Clostridium perfringens as foodborne pathogen

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Clostridium perfringens (Cp.) is a Gram-positive, anaerobic, nonmotile rod that forms subterminal spores. This bacterium has characteristics that contribute to its ability to cause foodborne illness by the thermotolerant spores. Meat and poultry products are identified as the main source of infection for humans. The diversity of toxins produced by Cp. has allowed it to be the cause of various diseases in humans and animals, due their rapid growth rate in warm food. In humans, it is associated with diseases related to food consumption that has been prepared or preserved in inadequate hygienic conditions, meanwhile the toxin causes necrotic enteritis in broilers.

Keywords: C. perfringens, pathogen ; Toxins, ; necrotic enteritis

1. Introduction

Clostridium perfringens is a Gram-positive, anaerobic, nonmotile rod that forms subterminal spores. The size of the bacillus on the environment where is found, for example, in culture media for sporulation based on starch the bacillus is long. Meanwhile, in media rich in glucose the bacillus is short. Vegetative cells are relatively cold resistant, and their spores are heat resistant [1][2]. *C. perfringens* can hydrolyze gelatin and reducing nitrates to nitrites; in sulphite media, it generates black colonies due to sulphite reduction. A characteristic test is the lactose fermentation produced by this microorganism, known as *stormy lactose fermentation in milk* due to the large amount of gas it generates [3][4]. This bacterium can develop under microaerophilic conditions due to its ability to produce high amounts of the enzyme superoxide dismutase [5][6]. Its ability to form spores allows it to be ubiquitous and can be found in the environment [7][8].

Beef and poultry, as well as other meat products, are the most important vehicles for this microorganism [9][10][11], although it has also been recovered from vegetables [12] and spices [13]. Butler et al. (2015) [14] described the transmission of *C. perfringens* through water by contact with animals and transmission from person to person. Considered a natural inhabitant of the gastrointestinal tract, the main source of contamination towards meat is fecal matter [15]. According to data reported by the CDC (2019) [16], *C. perfringens* is one of the five pathogens that most frequently cause foodborne illnesses in the United States, ranking second among the etiological agents identified, and, in Australia, it is considered one of the bacteria causing outbreaks [17]. The consumption of chicken meat is important worldwide and a 13% increase in its production is estimated for the year 2027 (OECD-FAO, 2017). In animal production, approximately 70% of the total cost is attributable to the feed. The diets for farm animals contain antibiotics or growth promoters that seek to improve the productive parameters on the farm; however, there is a tendency to use them less frequently, seeking to replace them with what is currently known as sustainable animal diets [18].

It is important to mention that some pathogens that cause disease in chickens can be transmitted to humans through their consumption. *Salmonella, Campylobacter jejuni*, and *C. perfringens* are the most studied so far. *C. perfringens* is the cause of subclinical necrotic enteritis in broilers, producing toxins and is the cause of disease in humans [9][19].

2. *C. perfringens* as a Foodborne Pathogen

Clostridium perfringens can produce a large amount of toxins (Table 1). Toxin types of *C. perfringens* cause different diseases in both humans and animals, ranging from subclinical manifestations to serious, life-threatening diseases (Table 2) [20].

Table 1. Types of *Clostridium perfringens* according to the toxins produced and the genes that encode the toxins.

Toxins						
Type	Alpha (α) (*plc* o *cpa*) *	Beta (β) (*cpb*) *	Epsilon (ε) (*etx*) *	Iota (ι) (*iap* y *ibp*) *	CPE (*cpe*) *	NetB (*netB*) *
A	+	−	−	−	−	−
B	+	+	+	−	−	−
C	+	+	−	−	+/−	−
D	+	−	+	−	+/−	-
E	+	−	−	+	+/−	−
F	+	−	−	−	+	−
G	+	−	−	−	−	+

*Gene for each toxin. Taken from Rood et al., 2018 [21].

Table 2. Toxigenic types of *Clostridium perfringens* and their association with diseases in humans and animals.

