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REVIEW ARTICLE

Integrating Alternative Therapies to Combat Multidrug-Resistant Bacteria Causing Infections in Equine

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ABSTRACT

Horses play an important role in many human activities. However, they are susceptible to bacterial infections, which may seriously impact their health and activity. These diseases are treated by using antibiotics. However, the increasing frequency of antibiotic resistance poses a significant concern since it reduces the efficacy of current therapies, resulting in extended illness, increased veterinary costs, higher fatality rates and potentially threat to human health through zoonotic transmissions. Consequentially, there is a growing interest in developing alternative medicines for tackling bacterial infections in horses. These alternatives include the use of bacteriophage, antimicrobial peptides, and nanoparticles. Integrating alternative therapies into veterinary practices may also assist in reducing antibiotic dependency and maintaining the efficacy of current antibiotics for future generations. Such treatments are intended to provide effective infection control while reducing the potential for antibiotic resistance. This review outlined the multidrug-resistant (MDR) pathogens causing different diseases in equine globally, the efficacy, advantages, applications, and limitations of innovative, emerging, or developing therapies currently under investigation that may offer potential solutions to combat MDR bacteria in equine. Ongoing research and innovation in this field of study are essential for maintaining long-term horse health management and tackling the broader effects on both animal and human health.

***Keywords*:** Antimicrobial resistance, Bacteriophage, Antimicrobial peptides, Nanoparticles, MDR.

Introduction

Horses occupy a unique position in our society. Whether as livestock, athletes, landscape caretakers, or companions for leisure activities, horses possess a diverse array of often-overlooked environmental benefits and attributes [1]. Bacterial diseases are the primary cause of equine infections, posing a serious health concern to horses. Recently, there has been a surge in severe outbreaks of infectious diseases caused by microorganisms that have evolved resistance to several antibiotics. This rise in drug resistance is a global phenomenon that poses a danger to our ability to successfully tackle prevalent diseases. As resistance spreads, it limits our ability to treat these diseases, resulting in longer illness and higher mortality rates [2, 3]. Horses serve as a potential reservoir of antimicrobial resistance (AMR) pathogens, which can be transmitted to their owners, caregivers, and the environment through direct or indirect contact. This transmission occurs through the excretion of antimicrobials and their metabolites in feces and urine [4, 5]. The overuse and misuse of antibiotics is a prevalent global issue that results in various detrimental consequences, including the emergence of

antimicrobial resistance, increased healthcare costs, and heightened risks of adverse drug reactions [6]. Certainly, the gravity of the issue has prompted the establishment of different classifications for multidrug-resistant (MDR) species. Several novel alternative approaches for combating these pathogenic bacteria have been discovered [3]. Novel therapies, such as combination antibiotics with adjuvants, employing bacteriophages, antimicrobial peptides, and nanoparticles, have been extensively studied. These techniques offer a variety of strategies for treating infections, particularly those caused by MDR bacteria, and show promise in enhancing clinical outcomes [7].

This review surveyed the MDR pathogens causing different diseases in equine globally. Additionally, this article introduces the factors contributing to multidrug resistance and exploration and application of innovative, emerging, or developing therapies currently under investigation that may offer potential solutions to combat MDR bacteria. Moreover, the efficacy, advantages, and limitations of previously outlined therapeutic approaches were included.

Equine infections caused by multidrug-resistant bacteria

Bacterial diseases play a crucial role in equine infections, and several of these can be transferred to human beings from horses [8]. Antimicrobial resistance results in high mortality rates and medical expenses, affecting the efficacy of antimicrobial treatments (Figure 1) [9]. Pneumonia is a serious disease in horses [10]. The most common cause of disease in horses and foals is a respiratory illness, which can be viral, bacterial, or immune-mediated [11]. The affected horses showed mucopurulent nasal discharge, fever, cough, and tachypnea [12]. *Klebsiella* is one of the most prevalent bacteria that can cause significant infections in human and animal's respiratory systems [11]. However, the most isolated pathogens from the equine respiratory system were Gram-negative bacteria, *Candida albicans*, *Streptococcus* species., and *Staphylococcus* species [13]. Strangles, caused by *Streptococcus equi subsp. equi*, is the most prevalent, serious, and extremely contagious respiratory disease of horses worldwide. It represents a severe threat to veterinary medicine, resulting in huge welfare and economic losses globally [14, 15].

