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RESEARCH ARTICLE

THE BACTERIA AND THEIR SURVIVAL IN ACIDIC ENVIRONMENTS

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ABSTRACT

One of the most significant environmental parameters affecting growth and survival of microorganisms is the local concentration of protons (H^+). When the proton concentration is high, acidic conditions prevail and cells must respond appropriately to ensure that macromolecules and metabolic processes are protected. The extreme acidophiles grow optimally at pH 3 or less and for that those bacteria have multiple strategies for tolerating stresses that accompany high levels of acidity.

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INTRODUCTION

As is known, most pathogenic bacteria for humans and animals grow and develop in environments whose pH is close to neutrality. However, there are examples of bacteria that have adapted to more aggressive environments, finding themselves living in extreme acidic environments (Guan and Liu, 2020). In this sense, the archaea are excluded. As it is known, one of the most significant environmental parameters impacting on growth and survival of microorganisms is the local concentration of protons (H^+). When the proton concentration is high, acidic conditions prevail and cells must respond appropriately to ensure that macromolecules and metabolic processes are sufficiently protected to sustain life (Lund *et al.*, 2020). For example, *Helicobacter pylori* is a clear example of a microorganism that has developed strategies that allow it to develop in the stomach of human beings, without the low pH values attributed to gastric secretions inhibiting its growth (Pop *et al*., 2022). Another example that can be cited is the case of acetic acid bacteria of *Acetobacter* spp. and other genera, where it has been observed that as a product of their metabolism they produce acid substances (such as acetic acid), and them considerably decrease the pH of its environment (Yang *et al*., 2019).

The lactic bacteria *Lactobacillus sp*., which is used in the production of fermented foods is another example (Flores-Encarnación *et al*., 2022; Nakano and Ebisuya, 2016). So, the extreme acidophiles grow optimally at pH 3 or less, they have multiple strategies for tolerating stresses that accompany high levels of acidity and are scattered in all domains of the tree of life (Quatrini and Johnson, 2018). Therefore, bacteria have developed different mechanisms that allow them to live and multiply in acidic environments. Tolerance to acidic pH is an adaptation of cells that have been exposed to a gradual decrease in environmental pH and have managed to survive against lethal stress. It is known that bacterial tolerance to stress conditions varies depending on the environmental factors (Álvarez-Ordóñez *et al*., 2012; Flores-Encarnación *et al*., 2022). This work shows some important molecular mechanisms that have been reported in some bacteria for survival during acid stress.

The case of *Escherichia coli:* Enteric bacteria are found naturally in the digestive tracts of mammals and include many species of commensal and pathogenic organisms, which typically grow best under neutral pH conditions (Kanjee and Houry, 2013). As is known, gastric juice functions as a chemical barrier for many microorganisms in the stomach, since most of them cannot tolerate low pH values (pH between 1.5 and 3.0).

By virtue of the above, different authors have estimated that most pathogenic bacteria require a large infectious dose to survive the passage through the stomach (for example, *Vibrio cholerae* requires 10^9 cells) (Gorden and Small, 1993; Kanjee and Houry, 2013; Lin *et al.*, 1996). In other cases, such as enterohemorrhagic *E. coli* require 10^2 cells indicating that bacteria have a robust survival and must be more resistant to the acid conditions of the stomach, in order to survive acid stresses as low as pH 2.0 (Kanjee and Houry, 2013; Lin *et al*., 1996; Xu *et al*., 2020). It has been also reported that the ability to grow at moderate acidic conditions (such as pH 4.0-5.0) is important to *E. coli* colonization into host's intestine. So, when *E. coli* is exposed to acidic conditions, the expression of various systems is induced. In this context, *E. coli* has developed some acidic stress response systems, including the acid-resistance systems (AR) to avoid extreme acid stress, and the acid-tolerance response system (ATR), under the mild and moderate acid stress (Foster, 2001; Lund *et al*., 2014; Xu *et al*., 2020). The acid-resistance systems arises owing to the buffering capacity of the amino acids, proteins, polyamines, polyphosphate, and inorganic phosphate present in the cytoplasm, that together contribute between 50 and 200 mM buffering capacity per pH unit. It includes also physiological, metabolic, and proton-consuming systems (Kanjee and Houry, 2013; Slonczewski *et al*., 2009). So these mechanisms protect cells from acid stress, which can range from pH 2 to 4.5. Xu *et al*., (2020) and Zhao and Houry (2010) reported that *E. coli* in exponential growth at pH 4.2 uses a regulatory circuit modulating the biosynthesis of unsaturated fatty acids and altering the lipid composition of membranes. Surmann *et al.*, (2016) reported the crosslinking between lipoproteins and peptidoglycan which increased the stability of bacterial cell wall. Other authors have reported the modification of phospholipids in the inner membrane to decrease the permeability of protons (Lund *et al*., 2014). Those changes in the composition of lipids, decreases the fluidity of the membrane improving the homeostasis of intracellular pH, allowing *E. coli* to grow at acidic pH (Surmann *et al.*, 2016; Xu *et al*., 2020).

