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Review Article

Listeriosis in Rabbits (*Oryctolagus cuniculus*): A Significant Bacterial Disease with an Emerging Zoonosis

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Abstract

Rabbit's rearing becomes one of the most important source of income in many countries world-wide. Rabbit's meat has many advantageous over any time of meat and it is recommended especially for sick people. Rabbits are susceptible to some important bacterial diseases such as listeriosis which causes severe economic losses. Listeriosis is a disease caused by many species of *Listeria* which may be environmental saprophytes or sometimes pathogenic for mammals, birds, and humans. *Listeria monocytogenes* (*L. monocytogenes*) is the most common cause of illness either in animals or humans. Infection with this bacterium usually occur in animals via ingestion, while in human via handling or consumption of uncooked or under-processed food. Most of signs in rabbits and humans are the same and including septicaemia especially in young, meningoencephalitis, and metritis and fetal mortality in pregnancy. Additionally, human may show the signs of severe febrile gastroenteritis due to food borne illness as well as skin and joint affections. Diagnosis of the disease depends mainly on the traditional methods of isolation and identification along with the recent molecular techniques for detection. Serological diagnosis is of little value. Prevention and control of listeriosis in rabbits are based on cleaning and disinfection of rabbit's cages, using of specific antibiotic treatment, and application of some natural alternatives such as probiotics and phytobiotics. In human, avoidances of the possible causes of *Listeria* infection and stressors and administration of a specific drug is the must. Besides, improvement of the quality control measures in processing plants or during handling of food are essential to effectively prevent and control listeriosis associated with food-borne illness. Accordingly, this article focuses on listeriosis in rabbits regarding the pathogenesis and virulence of the causative agent, clinical picture in rabbits, zoonotic importance in human, laboratory diagnosis, and the different strategies used for the prevention and control of the disease.

KEYWORDS
Listeria monocytogenes, Rabbits, Human, Virulence, Control

INTRODUCTION

Rabbit's industry has been developed in many countries due to several advantageous over other animal species including good feed conversion ratio, fast growth rate, high fertility rate, short production cycle, and big productive capability (Cullere and Dalle Zotte, 2018). In addition, rabbit's meat has gained popularity as a very healthy meat source due to ease digestibility, high level of protein, and low levels of fat, cholesterol, and sodium (Dalle Zotte and Szendro, 2011; Wang *et al*., 2019). However, rabbits are vulnerable to many important bacterial diseases that affect health and productivity such as listeriosis.

Listeriosis, silage disease, circling disease, or meningoencephalitis is caused by *Listeria monocytogenes* (*L. monocytogenes*). The bacterium was first isolated in 1926 from the livers of diseased rabbits (Murray *et al*., 1926). Later in 1966, *L. monocytogenes* was considered as a major foodborne bacterium and many experimental infections were done on different animal species to prove its pathogenicity (Gray and Killinger, 1966). *Listeria monocytogenes* is one of the most fastidious and opportunistic pathogen associated with life-threating listeriosis in a wide range of animals, birds, fish, and human being (Wesley, 2007; Johansson and Freitag, 2019). This pathogen is a facultative intracellular organism which is widely distributed in the environment. The bacterium may persist for many years in the facilities, grows at a wide temperature range from 0.5°C to 45°C, and tolerates environment with high salts or acids. *Listeria monocytogenes* is a Gram-positive, small, motile, non-sporulating, and bacillary to coccobacilli bacterium. Ingestion of contaminated food is regarded as the main route of the listeriosis transmission (Schlech *et al*., 1983). Listeriosis is commonly associated with septicaemia, meningitis, meningoencephalitis, brain stem encephalitis, abortion, stillbirth, and gastro-enteric infections in the affected hosts (Barbuddhe and Chakraborty, 2009; OIE, 2014).

