JOAVM
Journal of Alternative Veterinary Medicine
joavm.kazerun.iau.ir

Review Article

Islamic Azad University
Kazerun Branch
Fars, Iran

Enzybiotics, a Promising Era in Confronting Bacteria in the Poultry Industry

Gholam Hossein Habibi*

Department of Clinical Sciences, Faculty of Veterinary Medicine, Kazerun Branch, Islamic Azad University, Kazerun, Iran

Received: 15/Jun/2023 Revised: 06/Aug/2023 Accepted: 19/Aug/2023

Abstract

Since the discovery of antibiotics, they have been used widely for disease control. Antibiotics were also found to be useful in growth promotion in the poultry industry. However, their overuse and misuse have led to bacterial resistance against them. Antibiotic resistance is a global issue that results in considerable health and economic losses. Marked antibiotic resistance against various antibiotics has been observed in poultry infections. To counteract the burdens of antibiotic resistance, various alternatives for antibiotics are being studied. These alternative approaches have also been subjects of interest in the poultry industry, as poultry infections result in dramatic economic loss, and in cases of zoonotic infections, the transmission of infection from chicken leads to dramatic health burdens in humans. Phage therapy, probiotics, and anti-microbial peptides administration are some examples of these alternative approaches. Another antibiotic alternative approach is called “enzybiotics”. In enzybiotics, peptidoglycan hydrolases (endolysins) are used to degrade bacterial cell walls. These enzymes are mostly found in bacteriophages’ genomes because bacteriophages have to degrade the peptidoglycan layers of bacteria both to enter and exit their bacterial host. Bacterial genomes also contain some regions with peptidoglycan hydrolase properties which help bacteria in growth and division. The properties of various peptidoglycan hydrolases have been studied to find the more potent and applicable ones for future uses. Due to their advantages, endolysins are promising antibiotic alternatives. In this review, we will discuss the role of enzybiotics in the poultry industry. Also, endolysin advantages and limitations of their administration are discussed here.

Keywords: *Enzybiotics, Endolysin, Peptidoglycan hydrolase, Clostridium perfringens, poultry, Antibiotic resistance*

Cite this article as: Gholam Hossein Habibi. Enzybiotics, a promising era in confronting bacteria in the poultry industry. J Altern Vet Med. 2024; 7(20): 1202-1211.

[DOI: 10.61186/joavm.7.20.1202]

**** Corresponding Author***
Department of Clinical Sciences, Faculty of Veterinary Medicine, Kazerun Branch, Islamic Azad University, Kazerun, Iran.
E-mail: habibigh42@yahoo.com , Orcid: https://orcid.org/0000-0002-9239-1277

Introduction

Bacterial infections are among the major causes of global health burden (Antimicrobial Resistance Collaborators, 2022). In 2019, 13.7 million deaths were linked to bacterial infections (Antimicrobial Resistance Collaborators, 2022). Besides their role in human diseases, bacteria also cause dramatic effects on the veterinary industry. Approximately 50% of the mortality rate of the broilers in the first week of their lives seems to be caused by bacterial infections. Bacterial diseases contribute to half of the non-outbreak-related broilers' mortality rate. Additionally, bacteria-induced outbreaks increase broilers' mortality dramatically (Thøfner & Christensen 2021). Antibiotic discovery has provided remarkable benefits to societies, both in saving human lives and in decreasing economic losses (Hegemann *et al.,* 2023; Ogwuche *et al.,* 2021). Moreover, antibiotics benefited us in the field of veterinary due to their usage as animal growth promoters (Dibner & Richards 2005). Unfortunately, antibiotic overuse and misuse have contributed to a notable surge in antibiotic resistance (Organization World Health, 2017). About 5 million deaths in 2019 were found to be associated with bacterial resistance (Antimicrobial Resistance Collaborators, 2022). In the poultry industry, besides the treatment failure-caused economic losses, antibiotic resistance is considered a threat to human health, due to resistant zoonotic pathogen transfer (Nhung *et al.,* 2017). Regarding the dangers of antibiotic resistance, the USA, Europe, and China banned antibiotic usage as animal growth promoters in 2017, 2006, and 2020, respectively (Dibner & Richards 2005; Centner, 2016; Hu & Cowling, 2020). The application of an antibiotic alternative is another solution to combat bacterial infections without increasing antibiotic resistance (Murray *et al.,* 2021). Some antibiotic alternatives are probiotics, antimicrobial peptides, phage therapy, and enzybiotics (Łojewska & Sakowicz 2021; Murray *et al.,* 2021).