The case of *Acetobacter aceti:* The acetic acid bacteria are obligate aerobes that belong to *Proteobacteria*, with the ability to oxidize alcohols and sugars into their corresponding organic acids (Nakano and Ebisuya, 2016). Acetic acid resistance is a crucial ability that enables acetic acid bacteria to stably produce large amounts of acetic acid (Sakurai *et al*., 2013). *Acetobacter aceti* has been shown to survive exposure to acetic acid by tolerating cytoplasmic acidification, which implies an unusual adaptation of cytoplasmic components to acidic conditions (Francois *et al*., 2006). Matsushita *et al.,* (2005) reported that these bacteria are able to grow in media with high concentrations of acetic acid. They must possess a specific mechanism such as an efflux pump by which they can resist the toxic effects of acetic acid. In general, various authors have proposed different mechanisms of acid-tolerance by acetic acid bacteria and they are: the prevention of acetic acid influx into the cell (by optimizing the lipid component proportion of the membrane and by further forming polysaccharide on the surface of the cells to prevent the influx of acetic acid); the acetic acid assimilation (by acquiring the ability to convert the intracellular acetic acid in usable energy effectively via the alternative TCA cycle); the acetic acid efflux by transporter or pump (the acetic-acid bacteria possess two types of discharging intracellular acetic acid systems, one of which is a ABC transporter, and the other is an efflux pump driven by a proton motive force); the protection of cytoplasmic proteins against denaturing by general stress proteins (by inducing chaperones that stabilize the structure of proteins from acidification of the cell inside, and by synthesizing the enzymes which decompose reactive oxygen species to maintain the intracellular environment in good condition) (Francois *et al*., 2006; Kanchanarach *et al*., 2010; Matsushita *et al*., 2005; Mullins *et al*., 2008; Nakano and Ebisuya, 2016; Nakano and Fukaya, 2008; Sakurai *et al*., 2013; Yang *et al*., 2019).

The case of *Helicobacter pylori:* *Helicobacter pylori* is a Gram-negative helical bacterium. It has been estimated to this bacterium infects at least half the world's population. *H. pylori* has been established as the causative agent of human gastric mucosa infection with various gastro-duodenal diseases, such as chronic gastritis, gastric ulcer, duodenal ulcer, and increased risk of gastric cancer (Benoit *et al*., 2013; Pop *et al*., 2022). The ecological niche of this bacterium is the stomach, where the pH ranges from 2.0 to 6.5. So, *H. pylori* is highly adapted to the challenges encountered in this environment (Ansari and Yamaoka, 2017). In the gastric lumen, the pH is around 2.0 and above in the mucus layer, however *H. pylori* remains for little time within the lumen and enters the mucus layer, where the pH varies between 4.5 and 6.5. It's known that *H. pylori* is very capable of neutralizing the acidity of the gastric lumen (Ansari and Yamaoka, 2017; Kuwahara *et al*., 2000). Many studies have revealed that *H. pylori* has several mechanisms to overcome the lethal effects of acidic gastric secretion. One of the most studied mechanisms is the urease system. Several bacterial species (including normal flora and non-pathogens) require the enzymatic activity of several proteins, such as urease and hydrogenase to colonize the acidic niche. Urease has been demonstrated as a potent virulence factor for some species like *H. pylori. H. pylori* produces large amount of intracellular (cytoplasmic) urease (around 10% of total bacterial proteins). However, *H. pylori* also contains urease on the bacterial surface due to the lysis of some organisms (Ansari and Yamaoka, 2017; Eaton *et al.*, 1991). *H. pylori* infection is enhanced by the production of ammonia, which is of great importance as a source of nitrogen and to neutralize gastric acidity (Ansari and Yamaoka, 2017). The ammonia produced is transported outside the bacterial cell, which can act as a buffer, creating a neutral microenvironment. The resting pH of the human stomach can reach as low as 1.8 (Jones and Zamble, 2018). The hydrolyzing property of urea exhibited by the enzyme urease increases the pH in the mucus microenvironment and modifies it to less gelatinous, facilitating the movement of the bacteria (Ansari and Yamaoka, 2017).

CONCLUSION

Bacteria use different mechanisms that allow them to survive in extreme pH environments. These adaptation mechanisms include processes related to bacterial metabolism, or the production of proteins to remove protons through the membranes. The understanding of these mechanisms will allow the design of strategies to combat diseases related to public health or prevent the contamination of some foods.

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