Rabbits is regarded as a natural host for *L. monocytogenes* and the meat of affected animals is an important source of human food-borne infection (De Cesare *et al*., 2017; Zhao *et al*., 2020). Listeriosis has gained a great concern in rabbits due to its adverse effects on production as well as the food-born zoonosis and public health importance (Dhama *et al*., 2013; Johansson and

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Freitag, 2019). Infection of rabbits with *L. monocytogenes* causes infertility, abortion, and high mortality with severe losses in rabbitaries (Abdel Moteleb *et al*., 1990; Abd El-Ghaffar and Abd-El-Gwad, 1997). Despite *L. monocytogenes* may show low incidence rate, it often associated with high mortalities (Radoshevich and Cossart, 2018). The pathogen was isolated from diseased farmed rabbits in different localities including Egypt with incidences 20% or more (Abd El-Waneas, 1985; Abd El-Ghaffar and Abd El-Gwad, 1997; Hatab and Abd El-Latif, 2006; Moursi *et al*., 2006; Ibrahim and Ibrahim, 2016).

Therefore, this article focuses on listeriosis in rabbits regarding the pathogenesis and virulence of the causative bacterium, clinical picture in rabbits, zoonotic importance in human, laboratory diagnosis, and the different strategies used for the prevention and control of the disease.

PATHOGENESIS AND VIRULENCE

The intracellular nature of *L. monocytogenes* and the weak intracellular diffusion of many antimicrobials increase the ability of the pathogen to resist the environmental conditions and create difficulties in the eradication programs (Stratakos *et al*., 2020). The bacterium can survive at a wider range of temperature (4°C to 37°C), pH, and water activities (Janakiraman, 2008). Moreover, *L. monocytogenes* can grow in the presence or absence of oxygen and multiply at temperature of 0°C.

The soil, decayed tissues, or water are the sources of *L. monocytogenes* infection. The bacterium can enter the body via ingestion, inhalation, broken sin, or eyes. Un-processed or under-cooked food is an important source of human's infection. The predilection sites of *L. monocytogenes* are the intestinal wall, brain (medulla oblongata), and placenta of animals. The pathogen may cause encephalitis via tiny wounds in the buccal mucosa of infected animal.

It has been detected that *L. monocytogenes* is not acid tolerant and a large portion of the bacterium is likely to be killed in the stomach of the infected animal (D'Orazio, 2014). *Listeria monocytogenes* may invade the intestinal barrier through active endocytosis of the endothelial cells. This mechanism occurs via the interaction between the bacterial cell surface protein (internalin) and the epithelial cell surface receptor (E-cadherin). The bacterial cell could be passed from the intestinal cell to another in the host without exposure to the immune system which represented by antibodies, complement, or neutrophils. This could be achieved via pushing of the bacteria against the cell membrane and formation of pseudopods that ingested by some cells such as macrophages, enterocytes, and hepatocytes.

The virulence of *L. monocytogenes* is related to the ability of the pathogen to invade, adhere, and translocate across the barriers of the intestine during the gastrointestinal phase of infection (Radoshevich and Cossart, 2018). Consequently, hampering the bacterium during this phase is the best way to inhibit its spread to the deeper tissues and subsequent lethality. Moreover, *L. monocytogenes* has an intracellular life cycle which allows the pathogen to pass from one cell to another without leaving the cell. Moreover, presence of haemolytic factor (hlyA gene) which is known as listeriolysin O (Khan *et al*., 2013; Ibrahim and Ibrahim, 2016) and invasion associated protein (iap gene) are associated with the pathogenicity and virulence of *L. monocytogenes* (Wuenscher *et al*., 1993).

It has been reported that *L. monocytogenes* may proliferate in the liver, spleen, and immune organs (Regan *et al*., 2014) and also it can cross the placental and blood-brain barriers (Janakiraman, 2008) until attacking by the host's immune defense. During the early stage of infection, *L. monocytogenes* infected cells stimulate the infiltration of some inflammatory cells such as monocytes resulting in the formation of abscesses, and after the next days, the bacterium could be inactivated mainly by T-cells (Bortolussi *et al*., 1984).