Wounds are common in horses due to their natural flight urge and the harsh conditions of their surroundings; nevertheless, the high risk of infection by infectious agents complicates the healing process, often resulting in wounds becoming chronic [16]. Delayed wound healing is common in hor se limb wounds; this is mainly due to biofilm formation. Biofilms are bacterial aggregations in which bacteria are shielded from both antimicrobial agents and the host's immune system response [17]. Chronic wounds have an extensive range of types of bacteria at the spot of injury [18]. Pathogens that result in delayed wound he aling and infection include *Staphylococcu s aureus*, *Pseudomonas aeruginosa*, *Cand ida albicans*, and β-haemolytic *Streptococci* [19].

Bacterial infections are a significant cause of eye disorders in horses. Equine ocular disorders present a medical problem because of permanent and costly treatment, in addition to financial challenges linked with a potential loss in the market value of the infected horse [20]. These issues not only produce discomfort and distress for the horse, but they also pose a considerable danger of sight loss if not treated. Furthermore, in certain conditions, commensal microbes of the normal flora, notably Gram-negative bacteria and fungus, can transform into opportunistic infections,

worsening the ocular conditions and delaying treatment [21].

Diarrhea is one of the most popular clinical symptoms in foals and can cause severe morbidity and mortality [22]. Nearly 80% of foals have more than a sin gle attack of diarrhea during their lifetime [23]. Infectious causes of diarrhea in young horses are mostly bacterial, while viral or parasitic infections are less common [24]. Based on various examinations, the most popular bacterial pathogens isolated from diarrheic foals were *Salmonella* species, *Clostridium* species, and *Escherichia coli* (*E. coli*) [24].

Endometritis has long been acknowledged as one of the main causes of impaired fertility in mares, resulting in significant financial effects on the equine reproduction industry due to infertility and early embryonic loss [25]. Failure to deliver healthy foal is one of the primary causes of financial losses for horse breeders. This can be a result of infertility and fetal loss, abortion, stillbirth, or perinatal mortality [26]. In mares with severe endometritis, *E. coli*, *Pseudomonas aeruginosa (P. aeruginosa)*, *Klebsiella pneumoniae (K. pneumoniae)*, and *Streptococcus equi subsp. zooepidemicus (S. zooepidemicus)* were commonly identified pathogens [27]. Table 1 depicted the MDR bacteria causing equine infections.

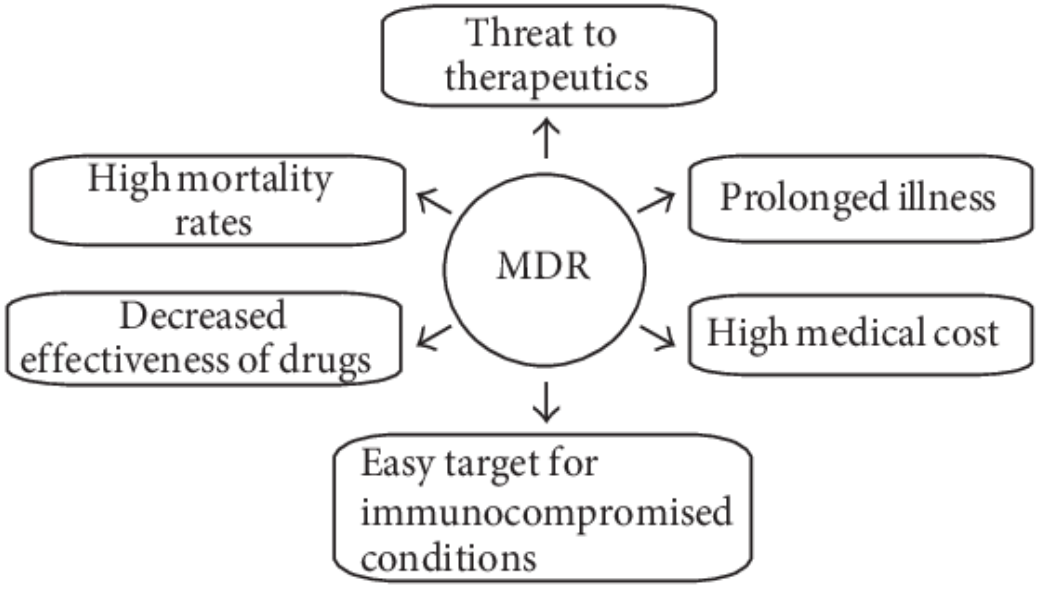

Figure 1: Multidrug-resistant bacteria (MDR) and a range of social and medical issues [9; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4124702/].

Table 1: Most common multidrug resistant isolates per site of infection isolated from infections in horses.