Enzybiotics

Enzybiotics definition consists of two words, antibiotics and enzymes. This category of antibacterials is comprised of enzymes with the ability to kill bacteria. Peptidoglycan hydrolases are a subtype of enzybiotics. Peptidoglycan hydrolases degrade bacterial cell walls by targeting the peptidoglycan layer of the bacteria. These enzymes are named endolysins and are mostly found in the bacteriophage genome. Bacteriophages use endolysins both for entering their host bacteria and exiting their progeny phages after a lytic cycle (Danis-Wlodarczyk *et al.,* 2021). Another source of peptidoglycan hydrolases is the prophage region of the bacterial genomes (Evseev *et al.,* 2023). Some sequences with hypothetical peptidoglycan hydrolase properties are found in the prophage region of many bacterial genomes. Peptidoglycan hydrolases are also needed for cell wall remodeling and division. These peptidoglycan hydrolases are named autolysins (Leonard *et al.,* 2023). According to the site of action of the peptidoglycan hydrolases on their target peptidoglycan layer, scientists divide these enzymes into 5 groups, including muramidase, glucosaminidase, endopeptidase, amidase, and lytic transglycosylase (Sekiya *et al.,* 2021a).

Endolysin structure

The endolysins that target gram-positive bacterial cell walls are composed of at least an enzymatically active domain (EAD) with peptidoglycan hydrolase properties in the N-terminal region, and a cell wall binding domain (CBD) in the C-terminal region, which helps in recognition of the target bacteria (Figure 1a) (Schmelcher *et al.,* 2012). In contrast, gram-negative bacterial endolysins don't contain CBD; however, the majority of them contain a C-terminal portion rich in charged amino acid residues (Ghose & Euler 2020). These charged portions help the endolysin in destabilizing the target bacteria's lipopolysaccharide (LPS) layer, thus facilitating the arrival of the endolysins to their site/place of action (Figure 1b) (Gutiérrez & Briers 2021).

Endolysin advantages

Both bacteriophages and endolysins have narrow host ranges, so commensal bacteria will be immune from unwanted eradication (Murray *et al.,* 2021). Bacteriophages are only capable of destroying their host bacterial strain; whereas, the bacteriophage endolysin host range is broader to some extent Bacteriophages are only capable of destroying their host bacterial strain; whereas, the bacteriophage endolysin host range is broader to some extent (Wang *et al.,* 2022).

[DOI: 10.61186/joavm.7.20.1202]

Figure 1. Endolysin structure. (a) Endolysin structure in gram-positive bacteria. (b) Endolysin structure in gram-negative bacteria.

Endolysins are preferred to phages because endolysins are usually less immunogenic. Moreover, some endolysins are capable of penetrating eukaryotic cells (Liu *et al.,* 2023a). So, unlike phages, endolysins can be used against intracellular bacteria (e.g. *Salmonella* species) (Liu *et al.,* 2023a; Diacovich *et al.,* 2017). There is a low risk for the development of resistance against endolysins (Rahman *et al.,* 2021). Although endolysins are promising factors to combat bacterial infections, they need much more investigation to reach the market (Schmelcher & Loessner 2021).

Bacterial infections in the poultry industry

The poultry industry is a widespread food industry, as more than 90 billion tons of chicken meat are produced annually (FAO, 2020). The average global amount of poultry meat consumption in 2011 was 14.5 kg per capita with an increasing trend over the years (Wahyono & Utami 2018). In Iran, the average poultry meat consumption was estimated to be 23 kg per capita (Ranaei *et al.,* 2021). One reason for their considerable production rate is that poultry industry costs are relatively reasonable. But it is notable that due to the improper use of antibiotics in poultry farming, antibacterial resistance has grown to a dangerous point (Nhung *et al.,* 2017). The most burdensome bacterial infections in poultry are caused by *Salmonella* species, Avian Pathogenic *Escherichia coli* (APEC), *Campylobacter jejuni*, *Clostridium perfringens*, *Clostridium botulinum*, *Pasteurella multocida*, and *Mycoplasma gallisepticum* (El-Saadony *et al.,* 2022; Kemmett *et al.,* 2014; Al Hakeem *et al.,* 2022; Ali & Islam 2021; Sato *et al.,* 2016; Li *et al.,* 2020; Awad *et al.,* 2022). The resistant bacteria increase poultry production costs because antibiotic usage becomes ineffective against them and they increase mortality rates in poultry. Antibiotic resistance in Avian Pathogenic *Escherichia coli* against amoxicillin, ampicillin, and tetracycline was more than 80% in several studies (Nhung *et al.,* 2017). In our previous study, we examined the antibiotic resistance of *Escherichia coli* extracted from yolk sac infections. We found that antibiotic resistance against ceftiofur and gentamycin was 42.5% and 40%, respectively. Additionally, 70% antibiotic resistance against colistin and phosphomycin was observed in *Escherichia coli*; whereas, its resistance against sultrim, fluorophenicol, and erythromycin was 90% (Habibi & Ziyaii 2021). *Salmonella* isolates that were found in raw poultry meat showed 21.44-32.6% resistance against the cephalosporin family (Castro-Vargas *et al.,* 2020). *Campylobacter jejuni* strains' resistance against ciprofloxacin, nalidixic acid, and tetracycline was 92.5%, 88.9%, and 68.4%, respectively (Wieczorek *et al.,* 2018). Resistance of *Clostridium perfringens* isolates against doxycycline and oxytetracycline was 98% and 71%, respectively (Osman & Elhariri 2013).

