147)
Candida albicans	Miconazole	Chitosan-based nanoparticles	Yes	Antifungal activity, Promising therapy for the treatment of vulvovaginal candidiasis	(148)
Cutaneous leishmaniasis	Amphotericin B	Poly(lactic-co-glycolic acid) (PLGA) nanoparticles	-	Topical therapy, useful for the local treatment of *Cutaneous leishmaniasis*	(149)
Cryptococcus neoformans	Amphotericin B	Methoxy poly(ethylene glycol)-poly(lactide)-poly(β-amino ester) nanocarriers	Yes	Reduce the *C. neoformans* burden in the lungs, liver and spleen, based on its improved biodistribution	(150)
Leishmania major	Amphotericin B	Nano-sized chitosan	Yes	Wound healing and parasite inhibition, successful treatment of *Leishmania major* pathological effects	(151)
Leishmania major	Amphotericin B	Anionic linear globular dendrimer	Yes	Successful treatment of *Leishmania's major* pathological effects	(151)
Visceral leishmaniasis (*Leishmania donovani*)	Amphotericin B	Peptide-coated iron oxide nanoparticles	-	Reduce total parasite burden in spleen, treatment of visceral leishmaniasis	(152)
Leishmaniasis (*Leishmania tropica*)	Paromomycin	Solid lipid nanoparticles	Yes	Inhibit the parasite propagation, treatment of leishmaniasis	(153)
Leishmania donovani	Amphotericin B	Glycol chitosan-stearic acid copolymer	Yes	Effective antileishmanial properties, efficacious drug delivery system	(154)
Fusarium solani	Amphotericin B	Eudragit RL 100 nanoparticles	Yes	Antifungal activity, suitable against eye irritation, Ophthalmic application	(155)
Paracoccidioides brasiliensis	Desoxycholate amphotericin B	Poly(lactic-co-glycolic acid) (PLGA) and dimercaptosuccinic acid (DMSA) polymeric blends	Yes	Useful to treat systemic fungal infections such as paracoccidioidomycosis, candidiasis, aspergillosis, and cryptococcosis	(149)
Systemic candidiasis	Amphotericin B	Sodium alginate nanospheres	Yes	Targeted antifungal therapy	(156)
Systemic candidiasis, *Candida albicans*	Caspofungin	-	Yes	Persistence of caspofungin in tissues to understand drug activity	(157)

Other examples include udder and ear helminthiases in cows, which can be effective in tackles in which topical drugs are ineffective. Thus, drug-material-based combined therapy with topical bioactive agents can be considered an alternative to topical drugs alone.

6. Current challenges, concluding remarks and outlook

As aforementioned, in different respective sections, the (re)-emergence of old and new lethal diseases along with recurring epidemics remains a massive challenge to the development of the animal sector in developing countries. Several critical factors play key roles in the impact and spread of the disease in various resource-limiting countries. Among these, poor animal care systems, non-hygienic maintenance, unsatisfactory livelihoods, unending intensification, reliance on external trade, and biosafety and biosecurity issues are the major examples. Under such unavoidable circumstances, the following question arises: That is, if the proximity of workers, along with their observational skills, could be used as a route for syndromic surveillance. Considering this thoughtful scenario, there is no reason to believe that such skillful workers could not notice the basic symptoms (e.g., as summarized in Table I) and deviations from the norm, such as first-hand contact, to highlight existing and emerging diseases. To tackle this challenge effectively, robust and aware-full epidemiological modeling and the design of surveillance, detection, and protection measures need to be deployed at the grassroots level to better understand the factors that influence individuals or collectively. To further strengthen such surveillance strategies, veterinarians should work in interdisciplinary and multidisciplinary areas of veterinary science, epidemiology, medicine, materials science, biology, chemistry, microbiology and social science to design robust systems that are inclusive of skillful individuals and state-of-the-art technology.

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Ethics approval and consent to participate

Not applicable.

Patient consent for publication

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Competing interests

The authors declare that they have no competing interests.

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