Type of infection	MDR bacteria	Country	N/total per organ system (%)	Reference
Respiratory Infection	*E. coli*	Equine Hospital of the University of Zurich, Switzerland.	25	[28]
	P. aeruginosa		25	
	K. pneumoniae	National Research Centre, Giza, Egypt.	4.4	[11]
	S. zooepidemicus	Animal Health Research Institute, Doll, Giza, Egypt.	83.5	[29]
	S. zooepidemicus	California.	48.5	[30]
	K. pneumoniae		12.1	
	Actinobacillus equuli subsp. Haemolyticus		9.1	
	K. pneumoniae	Equine Bacterial Diseases Unit, Giza, Egypt	26.3	[31]
	Staphylococcus aureus (*S. aureus*)		10.5	
	Streptococcus equi subsp. equi (*S. equi subsp. equi)*		4.5	
	P. aeruginosa		3.8	
	Proteus mirabilis (P. mirabilis)		2.3	
	S. zooepidemicus		2.3	
Wound Infections	*P. aeruginosa*	Equine Hospital of the	50	[28]

	CNS[1]	University of Zurich, Switzerland.	50	
	E. coli	East Nile Locality.	10	[32]
	Salmonella species.		15	
	Pseudomonas species.		12.5	
	S. aureus		40	
	Staphylococcus epidermidis (S. epidermidis)		40	
	Streptococcus species.		15	
	Klebsiella species.		5	
Eye Infections	*S. aureus* is the most important pathogen isolated from eye at different percentages.		73.8	[33]
			52.8	[34]
	Keratitis is mainly caused by methicillin-resistant *S. aureus*, *Streptococci*, and *P. aeruginosa.*			[35, 36]
Diarrhea	*E. coli*	Kingdom of Saudi Arabia.	14.28	[24]
	Salmonella enterica		5.72	
	E. coli	Pakistan.	48.77	[23]
	Clostridium perfringens (C. perfringens)		18.56	
	Salmonella species.		17.9	
Uterine Infection	*E. coli*	Cornell University, Ithaca.	38.7	[37]
	S. zooepidemicus		37.5	
	Enterococcus faecalis		6	
	Pseudomonas species.		5.2	
	Klebsiella species.		2.9	

History of repetitive infertility	Beta-hemolytic *Streptococcus* species.	British Equine Veterinary Association Congress.	52.5	[38]
	E. coli		25.8	
	S. zooepidemicus		68.3	[29]
	E. coli		17.3	[25]
	Staphylococcus species.		15.6	
	Streptococcus species.		13.5	
	P. aeruginosa		6.6	
	K. pneumoniae		4.6	

[1]CNS: coagulase negative staphylococci

Strategies to overcome multidrug resistant pathogens

Antimicrobial resistance (AMR) has developed against several types of antibiotics frequently administered against harmful bacteria as a result of repetitive drug administration and higher doses being common nowadays [39]. The biological pressure generated by repeated usage of multiple antibiotics during treatment has resulted in the development of resistant characteristics in crucial pathogens, leading to MDR bacteria that are virtually impossible to cure [40]. Specifically, face significant amounts of AMR as a result of antibiotic usage, particularly against ESKAPE pathogens: *Enterococcus faecium, Staphylococcus aureus, K. pneumoniae, Acinetobacter baumannii, P. aeruginosa,* and *Enterobacter* species [41-43]. ESKAPE bacteria are capable of "escaping" the biocidal activity of antimicrobial drugs [7]. ESKAPE's multidrug resistance mechanisms are divided into three categories: drug inactivation through enzyme-catalyzed cleavage, target site modification, and reduced drug buildup through reduced permeability or increased drug efflux or by forming biofilms suppress host immune response and drugs hinder pathogens [7].

The lack of innovative, powerful antibacterial agents is associated with an increase in MDR. Repeated use of antibiotics for resistant infections can harm patients by causing serious side effects, such as organ failure, and postponing recovery and treatment for a period of time [39]. To combat and prevent MDR development, a worldwide approach and multisectoral collaborative strategy are required [41]. Efforts could be focused on improving the efficacy of currently available antimicrobials through combination therapies, bacteriophage therapy, antimicrobial adjuvant therapy, or the use of nanotechnology [44], antimicrobial peptides, and photodynamic light therapy treatment has also been extensively reported [7].