The central nervous system is also a target for *L. monocytogenes* that causes meningitis, rhombencephalitis, and brain abscesses (Southwick and Purich, 1996, Vazquez-Boland *et al*., 2001; Orndorff *et al*., 2006). Infected animals show increased level of lactate dehydrogenase enzyme released from the cerebrospinal fluid causing brain tissue damage and/or increased permeability of the blood-brain barrier (Abate *et al*., 1998; Pamukcu *et al*., 2004). Furthermore, presence of inflammatory cells such as neutrophils, macrophages, and lymphocytes indicates the important role of these inflammatory cells in the brain tissue injury (Taha *et al*., 1991; Kruger *et al*., 1995; Najdenski and Vesselinova, 2002; Kabakci and Yarim, 2004). Inflammatory cells are related to secretion of pro-inflammatory cytokines and formation of toxic free radicals such as nitric oxides which is essential for the degeneration of the brain tissue (Greenberg *et al*., 1998; Shin *et al*., 2000).

Prompting of pro-inflammatory cytokines in rabbits in response to *L. monocytogenes* has been studied (Zhao *et al*., 2020). It has been reported that *L. monocytogenes* might upregulate pro-inflammatory cytokines genes such as tumor necrosis factor (TNF-α) and interleukin (IL-6), thus lead to increasing the permeability of the intestinal epithelium (Drolia *et al*., 2018). Moreover, the initial production of interferon gamma (IFNγ) is a very important step for stimulation of the immune response and regulation of *L. monocytogenes* infection (Harty and Bevant, 1995). In this context, increasing the expression levels of TNF-α, IFNγ, IL-6, IL-8, and IL-1β genes have been reported in *L. monocytogenes* infected rabbits compared with those infected and treated with either enrofloxacin or probiotics (Abd El-Hamid *et al*., 2022).

CLINICAL PICTURE

The forms of listeriosis are usually represented by septicaemia in bunnies, meningoencephalitis in adults, and metritis and fetal mortality in pregnant does (Vazquez-Boland *et al*., 2001; Malik *et al*., 2002).

Encephalitis is usually occur when *L. monocytogenes* ascends the trigeminal nerve causing localized infection of the brain stem. The severity of nervous signs vary according to the degree of neurons damage and the signs are usually manifested by trigeminal and facial nerve paralysis and circling (Kahn *et al*., 2006). The encephalitic form of listeriosis in rabbits is known as 'circling or rolling disease' as a result of walking of the animal around in circles in one direction with the head on "sideways" (OIE, 2014). Incoordination, loss of equilibrium, disorientation, immobility, and rolling sideways are another signs of the disease in the affected bunnies. The nervous signs may persist for some days or weeks, but the complete recovery is uncommon. Sometimes, affected bunnies may suddenly die without showing nervous signs.

Pregnant does may show purulent conjunctivitis, loses of weight, and lastly abortion (Hatab and Abd El-Latif, 2006). Intra-uterine death of feti or even death just after birth has been also reported (Okerman, 1999; Patton *et al*., 2000). Abortion associated listeriosis is due to the ability of the causative bacterium to cause myometrial contraction (Baker, 1998).

Experimental oral inoculation of 2-months-old rabbits with *L. monocytogenes* induced signs 2 weeks post-infection (Ibrahim and Ibrahim, 2016). Infected rabbits showed loss of appetite, depression, ruffled fur, lacrimation, conjunctivitis, urine retention, diarrhea, and finally emaciation followed by death. Moreover, nervous signs in the form of lateral deviation of the head and neck, convulsions, and death were also observed. Similar nervous signs have been also observed in rabbits following *L. monocytogenes* infection (Hoelzer *et al*., 2012; Ahmed, 2013). Oral or conjunctival inoculation with *L. monocytogenes* produced abortion in pregnant does (Gray and Killinger, 1966). Besides, abscess formation has been demonstrated in rabbits following *L. monocytogenes* subcutaneous inoculation (Gray and Killinger, 1966).

