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Review Article

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Interactions and Inhibition of Pathogenic Foodborne Bacteria with Individual Dissociated Organic Acid Species: A Review

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Abstract

The World Health Organization in 2017 named 12 pathogens that pose a threat to human health. Estimates of foodborne illnesses in 2011 by the Centers for Disease Control and Prevention and a summary report on foodborne outbreaks in 2015 by the European Food Safety Authority identified certain pathogens as a threat to human health. The pathogens described include the following: *Pseudomonas aeruginosa*, *Enterococcus faecium*, *Staphylococcus aureus*, *Campylobacter*, *Salmonella*, Shiga toxin-producing *Escherichia coli* O157 (O157 STECs), and non-O157 STECs. Researchers have suggested that new strategies must be developed to control foodborne pathogens, and the mechanism(s) of bacterial inhibition by organic acids (OAs) must be identified. This review focuses on eight major pathogens, *C. jejuni*, *C. coli*, *Salmonella* spp., *E. coli* O157:H7, non-O157 STECs, *Ps. aeruginosa*, vancomycin-resistant *E. faecium* (VRE), and *S. aureus* and their interactions with OAs. In the studies reviewed the pH was measured at the molar MICs (MIC_Ms), and the concentrations of undissociated and dissociated OAs were calculated at the MIC_Ms using the Henderson-Hasselbalch equation. The inhibition of bacterial strains was not solely dependent on pH or on the concentration of undissociated OAs, but inhibition was clearly correlated with the dissociated OA concentration. These studies show a dissociated OA level of acetic, formic, propionic, citric, L-lactic, and butyric acids at 21.83, 19.81, 18.18, 20.39, 22.23, and 22.56 mM, respectively, needed to inhibit 100% of the bacterial strains studied. It was further observed when a bacterium utilizes an OA for energy production, the concentration of that OA will require a significant increase to cause inhibition of the bacterium.

Keywords

Acetic acid, butyric acid, citric acid, formic acid, L-lactic acid, organic acids, propionic acid, foodborne pathogens

Abbreviations

[A^-]: molar concentration of the dissociated weak acid; BWL: body weight loss; CDC: Centers for Disease Control and Prevention; EFSA: European Food Safety Authority; FDH: formate dehydrogenase; [HA]: molar concentration of the undissociated weak acid; LDH: lactate dehydrogenase; L-iLDH: L-lactate dehydrogenase; MIC: minimum inhibitory concentration; MIC_M: molar minimum inhibitory concentration; NAD: nicotinamide adenine dinucleotide; O157 STEC: Shiga toxin-producing *Escherichia coli* O157; OA: organic acid; LPS: lipopolysaccharide; pK_a: $-\log_{10}$ of the acid dissociation constant (K_a); SA: staphyloferrin A; SB: staphyloferrin B; VRE: vancomycin-resistant *Enterococcus faecium*; WHO: World Health Organization

Introduction

The World Health Organization (WHO) named 12 pathogenic bacteria in 2017 that pose the greatest threat to human health [1, 2]. This was based on their pathogenicity to humans and propensity to become resistant to antibiotics. The bacteria were listed according to their priority: critical, high, and medium priority. *Pseudomonas aeruginosa* was in the critical priority group, and *Enterococcus faecium*, *Staphylococcus aureus*, *Campylobacter*, and *Salmonella* were listed in the high priority group [1, 2]. In a summary report on zoonotic agents and foodborne outbreaks in 2015 by the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control, *Campylobacter* was the most often reported human gastrointestinal pathogen, followed by *Salmonella*, and listed at number four were the STEC infections [3]. In 2011, the Centers for Disease Control and Prevention (CDC) published estimates of foodborne illnesses based on data from surveillance programs listing the 31 major pathogens in the United States [4]. *Campylobacter* spp. and nontyphoidal *Salmonella* spp. were number 1 and 2, respectively, in frequency causing gastrointestinal foodborne illness. Also listed in the report was Shiga toxin-producing *Escherichia coli* O157 (O157 STEC), non-O157 STEC, and *S. aureus* causing foodborne illness [4]. *Ps. aeruginosa* is an opportunistic pathogen [5] that generally causes infections in the blood, lungs, or in the tissues following surgeries [6]. *S. aureus* also is an opportunistic pathogen [5] that causes endocarditis, meningitis, sepsis, and skin diseases [7, 8]. An outbreak of foodborne MRSA caused septicemia [9]. Both *Ps. aeruginosa* and *S. aureus* can cause intestinal disease [5]. Gastrointestinal illness can be caused by *Ps. aeruginosa* [10, 11] and by foodborne *S. aureus* and MRSA [12, 13]. Eight major pathogens and their interactions with organic acids (OAs) are the focus of this review, *C. jejuni* [14], *C. coli* [15], *Salmonella* spp. [16], *E. coli* O157:H7 [17], non-O157 STECs [18], *Ps. aeruginosa* [19], vancomycin-resistant *E. faecium* (VRE) [20], and *S. aureus* [21].