Antibiotic in combination for overcoming multidrug resistant pathogens

Combining antibiotics in-vitro results in a greater therapeutic impact than individual medications. The most potent impact of combination therapies is their ability to revive the potency of old antibiotics against organisms that have already developed resistance to them, it also increases the range of coverage [7, 45]. Every year, the ESKAPE develop resistance to one or two antibiotics used in combination due to not only the selection of antibiotic-resistant strains but also the transfer of genes from them to sensitive organisms [7]. The issue of antibiotic resistance has escalated to the point where it is imperative to explore combinations of newly developed antibiotics or utilize last-resort antibiotics, to assess their efficacy in antimicrobial treatment. The Gram-positive representatives within the ESKAPE pathogens were evaluated with a blend of Fosfomycin and daptomycin, revealing a successful resolution of the infection. Fosfomycin, a wide-ranging antibiotic, displayed encouraging efficacy against Gram-negative bacteria, whereas daptomycin, a final line of defense antibiotic, was utilized for Gram-positive infections. Typically, in vitro experiments involving S. aureus have predominantly incorporated daptomycin or vancomycin, often in conjunction with other antibiotics such as cefazoline. The efficacy of these combinations, results in the successful eradication of S. aureus infections with no or minimal toxicity [7]. Carbapenems were once heralded as the most potent broad-spectrum β-lactam antibiotics for combating multidrug-resistant (MDR) Gram-negative bacteria. However, the emergence of carbapenem-resistant bacteria has become a pressing

concern, driven by resistance mechanisms such as mutations occurring in various chromosomal loci or the horizontal acquisition of resistance genes [46, 47]. Therefore, colistin (polymyxin E) and tigecycline have emerged as two antibiotics now classified as the "last resort" for treating carbapenem-resistant bacteria [7, 47]. However, paralleling the escalating usage of these two drugs, there has been a surge in reports of colistin- or tigecycline-resistant bacteria over the past five years [47, 48].

The benefits of reasoned antibiotic combination therapy compared to monotherapy are summarized in the following: broad-spectrum efficacy, resistance prevention, synergistic action, enhanced uptake and sequential blockage, reduced toxicity, and mortality. Certainly, there are drawbacks associated with the usage of these combinations, including Antagonism potentially resulting in the conversion of bactericidal agents to bacteriostatic ones, broad-spectrum antibiotics encouraging the overgrowth of Clostridium difficile, there is risk of fungal overgrowth, possibility of drug-drug interactions, and chance of drug toxicity [49].

Antibiotic Adjuvants

Antibiotic adjuvants have emerged as a promising strategy to tackle MDR pathogens by collaborating synergistically with antibiotics [7, 50]. Antibiotic adjuvants, which are non-antibiotic substances that target bacterial resistance, can be paired with antiquated drugs to improve the therapy regime [51]. Such compounds restore or boost the effectiveness of routinely used antibiotics against MDR bacteria by impeding the mechanisms responsible for conferring resistance, by enhancing their penetration into bacterial cells, augmenting their stability, or inhibiting efflux pumps that actively expel antibiotics from bacterial cells [50, 52]. Although the discovery of novel antibiotics remains crucial, the utilization of alternative approaches, such as implementing adjuvants to combat antibiotic resistance, offers an effective yet often overlooked strategy [53].

Direct-acting adjuvants directly target mechanisms involved in antibiotic resistance, while indirect resistance breakers act on pathways or processes that indirectly affect bacterial resistance mechanisms. Examples of both types are summarized in Figure 2.

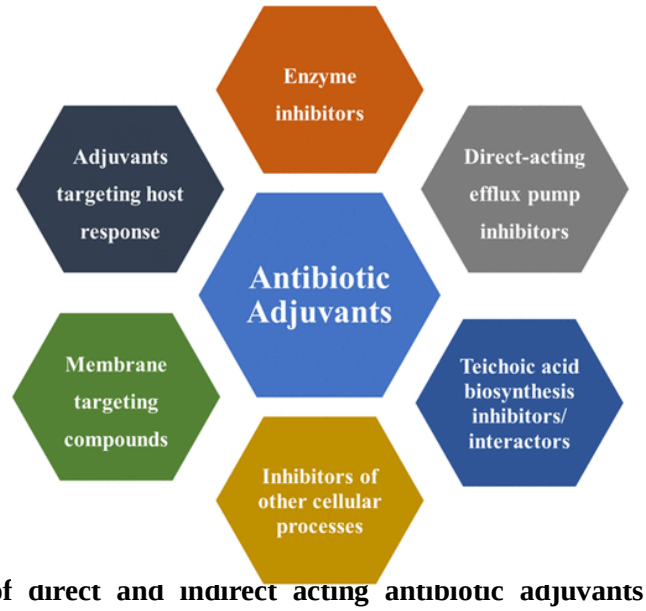

Figure 2: Examples of direct and indirect acting antibiotic adjuvants for tackling Multidrug resistant (MDR) pathogen [51; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10061514/].

Nanoparticles

Using nanoparticles (NPs) as alternatives for treating bacterial infections is an innovative approach that has gained considerable attention in recent years. NPs are made up of objects that range in size from 1 to 100 nanometers (nm) [39, 54]. Metals and metal oxide NPs seem to hold the most potential and have caught the attention of many researchers [55].