Significant pathological alterations in the livers, spleen, and brains of rabbits could be observed as a result of septicemia induced by *L. monocytogenes* infection (Watson and Evans, 1985; Abd El-Hamid *et al*., 2022). Dead rabbits with listeriosis showed severe generalized congestion of liver, spleen, kidneys, and lungs, along with softening of the brain (Okerman, 1999; Vazquez-Boland *et al*., 2001; Moursi *et al*., 2006; Ahmed, 2013; Ibrahim and Ibrahim, 2016). Necrosis of the live and spleen, atrophy of spleen, enteritis, cystitis, bloody vaginal discharge, peritonitis, endometritis, meningitis, and hydrocephalus could be also demonstrated in rabbits following such infection (Abd El-Ghaffar and Abd-El-Gwad, 1997). Listeriosis induced severe lesions in the mid brain, less severe lesions in the cerebellum, and rare lesions in the cerebrum (Pamukcu *et al*., 2004).

ZOONOSIS

Contamination of food with *L. monocytogenes* may occur during processing, handling, and packaging under poor quality control measures (Carpentier and Cerf, 2011). The pathogen is widely distributed in ready-to-eat and raw meat products (Mengesha *et al*., 2009). Moreover, direct contact with the contaminated materials such as aborted feti may be a possible way of *L. monocytogenes* infection in human. Food-born listeriosis and deaths of workers in retail and food service environments have been reported in many localities (Lianou and Sofos, 2007; Meloni *et al*., 2009). Human listeriosis may cause severe and life-threatening complications (Dhama *et al*., 2013). The disease in human is caused by all the 13 serotypes, especially 1/2a, 1/2b, and 4b, and the annual endemic infection rate varies from 2 to 15 cases/ millions of human (Munoz, 2012).

The clinical syndromes of listeriosis in people may appear as sporadic, endemic, or foodborne outbreak. The disease usually induces fatigue, chills, headache, and febrile gastroenteritis. Severe cases of listeriosis are associated with septicaemia, skin rashes, meningoencephalitis, abortion, infection of other organs, and finally death if the disease is neglected without probable treatment (Koopmans *et al*., 2014). Young and elderly individuals, pregnant women, and immuno-deficient debilitated people are at higher risk to *L. monocytogenes* serious illness, while healthy persons are usually vulnerable to gastroenteritis and pregnancy losses (Poulsen and Czuprynski, 2013; Popovic *et al*., 2014). Table 1, shows the different forms of listeriosis in humans.

LABORATORY DIAGNOSIS

Selection of the proper samples from infected rabbits is mainly depend on the prevalent signs in the infected farm. Samples could be collected from the aborted fetus, placenta, uterine discharges, blood, cerebrospinal fluid, brain, conjunctiva, liver, kidneys, spleen, and brain.

Isolates of *L. monocytogenes* grow on selective media such as Fraser broth after incubation at 37°C for 24 hrs followed by sub-culturing on PALCAM and incubation at 37°C for 24-48 hrs (Fraser and Sperber, 1988). Typical colonies appear as grey green with black sunken centers (Holt *et al*., 1994). The bacterium can grow at temperatures as low as -2°C in laboratory media broth (Bajard *et al*., 1996). On sheep blood agar, *L. monocytogenes* induces a complete zone of β-hemolysis which appears near to the line of the streak of *Staphylococcus aureus* (*S. aureus*) in CAMP test (Volokhovel *et al*., 2007).

Microscopic examination of suspected *L. monocytogenes* colonies revealed presence of non-sporulating Gram positive rods that arranged singly, in short chains, in pairs at V shape angle, or in parallel groups (Hass and Kreft, 1988; Warbureton *et al*., 2003).

The different biochemical reactions of *L. monocytogenes* are shown in Table 2. On semi solid agar media, *L. monocytogenes* strains show umbrella growth pattern with a characteristic tumbling motility using peritrichous flagella (Quinn *et al*., 2002).