Clostridium perfringens-induced necrotizing enteritis in poultry costs $6 billion each year (Yuan *et al.,* 2022). In addition to infection-related increased mortality rates in poultry, zoonotic pathogens contribute to foodborne diseases in humans *Campylobacter jejuni*-induced foodborne diseases cost $6.9 billion each year. Additionally, $2.8 billion is spent on combating foodborne infections caused by *Salmonella* species (Scharff, 2020).

[DOI: 10.61186/joavm.7.20.1202]

Endolysins against bacterial infections in poultry

Here, we explain some of the endolysins which were studied against burdensome bacterial infections in the poultry industry.

***Clostridium perfringens* endolysins**

The effects of various endolysins against *Clostridium perfringens* have been studied so far. The list of *Clostridium perfringens* endolysins and their properties are shown in Table 1. The optimal temperature and pH level for their activity varies between the endolysins. Hence, each endolysin reaches its highest activity in a specific condition (Jeong *et al.,* 2023). For example, an endolysin that is designed to be eaten by chicken must resist low pH levels of the gizzard (pH∼3) and intestine (pH∼6-6.8) (Swift *et al.,* 2015). Here, we mention some examples of reasonable endolysins for each condition. NaCl concentration in raw meat and fish is approximately 10 mM, so ZP173 can be used as a food preservative in them. The pH level of most meat-based foods is below 7; as a result, PlyCP39O and CP25L are not good preservative options in such a situation.Till now, only one antibacterial agent (nisin) has been approved by U.S. Food and Drug Administration (FDA) to be used as a food preservative. Two endolysins (Psm and ZP173) were found to have stronger antibacterial effects than nisin; therefore, they are promising agents for being used as food additives in the future (Kazanavičiūtė *et al.,* 2018).

Besides the existence of natural endolysins, scientists are using biotechnological approaches (e.g. chimeragenesis and mutagenesis) to make endolysins with improved functions (Heselpoth *et al.,* 2021). For oral use of the endolysins in the poultry industry, a plant-based endolysin expression system can be used instead of *E. coli*-based systems (Kazanavičiūtė *et al.,* 2018). Unlike *E. coli*- based systems, plant-based systems don't need endolysin purification and they work more efficiently in expressing endolysins (Hammond *et al.,* 2019; Kazanavičiūtė *et al.,* 2018). Using a gut-colonizing bacteria which is genetically engineered to express endolysin is another way to bring endolysins to the gastrointestinal tract. The expression system must be strong and work continuously. A previous study used an engineered *Lactobacillus johnsonii FI9785* which expressed CP25L (Gervasi *et al.,* 2014).

In addition to their role in killing bacteria, endolysins can be used for diagnosing bacteria in contaminated foods (Ha *et al.,* 2018).

Other endolysins

Salmonella spp. endolysins seem to lyse a broader range of bacterial species. Outer membrane permeabilizers (OMPs) (e.g. malic acid, EDTA, and citric acid) help *Salmonella* species endolysins in the elimination of bacteria. In the same conditions, adding citric acid to Lys68 resulted in a 2.89±0.27 Log reduction of *Salmonella Typhimurium* LT2; whereas, using Lys68 (without OMP) contributed to 0.14±0.16 log reduction of *Salmonella Typhimurium* LT2 (Oliveira *et al.,* 2014).

During *Salmonella pullorum* infection of poultry, LySP2 administration reduced the mortality rate significantly compared to the control group (Deng *et al.,* 2023). For combating *Campylobacter jejuni*, Zampara et al. made innolysins, by fusing an endolysin to a phage receptor binding protein (RBP) (Zampara *et al.,* 2021).

Conclusion

As antibiotic resistance is growing fast, antibiotic alternatives are receiving special attention (Murray *et al.,* 2021; Organization World Health, 2017). Nowadays, various types of antibacterials (e.g. endolysin administration) are being tested to find a solution for counteracting the burdens of antibiotic resistance (Murray *et al.,* 2021). Some endolysin features like their "narrow host range", "low immunogenicity", and "low probability of bacterial resistance development against them" are among the factors that make them potentially applicable antibacterials for the future (Murray *et al.,* 2021; Rahman *et al.,* 2021; Liu *et al.,* 2023b). Endolysin administration also faces some limitations, for example, in gram-negative bacterial species, endolysin causes a release of the LPS layer into the bloodstream and might contribute to cytokine storm (Briers *et al.,* 2011; Meng & Lowell 1997).