Metal oxide NPs are one of the most examined and studied families of NPs and are known to efficiently reduce the growth of a broad spectrum of susceptible as well as resistant Gram-positive and Gram-negative bacteria, developing as potential alternatives for combating MDR bacteria [56]. The most seriously investigated metal nanoparticles are gold NPs and silver NPs [55]. Gold nanoparticles have ideal antibacterial activity and biosafety, which makes them antibacterial alternatives [57]. Nanoparticles have received considerable attention due to their wide use in the agricultural sector, pharmaceuticals, consumer items, transportation, energy, cosmetics, and, most critically, as antibacterial agents [55]. They have several properties that make them attractive as carriers for drugs to treat disease-causing microorganisms. Also, increased drug solubility and stability, ease of manufacturing, biocompatibility with target agents, and regulated release, which can be regulated through stimulation such as light, pH, and heat [56]. In addition, Nps have been examined as an adjuvant for improving antibiotic stability and efficacy. Different forms of NPs have sparked significant interest in their ability to improve medication availability and targeting efficacy, thus improving antibiotic effectiveness [50, 58].However, reports on nanoparticle-resistant bacteria are steadily arising. Its widespread application increases the possibility of resistance to such potential compounds. Actually, incorporating NPs with antibiotics may help decrease bacterial resistance [55].

Antimicrobial peptides therapy

Antimicrobial peptides (AMPs) are naturally occurring molecules found in various organisms, including humans, animals, plants, and bacteria. AMPs exhibit broad-spectrum antimicrobial activity against bacteria, fungi, viruses, and even parasites [7, 59]. Equine antimicrobial peptides, including lysozymes, cathelicidins (eCATH-1, -2, -3), defensins (α- and β-defensin), neutrophilic AMP, NK-lysin, psoriasin, hepcidin, and equinins, are now being studied [60, 61].With the rise of MDR, extensively drug-resistant(XDR), and pandrug-resistant (PDR) bacteria, there has been increasing interest in exploring AMPs as potential therapeutics for combating drug-resistant infections [59]. One key advantage of AMPs is their ability to disrupt bacterial cell membranes, a mechanism that is distinct from traditional antibiotics and less prone to resistance development. Additionally, AMPs exhibit immunomodulatory effects, enhancing the host immune response and promoting tissue repair [59, 62]. AMPs also work synergistically with traditional antibiotics, neutralize toxins, and are effective in animal models [62]. They primarily exert their antimicrobial action against MDR bacteria through membrane disruption and cell lysis [62, 63].

Indeed, the combination of NPs and AMPs represents a potentially promising technique for treating infections, particularly those caused by MDR bacteria. Polymer-based NPs are widely used alongside AMPs to treat illnesses such as sepsis, pulmonary infections, and different bacterial infections [63].

Bacteriophage therapy

The investigation of bacteriophage (Bps) particles could shed light on the invention of novel biotechnology items [64]. Bps, classified as viruses that infect and destroy bacteria, are an exciting approach for tackling antibiotic-resistant bacteria. These viruses, which multiply within bacterial cells have the potential to be an important advance in overcoming bacterial diseases [41, 65]. They tend to be highly specific, with the majority infecting only one type of bacteria. It penetrates bacterial cells by adhering to certain receptors on the host cell's surface that make them ideal candidates to treat bacterial infections [66]. More specifically, after a Bp connects to a susceptible host, it uses one of two replication mechanisms: lytic or lysogenic replication (Figure 3) [67]. During the lytic phase, the phage duplicates, and recently replicated phage parts kill the bacteria before attacking more bacteria [68]. While lysogenic phages incorporate into the host genomes and transmit them to their offspring during replication [69]. The most likely possibilities for phage therapy innovation seem to be obligately lytic phages [69].