The Anton's test revealed that inoculation of two to three drops of *L. monocytogenes* in the eyes of rabbits induced purulent conjunctivitis and keratitis 24-48 hrs post-inoculation (An-

Table 1. Clinical forms of listeriosis in humans

Form	Signs
Gastrointestinal	Abdominal pain, vomiting, diarrhea, and flue like signs such as fever, nausea, headache, and myalgia. Most of these cases are usually self-limiting within few days.
Nervous	Meningitis, meningoencephalitis, rhombencephalitis or brain abscesses. Unilateral or bilateral cranial nerve deficits, ataxia, cerebellar dysfunction, hemiparesis, impaired consciousness, and death. Sometimes death result from cardiac and respiratory failure.
Reproductive	Pregnant women may remain asymptomatic or shows mild flu-like signs and/or gastroenteritis. However, she may later abort or give birth to a stillborn or premature infant. Neonates usually have septicemia and sometimes granulomas, skin lesions and/or abscesses. Pneumonia and meningitis are less commonly reported syndromes. In the later stage, meningitis is most common.
Skin	Rashes, papule, vesicle, or pustule which may be localized and non-pruritic, and may sometimes be disseminated especially in immunosuppressed persons. Some cases showed fever, chills, lymphadenopathy, and general pain.
Bone and joint	Arthritis and osteomyelitis
Eye	Conjunctivitis, keratoconjunctivitis, chorioretinitis, and unilateral endophthalmitis.
Others	Cholecystitis, cholangitis, biliary cyst, hepatitis or liver abscesses. Pyelonephritis. Endocarditis. Peritonitis Pneumonia and pleuritis

ton, 1934). Moreover, the pathogenicity test in mice showed that intraperitoneal injection of *L. monocytogenes* lead to 100% mortality rate within 24-48 hrs after injection with severe congestion of the internal organs and brain (Seeliger and Jones, 1986; Marco *et al*., 1992).

Table 2. The biochemical reactions of *Listeria monocytogenes*.

Reaction	Result
Catalase	+
Vogues Proskaur	+
Oxidase	-
Urease	-
Indole	-
H_2S production	-
Sugar fermentation	
Maltose	+
Sucrose	+
Dextrose	+
Sorbitol	+
Xylose	-
lactose	±
Mannitol	±

+: Positive; - = Negative

Immunohistochemistry, immunofluorescence, polymerase chain reaction, or loop-mediated isothermal amplification may provide a more rapid diagnosis of *L. monocytogenes* in the tissues. Moreover, *L. monocytogenes* could be subtyped genetically using pulsed field gel electrophoresis, whole genome sequencing, DNA hybridization, multi-virulence-locus sequence typing, or multilocus sequence typing. These testes are usually used in epidemiological investigations of human listeriosis and detection of out-breaks sources.

Serological tests can detect immunoglobulins (IgG) to listeriolysin. Serological diagnosis of listeriosis using agglutination or enzyme linked immunosorbent assay test is not common because most of cases are caused by few common serotypes, and each of these serotypes can contain more than one *Listeria* species. In addition, some apparently healthy rabbits show high antibody titers and cross-reactions with *Enterococci* species or *Staphylococcus aureus (S. aureus)* in some tests. The serological response against *L. monocytogenes* in the absence of clinical signs has been detected (Low and Donachie, 1991). Frequent ingestion of low doses of the bacterium induced high titers of anti-*Listeria* agglutinins in apparent healthy animals and humans (Seeliger, 1987). Anti-*L. monocytogenes* antibodies could be produced in rabbits to demonstrate the immune response to the bacterium (Larsen *et al*., 1974). Belen Lopez *et al*. (1993) hypothesized the interaction between *L. monocytogenes* and the host immune system in the tonsils after oral and gastric inoculation of rabbits with the bacteria. The IgM and IgG were produced in rabbits in response to oral inoculation of *L. monocytogenes* and/or *S. aureus* with a cross immunity (Larsen *et al*., 1974). Thirteen serovars of this bacterium are highly virulent and common in animals such as serovars 4b, 1/2a, 1/2b and 3, while serovars 4b, 1/2a, 1/2b, and 1/2c are thought to be the cause of more than 95% of the clinical cases in humans.