Most of the endolysin-related research is conducted *in vitro* (Murray *et al.,* 2021). Engineering methods are also an important part of making efficient endolysins. Collectively, it must be noted that we're just at the start of the road of endolysin administration and several additional studies are

[DOI: 10.61186/joavm.7.20.1202]

Endolysin	Source	Predicted enzymatic activity	Additional information	References
LysCPAS15	Bacteriophage CPAS-15	Amidase	- Optimum pH = 2-10 - Optimum temperature = <50 °C - After adding a CBD to LysCPAS15, the chimer was stable in temperature<60 °C, and in pH range between 4-12	(Cho *et al.,* 2021)
Ply3626	Bacteriophage phi3626	Amidase	-	(Zimmer *et al.,* 2002)
CP25L	prophage region of *C. perfringens* 5416–97, vB_CpeS-CP51	Amidase	- Optimum pH = 7.5 - Optimum NaCl concentration = 200-500 mM - Optimum temperature = 4-25 °C (its activity unchanged for 2 days in 37 °C but 30 min incubation in 65 °C inactivated CP25L)	(Gervasi *et al.,* 2014; Kazanavičiūtė *et al.,* 2018)
Psm	Episomal phage phiSM101	Muramidase	- Optimum pH = 6.5-7 - Optimum NaCl concentration = 250 mM	(Nariya *et al.,* 2011)
PlyCP10	Prophage region of *C.perfringens* Cp10	Muramidase	- Optimum pH = 6 - Optimum temperature = 4-42 °C - Optimum NaCl concentration = 50-100 mM	(Swift *et al.,* 2018)
PlyCP41	Prophage region of *C.perfringens* Cp10	Muramidase	- Optimum pH = 6.5 - Optimum temperature = 4-42 °C (but it was more thermostable than PlyCP10) - Optimum NaCl concentration = 50-100 mM (but 60% of its activity was retained in 600 mM)	(Swift *et al.,* 2018)
PlyCM	Prophage region of *C. perfringens* ATCC 13124	Muramidase	- Optimum pH = 6.4 - Optimum temperature = 35-45 °C	(Schmitz *et al.,* 2011)
Acp	*C. perfringens* strain 13	*N*-acetylglucosaminidase	-	(Camiade *et al.,* 2010)
PlyCP39O	*C. perfringens* phage phiCP39-O	Amidase	- Optimum pH = 8.2	(Simmons *et al.,* 2010)
PlyCPS2	Phage CPS2	Amidase	- Optimum pH = 7.5-10 - Optimum temperature = 25 °C - Optimum NaCl concentration = up to 500 mM	(Ha *et al.,* 2018)
PlyCP26F	*C. perfringens* phage phiCP26F	Amidase	- Optimum pH = 6.8	(Simmons *et al.,* 2010)
Psa	prophage region of *C. perfringens* st13	Amidase	- Optimum temperature = 37 °C - Optimum NaCl concentration = 300 mM	(Sekiya *et al.,* 2021b)
GVE2EAD-CP26FCBD	Chimeragenesis	Amidase	- Optimum temperature = 22 °C (95% of its activity retained after incubation in 50°C for 30 min) - Optimum pH = 8 - Optimum NaCl concentration = 10 mM	(Swift *et al.,* 2015; Swift *et al.,* 2019)
ZP278	*C. perfringens* CPE str.4969, prophage region	Muramidase	- Optimum pH = 4-8 - Optimum NaCl concentration = 500 mM	(Kazanavičiūtė *et al.,* 2018)
LysCP28	*C. perfringens* phage, vB_CpeS_BG3P	Muramidase	- Optimum temperature = 37-42 °C - Optimum pH = 7	(Lu *et al.,* 2023)
PlyCpAmi	*C. perfringens* 13124	Amidase	-	(Tillman *et al.,* 2013)
ZP173	*C. perfringens* CPE str.4969, prophage region	Muramidase	- Optimum temperature = 4 °C (More than 70% of its activity retained after 1 week in 37 °C) - Optimum pH = 5.2 - Optimum NaCl concentration = 50 mM and higher NaCl concentrations	(Kazanavičiūtė *et al.,* 2018)
LysCPD9	bacteriophage CPD9	Muramidase	- Optimum temperature = 25 °C - Optimum pH = 6 - Optimum NaCl concentration = 0 mM (50% of LysCPD9 activity was conserved in 500 mM)	(Choi *et al.,* 2023)
ClyY	Chimeragenesis	Muramidase	- Optimum temperature = up to 95 °C - Optimum pH = 5-9 (6) - Optimum NaCl concentration = 0-1000 mM	(Choi *et al.,* 2023)

Table 1. *Clostridium perfringens* endolysins and their properties

[DOI: 10.61186/joavm.7.20.1202]

needed to elucidate all aspects of their usage (Abdelrahman *et al.,* 2021). Till the time of the availability of these antibiotic alternatives on the market, we must consider some points to slower the antibiotic resistance progression. Some of these points are that antibiotics must be prescribed by the in-charge veterinarians, and only after the determination of the antibiogram tests of the bacterial strains (Darboe *et al.,* 2023). It is also beneficial to set a cut-off point for antibiotic residue in poultry tissues for their usage as important human foods. Antibiotic residue can be reduced if we leave a long time between poultry antibiotic consumption and slaughter. This lag (withdrawal time) varies among different antibiotics (Habibi, 2018).