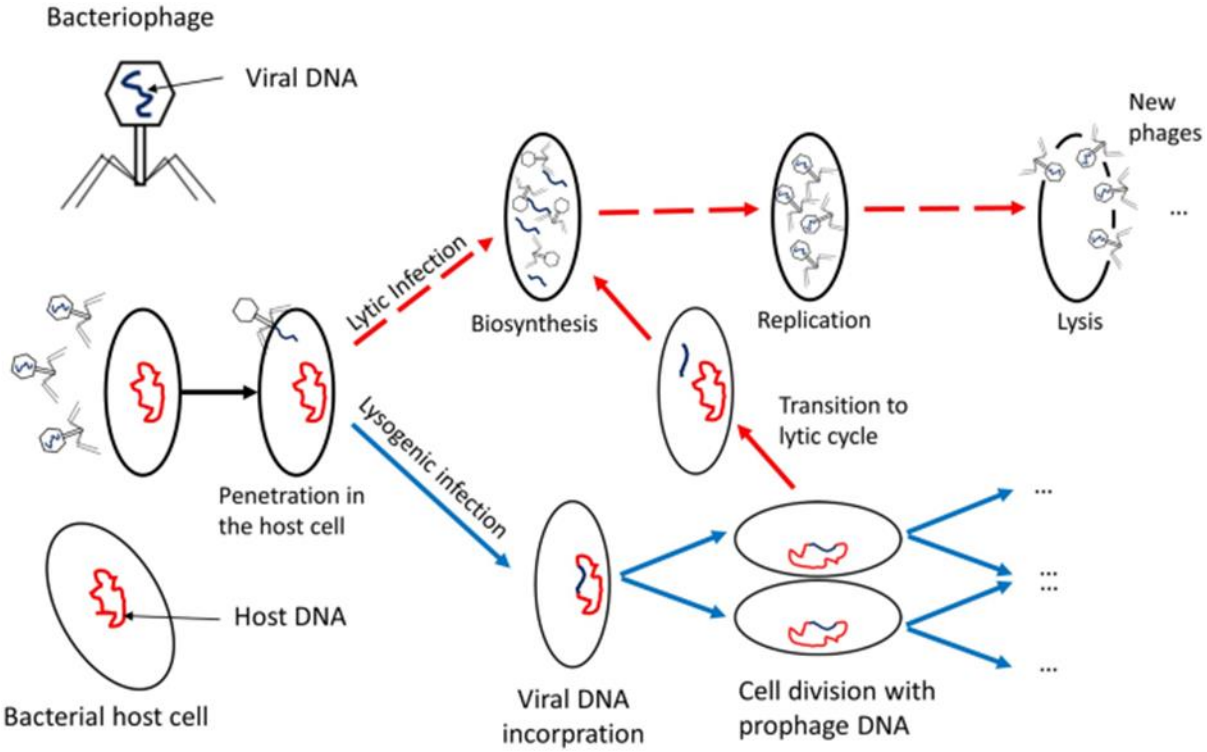

Figure 3: The lytic and lysogenic phase of bacteriophages [70; https://www.nature.com/articles/s41598-021-83773-1].

Overall, phages have a high level of ge netic variation, and each phage only infect s one type of bacteria [41]. Large phages have genomes that are 200 Kbp or more. They can infect a wide variety of bacteria and maintain a permanent infection [71]. They can be found in a variety of natural niches, including oceans, lakes, sand, soil, plants, and the gastrointestinal tract of humans [41]. They are being recognized, isolated, and developed as therapeutically acceptable drugs, all while being subjected to stringent quality control [68]. Collecting effluent fluid from a significantly larger sewage treatment facility would very likely have resulted in greater phage diversity [72].

Several investigations on the use of Bp *in-vitro*, in experimental animals, and in humans have been carried out in the United States and Europe [73]. As a result, therapeutic phages are administered in a variety of ways, including intravenous, oral, nasal, rectal, vaginal, and topical delivery, as well as joint or muscle injection and inhalation [41].However, phage therapy has major drawbacks due to a limited host range, lysogenic phenomena, a lack of relevant laws, and a lack of pharmacokinetic data [74]. The drawbacks of phage therapy versus antibiotics are that you must first identify an etiological element producing a disease by cultivating a sample, and then identify a pathogen using microbiological diagnostic techniques [66]. Loss-of-function mutations in genes involved in capsule production were found in phage-resistant mutants, resulting in capsule degradation and disruption of phage adsorption [75].

Monophage therapy requires confirming the phage's activity against disease-causing bacteria in vitro before administering it to patients, which can be a difficult and costly process, using phage cocktail for different bacterial species can avoid this issue [7]. Previous research has shown that a bacteriophage cocktail can postpone the development of bacteriophage-resistant bacterial strains while also improving therapeutic efficiency [67]. This diverse phage combination served as the foundation for a phage cocktail, which displayed improved efficacy in preventing the development of phage resistance, as demonstrated by the significant stability gained by 3- and 4-phage combinations [76]. These combinations provide a wider range of action than a single phage particle and prevent resistance from developing quickly [68]. Also, the combination of phages and antibiotics used in therapeutic regimens reduces the development of resistant copies, which results in decreased usage of multiple antibiotics [77]. Figure 4 highlights the primary drawbacks of each alternative treatment that has been thoroughly reviewed in the previous sections.