PREVENTION AND CONTROL

Once the outbreak of listeriosis occurs in certain countries such as United States of America (USA), Veterinarians should report the national and/or local authority. Diseased rabbits should be isolated and sources of contamination, such as the aborted feti, should be hygienically disposed. Thorough cleaning and disinfection of fomites including water tanks or feeders is the must. Eradication of mechanical vectors such as rodents which can shed *L. monocytogenes* in feces. Minimize stressors and concomitant infections which are suspected to increase exposure to listeriosis.

Listeria organism can be inactivated by heating or autoclaving. Many disinfectants such as quaternary ammonium compounds, glutaraldehyde, ethanol, sodium hypochlorite, iodine, and chlorhexidine can effectively dissolve on the organic matters covering *L. monocytogenes*. Sometimes presence of biofilm layer on the bacterium surface makes destroying of bacterium is difficult especially in food processing facilities.

Improved quality control measures are essential to effectively prevent and control listeriosis associated with food-borne illness (Nakari *et al*., 2014). Measures including good cooking of animal products, well washing of raw vegetables, and avoidance of undercooked food should be considered to reduce the risk of food-borne listeriosis, Monitoring of environment, testing of products, as well as cleaning and sanitation are also crucial. In certain countries, such as USA, detection of *L. monocytogenes* in any concentration in food prompts a recall, and measures are carried-out.

ANTIBIOTIC TREATMENT

Antibiotic treatment is the most important way for controlling *L. monocytogenes*. The treatment course varies according to the level of infection. Sometimes, treatment may be difficult because the pathogen can invade all types of cells. Moreover, treatment of encephalitic or immunocompromised host is usually not effective. However, high doses of early medication along with supportive treatment are important for rabbits suffering rhombencephalitis. Monitoring of antibiotic sensitivity is very important (Okada *et al*., 2011; Barbosa *et al*., 2013). Penicillin's classes are regarded to be the most effective treatment of *L. monocytogenes* infection particularly for humans, but other drugs have sometimes been used. Despite the highest effectiveness of penicillin against *L. monocytogenes* infection, resistance has been reported (Rivero *et al*., 2003). Some strains of *L. monocytogenes* showed resistance to cephalosporins, especially cefotaxime (Boisivon *et al*., 1990). Moreover, *L. monocytogenes* strains from food, environment, animal, and human origins showed resistance to gentamicin, cotrimixazole, and ofloxacin (Rahimi *et al*., 2012; Soni *et al*., 2013; Ndahi *et al*., 2014). It is important to mention that haphazard using of penicillin for the treatment of listeriosis in farmed animals has been suggested as one of the causes of resistance in *Listeria*-infected human via animal derived foods (Tiwari *et al*., 2013).

Though some *L. monocytogenes* strains are sensitive to several antibiotics *In-vitro*, some of these antimicrobials may not be effective *in-vivo*. An early *in-vitro* study revealed that *L. monocytogenes* strains from rabbits-origin were highly sensitive to gentamycin, tetracycline, and spictinomycin, while resistant to chloramphenicol, lincomycine, and streptomycin (Abd El-Ghaffar and Abd-El-Gwad, 1997). Additionally, *L. monocytogenes* isolated from diseased rabbits were highly susceptible to ampicillin, amoxicillin, penicillin, tetracycline, doxycycllin, trimethoprim, neomycin, and gentamycin, but less susceptible to streptomycin, cefotaxime, and nalidixic acid *In-vitro* (Charpentier and Courvalin, 1999; Moursi *et al*., 2006).

Prophylactic medication with sulphonamides, penicillin, or tetracycline may be effective in prevention of listeriosis (Radostits *et al*., 2008), while ampicillin and erythromycin are the drugs of choice for treatment.