References

Abdelrahman F., Easwaran M., Daramola OI., Ragab S., Lynch S., Oduselu TJ., et al. Phage-Encoded Endolysins. Antibiotics (Basel), 2021; 10(2):124.

Al Hakeem WG., Fathima S., Shanmugasundaram R. and Selvaraj RK. Campylobacter jejuni in poultry: pathogenesis and control strategies. Microorganisms, 2022;10 (11): 2134.

Ali MZ. and Islam MM. Characterization of β-lactamase and quinolone resistant Clostridium perfringens recovered from broiler chickens with necrotic enteritis in Bangladesh. Iran J Vet Res, 2021; 22(1): 48-54.

Awad NFS., Hashem YM., Elshater NS., Khalifa E., Hamed RI., Nossieur HH., et al. Therapeutic potentials of aivlosin and/or zinc oxide nanoparticles against Mycoplasma gallisepticum and/or Ornithobacterium rhinotracheale with a special reference to the effect of zinc oxide nanoparticles on aivlosin tissue residues: an in vivo approach. Poult Sci, 2022; 101(6): 101884.

Briers Y., Walmagh M. and Lavigne R. Use of bacteriophage endolysin EL188 and outer membrane permeabilizers against Pseudomonas aeruginosa. J Appl Microbiol, 2011; 110(3): 778-785.

Camiade E., Peltier J., Bourgeois I., Couture-Tosi E., Courtin P., Antunes A., et al. Characterization of Acp, a peptidoglycan hydrolase of Clostridium perfringens with N-acetylglucosaminidase activity that is implicated in cell separation and stress-induced autolysis. J Bacteriol, 2010 May;192(9):2373-84.

Castro-Vargas RE., Herrera-Sánchez MP., Rodríguez-Hernández R. and Rondón-Barragán IS. Antibiotic resistance in Salmonella spp. isolated from poultry: A global overview. Vet World, 2020; 13(10): 2070-2084.

Centner TJ. Recent government regulations in the United States seek to ensure the effectiveness of antibiotics by limiting their agricultural use. Enviro Int, 2016; 94: 1-7.

Cho JH., Kwon JG., O'Sullivan DJ., Ryu S. and Lee JH. Development of an endolysin enzyme and its cell wall-binding domain protein and their applications for biocontrol and rapid detection of Clostridium perfringens in food. Food Chem, 2021; 345: 128562.

Choi Y., Ha E., Kong M. and Ryu S. A novel chimeric endolysin with enhanced lytic and binding activity against Clostridium perfringens. LWT, 2023; 181: 114776.

Danis-Wlodarczyk KM., Wozniak DJ. and Abedon ST. Treating bacterial infections with bacteriophage-based enzybiotics: in vitro, in vivo and clinical application. Antibiotics (Basel), 2021; 10(12): 1497.

Darboe S., Mirasol R., Adejuyigbe B., Muhammad AK., Nadjm B., De St Maurice A., et al. Using an antibiogram profile to improve infection control and rational antimicrobial therapy in an urban hospital in the gambia, strategies and lessons for low- and middle-income countries. Antibiotics (Basel), 2023; 12(4): 790.

Deng H., Li M., Zhang Q., Gao C., Song Z., Chen C., et al. The broad-spectrum endolysin lysp2 improves chick survival after Salmonella pullorum infection. Viruses, 2023; 15: 836.

Diacovich L., Lorenzi L., Tomassetti M., Méresse S. and Gramajo H. The infectious intracellular lifestyle of Salmonella enterica relies on the adaptation to nutritional conditions within the Salmonella-containing vacuole. Virulence, 2017; 8(6): 975-992.

[DOI: 10.61186/joavm.7.20.1202]

Dibner JJ. and Richards JD. Antibiotic growth promoters in agriculture: history and mode of action. Poult Sci, 2005; 84: 634-43.

El-Saadony MT., Salem HM., El-Tahan AM., Abd El-Mageed TA., Soliman SM., Khafaga AF., et al. The control of poultry salmonellosis using organic agents: an updated overview. Poult Sci, 2022; 101(4): 101716.

Evseev P., Lukianova A., Tarakanov R., Tokmakova A., Popova A, Kulikov E., Shneider M, Ignatov A., et al. Prophage-derived regions in curtobacterium genomes: good things, small packages. Int J Mol Sci, 2023; 24(2): 1586.

FAO. Food and Agriculture Organization of the United Nations-FAOStat, Land Use Data, 2020.

Gervasi T., Horn N., Wegmann U., Dugo G., Narbad A. and Mayer MJ. Expression and delivery of an endolysin to combat Clostridium perfringens. Appl Microbiol Biotechnol, 2014; 98(6): 2495-505.

Ghose C., and Euler CW. Gram-negative bacterial lysins. Antibiotics (Basel), 2020; 9: 74.

Gutiérrez D. and Briers Y. Lysins breaking down the walls of Gram-negative bacteria, no longer a no-go. Curr Opin Biotechnol, 2021; 68: 15-22.