Type of Toxin	Main Toxin	Diseases that Cause
A	α	Wound infection in humans (gas gangrene or clostridial myonecrosis), necrotic enteritis in birds, ulcerative abomasitis, mild necrotizing enteritis in piglets, and endotoxemia in South American camelids.
	α, CPE	Food poisoning in humans, non-food gastrointestinal diseases in humans, and diarrhea in animals such as dogs, pigs, and foals.
	α, β2	Gastrointestinal disease in swine.
B	α, β, ε	Dysentery and hemorrhagic enteritis in lambs and kids.
C	α, β	Necrotizing enteritis in humans, enteritis in dogs, chickens, and South American camelids.
	α, β, β2	Gastrointestinal disease in swine.
D	α, ε	Enterotoxemia in sheep and goats (pulpy kidney disease).
E	α, ι	Enterotoxemia in rabbits, dogs, cattle, and sheep.
F	α, CPE	Human food poisoning and non-food associated diarrhea.
G	α, NetB	Subclinical necrotic enteritis in chickens.

Bruce et al., 2006; Kiu& Hall, 2018 and Rood et al., 2018 [20][21].

These diseases are mediated by one or more *C. perfringens* toxins [21][22]. Enteric infections in humans and animals have been shown to be associated with *C. perfringens* type C [23][24], while the other type of toxins have been confirmed to cause disease in humans or animals, but not both (Table 2). Of the seven *C. perfringens* toxin types described, type A is the most frequently identified strain [12][25]. However, type F is the one that causes food-related poisoning in humans [21][26].

The diversity of toxins produced by *C. perfringens* has allowed it to be the cause of various diseases in humans and animals. In humans, it is associated with diseases related to food consumption that has been prepared or preserved in inadequate hygienic conditions [17][27][18]. This type of illness is usually characterized by watery diarrhea and abdominal pain, without fever or vomiting, and the symptoms disappear after 12 to 24 hours [29]. Non-food associated diarrhea due to *C. perfringens* has also been described, which usually occurs after a treatment with broad-spectrum antibiotics, and it is common in older adults. It is worth mentioning that this type of diarrhea usually last longer than those associated with contaminated food [30]. Another symptom is necrotic enteritis (NE) caused by *C. perfringens* type C [31]. Myonecrosis due to *C. perfringens* (also known as gas gangrene) is another condition that can occur in people because of wound infection, generating significant pain, gas accumulation at the site of infection and extensive muscle necrosis, which can put people’s life at risk [32][33].

The toxin of this bacterium also affects some animal species. For example, in broilers the toxin causes necrotic enteritis, which could lead economic losses. The role of the necrotic enteritis B-like toxin (NetB) present in G strains causes NE, which is more frequent in chickens fed wheat or barley-based diets than in those fed with corn [34][35], due to the difference in clostridia proliferation in the diets resulting in a higher number of bacteria in the intestine, as well as a lack of fluidity and digestion, generating an increase in the incidence of NE in chickens and increasing the viscosity of the intestinal contents, mucus production, and growing bacteria [35][36].

3. Conclusions

Clostridium perfringens is an important microorganism in the clinical, food and veterinary areas. The diversity of toxins produced by this microorganism not only makes it a risk to human health, but also to animal health. In the latter, the problem is that it causes subclinical diseases that generate great losses, particularly in the poultry industry, because *C. perfringens* is capable of producing various toxins and bacteriocins, some of which have already been identified and characterized. However, other pathogenicity factors cannot be discarded.

Currently, the infection produced in broilers, known as necrotic enteritis (NE), associated with this microorganism, has become a problem to maintaining the health of birds, affecting reproduction and conservation, and the supply for human consumption, due to the fact that the disease occurs subclinically, and diagnosis cannot be made in a timely manner, generating significant economic losses for the producer.

Chicken meat is the most consumed animal protein and enough supply for consumers requires mass production strategies, exacerbating the problem of by infections by pathogens such as *C. perfringens.* Due to this, there is a need to find economical, environmentally friendly and efficient alternatives in the modulation of the intestinal microbiota, which contribute to the efficient production of broiler chicken to meet current and future demand.

The use of various food additives based on probiotics, prebiotics, symbiotics, essential oils, organic acids and enzymes have been presented as alternatives to mitigate the incidence of NE, achieving an improvement in the general intestinal health of birds, with the opportunity to produce healthy birds for consumption.

Perspectives: It is imperative to carry out more research on alternative and efficient products for the modulation of the intestinal microbiota, in addition to the role they play in the immune system, where consistent positive effects are needed to fulfill the current demand, while keeping a safe environment. It is also important to establish standardized protocols that consider individual and inter-sample variability, and consider the utility of molecular detection mechanisms and epigenetic modifications underlying treatment with alternative products such as essential oils and organic acids where research has not yet been clarified.

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