PROBIOTICS

Antibiotics treatment can harm the gut microbiota and the host immune response, enhances the development of resistant bacteria, and accumulates in the tissues as residues. Accordingly, new antibiotics alternatives have been developed to control *L. monocytogenes* infection (Suez *et al*., 2019). Such alternatives include using of probiotics (Amalaradjou and Bhunia, 2012). They may compete with the pathogenic bacteria for adhesion sites, prevent the disruption of intestinal integrity, and enhance the host's immune system, thus conferring resistance to *L. monocytogenes* (Amalaradjou and Bhunia, 2012). It has been proposed that probiotics block the bacterial attachment and consequently its invasion to the intestinal epithelial cells that resulting in improved growth performance of rabbits and provide protection against *L. monocytogenes* infection. Drolia *et al*. (2020) demonstrated that that probiotics contain Lactobacilli species inhibited *L. monocytogenes*-induced intestinal permeability via the preservation of the cell junctional configuration of claudin-1, occludin, and E-cadherin biomarkers. Besides, this species of probiotic stimulated the secretion of tight junction protein gene (MUC), hence fortified the mucus barrier and decreased *L. monocytogenes*-induced MUC-2 loss and apoptotic responses (Drolia *et al*., 2020).

In-vitro studies showed that *Lactobacillus* (L) producing bacteria such as *L. acidophilus, L. plantarum*, and *Enterococcus faecium* (*E. faecium*), or even their metabolites inhibited the formation of *L. monocytogenes* biofilm (Rocha *et al*., 2019). Addition of *L. acidophilus* at concentration of 10^9 or 10^{12} colony forming unit (CFU)/mL to the milk revealed a significant inhibitory effect *L. monocytogenes* growth (Ehsani *et al*., 2019). Moreover, a strain of *L. plantarum* or its cell-free supernatants significantly prevented the growth of *L. monocytogenes*, *Salmonella enteritidis*, *Escherichia coli,* and *S. aureus* (Arena *et al*., 2016). The proliferation of spoilage bacteria such as *L. monocytogenes* and *Salmonella* species has been inactivated following inoculation of *L. plantarum* at a level of 10^8 CFU/g of raw minced beef meat (Trabelsi *et al*., 2019). In milk, the multiplication of *L. monocytogenes* was significantly inhibited by incorporation of *E. faecium* and its enterocins A and B (Vandera *et al*., 2017).

Van Zyl *et al*. (2016) found that *L. plantarum* excluded *L. monocytogenes* from the gut of mice. There are limited data regarding using of probiotics to prevent or treat *L. monocytogenes* infections in farmed rabbits. Zhao *et al*. (2020) demonstrated that lactic acid bacteria can reduce *L. monocytogenes* infection and modulate the cellular and humoral immune responses of infected rabbits. Recently, treatment of *L. monocytogenes* infected rabbits with multi-strains probiotics (a mixture of *L. acidophilus*, *Bacillus subtilis*, and *E. faecium* strains) restored the reduced growth and intestinal barriers, decreased the severity of signs and mortalities, attenuated the excessive inflammatory reactions, and ameliorated the microscopic lesions in liver, brain, and spleen compared with enrofloxacin treatment (Abd El-Hamid *et al*., 2022).

PHYTOBIOTICS

The anti-*Listeria* effect of some herbs and their extracts has been studied. For instance, Thai spices proved efficacy in the treatment of listerosis associated food poisoning (Thongson *et al*., 2005). In addition, extracts of many plants such as *Prangos ferulacea*, *Allium vineale, Chaerophyllum macropodum, Sophorae radix, Psoraleae semen*, oregano, rosemary, clove, and sage showed high efficacy against *L. monocytogenes* infection (Sagun *et al*., 2006; Yoon and Choi, 2012; Witkowska *et al*., 2013). Skariyachan *et al*. (2015) demonstrated that cinnamon extract could be very effective against *L. monocytogenes* via inhibition of the general secretory pathway, thus decreasing the pathogen virulence.

CONCLUSION

Listeriosis is regarded as a disease of clinical and productive significance for rabbits industry. Therefore, the pathogenesis and mechanism of *L. monocytogenes* virulence in rabbit should be more studied and explained. In addition, successful preventive control measures against listeriosis in rabbit farms should be implemented.

CONFLICT OF INTEREST

The author declare that they have no conflict of interest.

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