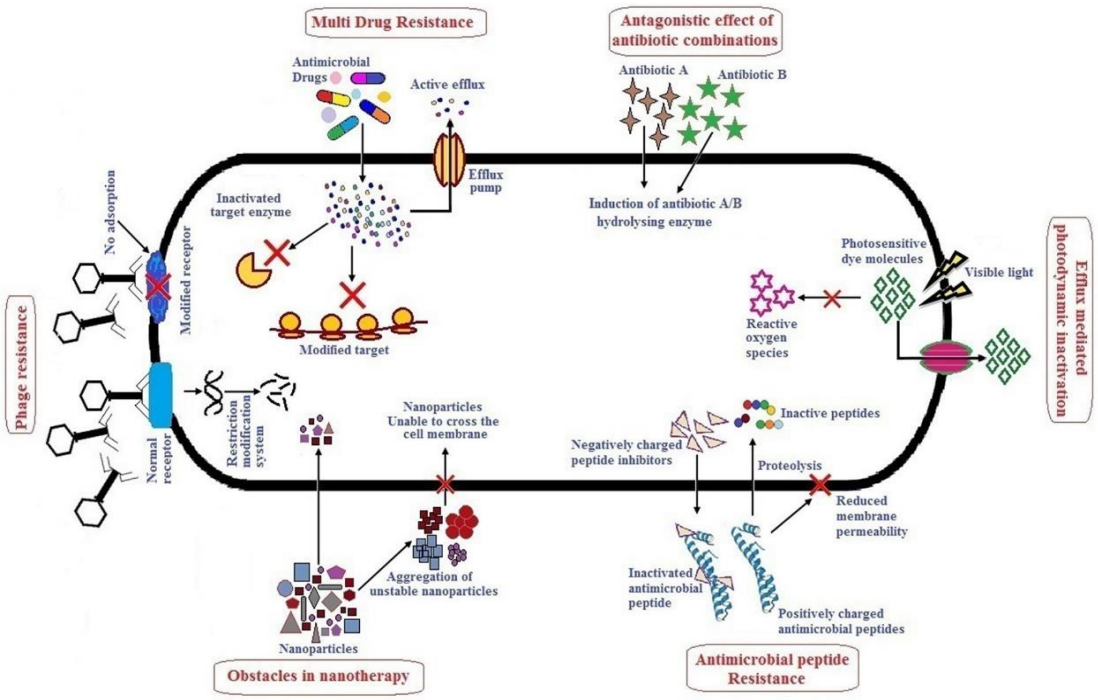

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Figure 4: The limitations of each alternative therapy [7; https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2019.00539/full].

Application of different approaches for overcoming bacterial infections in Equine

Antimicrobial resistance has become one of the most critical concerns facing the health-care system currently, posing a significant threat to public health [78]. As a result, various unique alternative tactics for combating these MDR bacteria have been developed [3]. These alternative techniques are summarized in Table 2.

Alternative Approaches	Types	Bacterial strains	Outcomes	Testing method	Reference
Antimicrobial peptides	1-alpha-helical equine antimicrobial peptide eCATH1.	*R. equi*	eCATH1 decreased the number of bacteria within macrophages in vitro while in mice it resulted in reduction in number of bacteria compared to that obtained when treated by Rifampin.	In-vitro and in-vivo tests by inducing rhodococcosis in mice.	[79]
	2-Two AMPs[1], eCATH1 and DEFA1.	*R. equi* and its associated pathogens (*K. pneumoniae* or *S. zooepidemicus*).	Cause inhibition of *R. equi* and *S. zooepidemicus* at low micromolar concentrations and eCATH1 inhibit growth of *K. pneumoniae.*	Evaluation of 2 AMPs to control *R. equi* in single or co-infections.	[80]
	3-A biomimetic substance (Ceragyn).	against *S. equi subsp. zooepidemicus, E. coli, K. pneumoniae* and *P. aeroginosa* in free-floating state only.	Studies have yielded promising results.	In-vitro examination of its efficacy against bacteria causing equine endometritis and used as uterine infusion and as a lavage device.	[81]
Bacteriophages	1-Bacteriophage cocktail	*E. coli, S. aureus, Streptococcus* species., *Diplococcus* species., *P. aeruginosa*	Effective in a short period	Treating ulcerative keratitis in 30 horses.	[36]
	2-combination of ciprofloxacin with commercial phages (Pyophage or Pyophage + Staphylococcal phage followed by 1 mg/L of ciprofloxacin)	*P. aeruginosa* and *Methicillin-resistant S. aureus* (MRSA).	Complete elimination of dual-species biofilms.	*S. aureus/P. aeruginosa* dual-species biofilms *in- vitro*.	[82]