Ha E., Son B. and Ryu S. Clostridium perfringens virulent bacteriophage CPS2 and its thermostable endolysin lysCPS2. Viruses, 2018; 10: 251.

Habibi GH. Evaluation of antibiotic residues in the liver of broiler by four-plate method in Kazerun city. J Altern Vet Med, 2018; 2: 273-82.

Hammond RW., Swift SM., Foster-Frey JA., Kovalskaya NY. and Donovan DM. Optimized production of a biologically active Clostridium perfringens glycosyl hydrolase phage endolysin PlyCP41 in plants using virus-based systemic expression. BMC Biotechnol, 2019; 19: 1-10.

Hegemann JD., Birkelbach J., Walesch S. and Müller R. Current developments in antibiotic discovery: Global microbial diversity as a source for evolutionary optimized anti-bacterials. EMBO Rep, 2023; 24: e56184.

Heselpoth RD., Swift SM., Linden SB., Mitchell MS. and Nelson DC. Enzybiotics: Endolysins and Bacteriocins. In: Harper DR., Abedon ST., Burrowes BH., McConville ML. (eds) Bacteriophages., Springer, 2021; PP: 989-1030.

Habibi GH. and Ziyaii M. Isolation of Escherichia coli from the yolk sac of one-day old chicks with their antibiogram in Mashhad-Iran. J Altern Vet Med, 2021; 4(10): 579-585.

Hu YJ. and Cowling BJ. Reducing antibiotic use in livestock, China. Bull World Health Organ, 2020; 98(5): 360-361.

Jeong TH., Hong HW., Kim MS., Song M. and Myung H. Characterization of three different endolysins effective against gram-negative bacteria. Viruses, 2023;15(3):679.

Kazanavičiūtė V., Misiūnas A., Gleba Y., Giritch A. and Ražanskienė A. Plant-expressed bacteriophage lysins control pathogenic strains of Clostridium perfringens. Sci Rep, 2018; 8(1): 10589.

Kemmett K., Williams NJ., Chaloner G., Humphrey S., Wigley P. and Humphrey T. The contribution of systemic Escherichia coli infection to the early mortalities of commercial broiler chickens. Avian Pathol, 2014; 43(1): 37-42.

Leonard AC., Goncheva MI., Gilbert SE., Shareefdeen H., Petrie LE., Thompson LK., et al. Autolysin-mediated peptidoglycan hydrolysis is required for the surface display of Staphylococcus aureus cell wall-anchored proteins. Proc Natl Acad Sci U S A, 2023; 120(12): e2301414120.

Li P., He F., Wu C., Zhao G., Hardwidge PR., Li N., et al. Transcriptomic analysis of chicken lungs infected with avian and bovine pasteurella multocida serotype A. Front Vet Sci, 2020; 7: 452.

Liu, H., Z. Hu, M. Li, Y. Yang, S. Lu, and X. Rao. 2023a. 'Therapeutic potential of bacteriophage endolysins for infections caused by Gram-positive bacteria', J Biomed Sci, 30: 29.

Liu H., Hu Z., Li M., Yang Y., Lu S. and Rao X. Therapeutic potential of bacteriophage endolysins

[DOI: 10.61186/joavm.7.20.1202]

for infections caused by Gram-positive bacteria. J Biomed Sci. 2023b; 30(1): 29.

Łojewska E. and Sakowicz T. An alternative to antibiotics: selected methods to combat zoonotic foodborne bacterial infections. Curr Microbiol, 2021; 78(12): 4037-4049.

Lu R., Liu B., Wu L., Bao H., García P., Wang Y., et al. 2023. A broad-spectrum phage endolysin (LysCP28) able to remove biofilms and inactivate clostridium perfringens strains. Foods, 2023; 12: 411.

Meng F., and Lowell CA. Lipopolysaccharide (LPS)-induced macrophage activation and signal transduction in the absence of Src-family kinases Hck, Fgr, and Lyn. J Exp Med, 1997; 185: 1661-70.

Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022; 399(10325): 629-655.

Murray E., Draper LA., Ross RP. and Hill C. The advantages and challenges of using endolysins in a clinical setting. Viruses, 2021; 13(4): 680.

Nariya H., Miyata S., Tamai E., Sekiya H., Maki J. nad Okabe A. Identification and characterization of a putative endolysin encoded by episomal phage phiSM101 of Clostridium perfringens. Appl Microbiol Biotechnol, 2011; 90(6): 1973-9.

Nhung NT., Chansiripornchai N. and Carrique-Mas JJ. Antimicrobial resistance in bacterial poultry pathogens: a review. Front Vet Sci, 2017; 4: 126.

Ogwuche A., Ekiri AB., Endacott I., Maikai BV., Idoga ES., Alafiatayo R., et al. Antibiotic use practices of veterinarians and para-veterinarians and the implications for antibiotic stewardship in Nigeria. J S Afr Vet Assoc, 2021; 92(0): e1-e14.

Oliveira H., Thiagarajan V., Walmagh M., Sillankorva S., Lavigne R., Neves-Petersen MT., et al. A thermostable Salmonella phage endolysin, Lys68, with broad bactericidal properties against gram-negative pathogens in presence of weak acids. PLoS One, 2014; 9(10): e108376.

Organization World Health. Stop overuse and misuse of antibiotics: combat resistance. 2017.

Osman KM. and Elhariri M. Antibiotic resistance of Clostridium perfringens isolates from broiler chickens in Egypt. Rev Sci Tech, 2013; 32(3): 841-50.

Rahman MU., Wang W., Sun Q., Shah JA., Li C., Sun Y., et al. Endolysin, a promising solution against antimicrobial resistance. Antibiotics (Basel), 2021; 10(11): 1277.

Ranaei V, Pilevar Z, Esfandiari C, Khaneghah AM, Dhakal R, Vargas-Bello-Pérez E, Hosseini H. Meat value chain losses in Iran. Food Sci Anim Resour, 2021; 41(1): 16-33.

Sato Y., Wigle WL., Gallagher S., Johnson AL., Sweeney RW. and Wakenell PS. Outbreak of type C botulism in commercial layer chickens. Avian Dis, 2016; 60(1): 90-94.

Scharff RL. Food attribution and economic cost estimates for meat-and poultry-related illnesses. J Food Prot, 2020; 83: 959-67.

Schmelcher M., Donovan DM. and Loessner MJ. Bacteriophage endolysins as novel antimicrobials. Future Microbiol, 2012; 7: 1147-71.

Schmelcher M. and Loessner MJ. Bacteriophage endolysins—extending their application to tissues and the bloodstream. Curr Opin Biotechnol, 2021; 68: 51-59.

Schmitz JE., Ossiprandi MC., Rumah KR. and Fischetti VA. Lytic enzyme discovery through multigenomic sequence analysis in Clostridium perfringens. Appl Microbiol Biotechnol, 2011; 89(6): 1783-1795.

Sekiya H., Kamitori S., Nariya H., Matsunami R. and Tamai E. Structural and biochemical characterization of the Clostridium perfringens-specific Zn2+-dependent amidase endolysin, Psa, catalytic domain. Biochem Biophys Res Commun, 2021a; 576: 66-72.

Sekiya H., Okada M., Tamai E., Shimamoto T., Shimamoto T. and Nariya H. A putative amidase endolysin encoded by clostridium perfringens st13 exhibits specific lytic activity and synergizes with

[DOI: 10.61186/joavm.7.20.1202]

the muramidase endolysin psm. Antibiotics (Basel), 2021b; 10(3): 245.

Simmons M., Donovan DM., Siragusa GR. and Seal BS. Recombinant expression of two bacteriophage proteins that lyse clostridium perfringens and share identical sequences in the C-terminal cell wall binding domain of the molecules but are dissimilar in their N-terminal active domains. J Agric Food Chem, 2010; 58(19): 10330-10337.

Swift SM., Reid KP., Donovan DM. and Ramsay TG. Thermophile lytic enzyme fusion proteins that target clostridium perfringens. Antibiotics (Basel), 2019; 8(4): 214.

Swift SM., Seal BS., Garrish JK., Oakley BB., Hiett K., Yeh HY., et al. A Thermophilic phage endolysin fusion to a clostridium perfringens-specific cell wall binding domain creates an anti-clostridium antimicrobial with improved thermostability. Viruses, 2015; 7(6): 3019-34.

Swift SM., Waters JJ., Rowley DT., Oakley BB. and Donovan DM. Characterization of two glycosyl hydrolases, putative prophage endolysins, that target Clostridium perfringens. FEMS Microbiol Lett, 2018; 365(16): fny179.

Thøfner IDA. and Christensen JP. Bacterial diseases in poultry. In: Advancements and technologies in pig and poultry bacterial disease control (Elsevier), 2021.

Tillman GE., Simmons M., Garrish JK. and Seal BS. Expression of a Clostridium perfringens genome-encoded putative N-acetylmuramoyl-L-alanine amidase as a potential antimicrobial to control the bacterium. Arch Microbiol, 2013; 195(10-11): 675-81.

Wahyono ND. and Utami MMD. A review of the poultry meat production industry for food safety in Indonesia. J Phys Conf Ser, 2018; 012125.

Wang X., Han L., Rong J., Ren H., Liu W. and Zhang C. Endolysins of bacteriophage vB_Sal-S-S10 can naturally lyse Salmonella enteritidis. BMC Vet Res, 2022; 18(1): 410.

Wieczorek K., Wołkowicz T. and Osek J. Antimicrobial resistance and virulence-associated traits of campylobacter jejuni isolated from poultry food chain and humans with diarrhea. Front Microbiol, 2018; 9: 1508.

Yuan B., Sun Z., Lu M., Lillehoj H., Lee Y., Liu L., et al. Immunization with pooled antigens for clostridium perfringens conferred partial protection against experimental necrotic enteritis in broiler chickens. Vaccines (Basel), 2022; 10(6): 979.