	3-A cocktail of two phages *Myoviridae* and *Podoviridae* phages	*P. aeruginosa*	Inhibit bacteria	Keratitis mouse model.	[35]
	4-Two lytic phage combination	*S. aureus*	100% in vitro inhibition coverage.	In-vitro phage susceptibility test.	[67]
Nanoparticles	1-green and chemical ZnO-NPs[2] gels.	----------	Clinically evaluated for 3 weeks after the start of the application of the gel.	Animals were topically treated with NPs and monitored for 3 weeks.	[83]
	2-Nebulized AgNP[3]	*Streptococcus equi subsp. zooepidemicus and Actinobacillus equuli subsp. equuli* isolated from respiratory tract.	Both low and high doses of AgNP completely inhibited bacterial growth in *A. equuli* and *S. zooepidemicus*, respectively	Bacterial growth inhibition by AgNP on agar media after instillation and nebulization.	[84]
	3-AgNP	*E. coli* isolated from horse manure.	The examined=AgNP has high antibacterial capabilities, which increase with concentration.	Disk diffusion method.	[85]
	4-AgNP complexes	Controlling *R. equi* the causative agent of pneumonia in horse.	AgNP complexes have a considerable effect on the survivability of *R. equi* when cultivated in pure culture.	In-vitro examination of viability of bacterial and host cells when cultivated in media containing AgNP by counting colony forming unit per milliliter (CFU/ml).	[86]

Table 2: Summary of alternative approaches for overcoming multidrug resistant bacteria causing infections in equine.
[1]AMP: Antimicrobial peptides, [2]ZnO-NP: Zinc Oxide-nanoparticles, [3]AgNP: Silver nanoparticles.

Conclusions and future perspective

Antimicrobial resistance continues to develop and spread throughout all boundaries. Hence, there is an urgent need to develop novel approaches for reducing the spread of infectious diseases to protect human and animal health. The illegal advocate for antibiotics needs to be curbed and efforts to reduce overuse and misuse must be implemented. Fortunately, numerous new approaches are being investigated to combat current and emerging resistance of bacteria causing equine diseases. Employing combinatorial methods in which two or more therapies are employed together such as antibiotics combined with adjuvants, phages, antimicrobial peptides, and nanoparticles are recommended to enhance the effectiveness of treatments and lessen their limitations.

Conflict of Interest: The authors have no conflict of interest to declare.

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الملخص العربي
العلاجات البديلة لمكافحة البكتيريا المقاومة للأدوية المسببة للعدوى في الخيول

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تلعب الخيول دورًا هاماً في العديد من الأنشطة البشرية. ومع ذلك، فهم عرضة للإصابة بالعدوى البكتيرية، مما قد يؤثر بشكل خطير على صحتهم ونشاطهم. يتم علاج هذه الأمراض باستخدام المضادات الحيوية. ومع ذلك، فإن التكرار المتزايد لمقاومة المضادات الحيوية يشكل مصدر قلق كبير لأنه يقلل من فعالية العلاجات الحالية، مما يؤدي إلى زيادة فترة العلاج، وزيادة التكاليف البيطرية، وارتفاع معدلات الوفيات، ويحتمل أن يهدد صحة الإنسان من خلال انتقال الأمراض الحيوانية المنشأ. وبالتالي، هناك اهتمام متزايد بتطوير أدوية بديلة لمعالجة الالتهابات البكتيرية في الخيول. وتشمل هذه البدائل استخدام العاثيات والببتيدات المضادة للميكروبات والجسيمات النانوية. قد يساعد دمج العلاجات البديلة في الممارسات البيطرية أيضًا في تقليل الاعتماد على المضادات الحيوية والحفاظ على فعالية المضادات الحيوية الحالية للأجيال القادمة. تهدف هذه العلاجات إلى توفير مكافحة فعالة للعدوى مع تقليل احتمالية مقاومة المضادات الحيوية. أوضحت هذه المراجعة مسببات الأمراض المقاومة للأدوية المتعددة التي تسبب أمراضًا مختلفة في الخيول على مستوى العالم، وفعالية ومزايا وتطبيقات وقيود العلاجات المبتكرة أو الناشئة أو المتطورة قيد البحث حاليًا والتي قد تقدم حلولاً محتملة لمكافحة البكتيريا المقاومة للأدوية المتعددة في الخيول. يعد البحث والابتكار المستمر في هذا المجال من الدراسة ضروريين للحفاظ على إدارة صحة الخيول على المدى الطويل ومعالجة التأثيرات الأوسع على صحة الحيوان والإنسان.