Zampara A., Sørensen MCH., Gencay YE., Grimon D., Kristiansen SH., Jørgensen LS., et al. Developing Innolysins against campylobacter jejuni using a novel prophage receptor-binding protein. Front Microbiol, 2021; 12: 619028.

Zimmer M., Vukov N., Scherer S. and Loessner MJ. The murein hydrolase of the bacteriophage phi3626 dual lysis system is active against all tested Clostridium perfringens strains. Appl Environ Microbiol, 2002; 68(11): 5311-7.

[DOI: 10.61186/joavm.7.20.1202]

مجله طب دامپزشکی جایگزین | بهار ۱۴۰۳ |دوره ۷ | شماره ۲۰

JOAVM
Journal of
Alternative Veterinary Medicine
joavm.kazerun.iau.ir

مقاله مروری

Islamic Azad University
Kazerun Branch
Fars, Iran

آنزی بیوتیک ها، راه حلی امیدوارکننده در مقابله با باکتری ها در صنعت طیور

غلامحسین حبیبی*

گروه علوم بالینی، دانشکده دامپزشکی، واحد کازرون، دانشگاه آزاد اسلامی، کازرون، ایران

تاریخ دریافت: ۱۴۰۲/۰۳/۲۵ اصلاح نهایی: ۱۴۰۲/۰۴/۲۶ تاریخ پذیرش: ۱۴۰۲/۰۵/۲۸

چکیده

از زمان کشف آنتی بیوتیک ها، آنها به طور گسترده ای برای کنترل بیماری ها استفاده شده اند. همچنین مشخص شد که آنتی بیوتیک ها در تقویت رشد در صنعت طیور مفید هستند. با این حال، استفاده بیش از حد و سوء استفاده از آنها منجر به ایجاد مقاومت باکتریایی در برابر آنها شده است. مقاومت به آنتی بیوتیک یک معضل جهانی است که منجر به خسارات بهداشتی و اقتصادی قابل توجهی می شود. مقاومت آنتی بیوتیکی در برابر آنتی بیوتیک های مختلف در عفونت های طیور نیز مشاهده شده است. برای مقابله با بار مقاومت آنتی بیوتیکی، جایگزین های مختلفی برای آنتی بیوتیک ها مورد مطالعه قرار گرفته است. این رویکردهای جایگزین در صنعت طیور نیز مورد توجه قرار گرفته‌اند؛ زیرا عفونت های طیور منجر به زیان اقتصادی چشمگیری می‌شوند و در موارد عفونت‌های مشترک بین انسان و طیور، انتقال عفونت از مرغ سلامت انسان را به مخاطره می اندازد. فاژ درمانی، استفاده از پروبیوتیک ها و تجویز پپتیدهای ضد میکروبی نمونه هایی از این رویکردهای جایگزین هستند. از دیگر روش های جایگزین آنتی بیوتیک به "آنزی بیوتیک" می توان اشاره کرد. در آنزیبیوتیک ها، پپتیدوگلیکان هیدرولازها (اندولیزین ها) برای تخریب دیواره سلولی باکتری استفاده می شود. این آنزیم ها بیشتر در ژنوم باکتریوفاژها یافت می شوند؛ زیرا باکتریوفاژها باید لایه های پپتیدوگلیکان باکتری ها را هم برای ورود و هم برای خروج از میزبان باکتریایی خود تجزیه کنند. ژنوم باکتری ها همچنین حاوی توالی هایی با خواص پپتیدوگلیکان هیدرولاز است که به رشد و تقسیم باکتری ها کمک می کند. خواص پپتیدوگلیکان هیدرولازهای مختلف برای یافتن انواع قوی تر و کاربردی برای استفاده در آینده مورد مطالعه قرار گرفته است. با توجه به مزایای آنها، اندولیزین ها جایگزین های آنتی بیوتیکی امیدوارکننده ای هستند. در این مقاله به نقش آنزی بیوتیک ها در صنعت طیور خواهیم پرداخت. همچنین، مزایا و محدودیت های تجویز اندولیزین ها مورد بحث قرار می گیرد.

واژه‌های کلیدی: *آنزی بیوتیک ها، اندولیزین، پپتیدوگلیکان هیدرولاز، کلستریدیوم پرفرنجنس، طیور، مقاومت آنتی بیوتیکی*

غلامحسین حبیبی. آنزی بیوتیک ها، راه حلی امیدوارکننده در مقابله با باکتری ها در صنعت طیور. مجله طب دامپزشکی جایگزین. ۱۴۰۳؛ ۷(۲۰): ۱۲۰۲-۱۲۱۱.

[DOI: 10.61186/joavm.7.20.1202]

* نویسنده مسئول: *گروه علوم بالینی، دانشکده دامپزشکی، واحد کازرون، دانشگاه آزاد اسلامی، کازرون، ایران.*

Orcid: https://orcid.org/0000-0002-9239-1277 ،Email: habibigh42@gmail.com