Wachsmuth and coworkers suggested that new strategies must be developed to control foodborne pathogens that cause human illnesses [22], and successful new strategies may include biocides, disinfectants, and OAs. OAs are currently used on the farm and in the processing plant. During poultry production OAs, such as butyric, formic and L-lactic acids are often used to treat the feed [23-26] and the drinking water [27, 28] to reduce pathogens carried by the birds. Evaluations of OA treatments in the poultry industry to reduce body weight loss (BWL) while improving meat quality characteristics was successful, and OA treatments may be a way to improve animal welfare and economic concerns [29]. Enhanced growth performance has been observed in weaned pigs following treatment with citric, formic and propionic acids [30-32]. Also, dietary acidifiers, like the OAs, can improve both growth rate and feed efficiency in pigs [33]. Lactic acid sprays are used to remove *Campylobacter* spp. and *Salmonella* spp. from pork carcasses [34, 35]. Feedlot cattle may experience a grain overload resulting in ruminal acidosis, which can result in reduced performance and production efficiency. However, when OAs were used to replace antimicrobial compounds in the feed (like monensin), they were effective in controlling ruminal acidosis in beef cattle [36]. Acetic and lactic acids are used as warm surface rinses to treat beef and lamb carcasses post slaughter for the removal of surface bacteria [37], and OA sprays are also used to remove carcass surface bacteria [35, 38, 39]. Citric and lactic acid applications applied to beef shoulder clods used for ground beef can remove *E. coli* O157:H7 and other STEC contamination [40], and studies have been conducted using OAs for marinating meat to remove foodborne pathogens [41]. Food processing plants in the United States commonly use acetic [39, 43-47], formic [37, 44], propionic [44-46], citric [39, 46] and lactic acid [34, 35, 37-39, 44-47] to remove bacteria from the hides, carcasses and meats, and these treatments are fast, cost efficient, and effective [42]. Also, short chain OAs like butyric acid are fed to broiler chickens to help maintain carcass quality and performance [48, 49]. After meat processing, the bacteria not removed by the OA washes remains on the meat and can be found in the final meat products. A thorough understanding of the mechanism(s) by which OAs inhibit pathogenic bacteria will allow the food processor to incorporate this information into their disinfection strategy to enhance their ability to mitigate foodborne pathogen contamination. The studies reviewed here evaluated some or all of the six OAs: acetic, butyric, citric, formic, L-lactic, and propionic acids along with eight foodborne pathogens.

The historical traditional assumption for OA inhibition of bacteria

As early as 1929 and through the first half of the 1900's researchers observing weak acid effects on microorganisms felt there was a clear pH-dependency on bacterial inhibition, because weak acids were less effective as the pH increased [50-52]. In a symposium it was discussed how these earlier researchers had not calculated the concentration of undissociated acid present at the point of inhibition of the microorganisms [53]. It appears researchers at that time assumed OAs used as food preservatives were active in the undissociated form [54, 55]. This point of view also suggests that the inhibition of microorganisms is primarily pH-dependent [56]. However, some researchers did not agree with the pH dependency theory because they noticed trends of inhibition by weak acids that were not dependent on pH changes [57-60]. Quantification of the undissociated and dissociated forms of sorbic acid was investigated, and the results suggested that the dissociated acid may also have antimicrobial activity [57]. Others calculated the undissociated and dissociated forms of sorbic acid [56], and benzoic and propionic acids [61], showing that both the undissociated and dissociated acids caused inhibition. However, the final formula used by these researchers was flawed; therefore, the results are suspect. Since those earlier times researchers have continued to assume that the undissociated forms of OAs are the form that enters bacterial cells and result in causing bacterial inhibition [46, 62-69]. However, there appears to be no definitive study showing that the undissociated OA form is the active form of the OAs that enters the bacterial cell

and causes inhibition, and the actual mechanism(s) that are involved in OA caused bacterial inhibition remains unknown [21, 70-73]. It is however, relatively clear that intracellular accumulation of anions is a primary reason for inhibition of bacteria by OAs [46, 71, 74, 75].

Bacterial utilization of OAs for energy or for metabolic products

We have observed that when a bacterium utilizes an OA as an energy source it will significantly increase the susceptibility values of that bacterium against that same OA [15]. Researchers have observed *S. aureus* utilizing citrate in two different siderophores for iron sequestration [76, 77], and our laboratory has observed that high concentrations of dissociated citric acid were required for inhibition of *S. aureus* [21]. Bacterial utilization of OAs (with some bacteria–OA combinations) is an important limitation on the application of OAs used for removal of bacteria. Therefore, the utilization of OAs by the eight pathogenic bacteria and the 6 OAs reviewed here are discussed below.

Campylobacter jejuni utilization of OAs

C. jejuni utilizes the following five OAs: acetic, butyric, formic, propionic, and L-lactic acid [5]. Formic and L-lactic acid are the most readily utilized OAs. *C. jejuni* metabolizes formate using a multi-subunit formate dehydrogenase (FDH) [78]. The metabolism of formate leads to chemoattraction of formate and results in further bacterial respiration using formate; therefore, formic acid is used as a primary energy source for *C. jejuni* [79, 80]. *C. jejuni* also utilizes acetic [79, 81], butyric [79, 81], propionic [81], and L-lactic acid [81, 82] as energy sources. *C. jejuni* utilization of L-lactate is mediated through two nicotinamide adenine dinucleotide (NAD)-independent L-lactate dehydrogenases (L-LDHs), in which one L-LDH enzyme contains a non-flavin iron-sulfur containing a three-subunit membrane-associated enzyme and the other L-LDH contains both a flavin and iron-sulfur containing membrane-associated oxidoreductase [82]. Formic and L-lactic acid were observed to be the most utilized OA energy sources for *C. jejuni*, as revealed by the high dissociated acid concentrations at the molar minimum inhibitory concentrations (MIC_Ms) of the bacteria for these two OAs [14]. Molar units were used for the MIC concentrations to give an accurate presentation of the MICs of bacteria against OAs having differing molecular weights [17].

Campylobacter coli utilization of OAs

C. coli has been shown to utilize the three OAs: formic, lactic, and propionic acid [83]. In a study by Elharrif and Mégraud, *C. coli* wild type strains did not utilize butyrate, and they did not uniformly utilize citric acid [84]. In the swine study, 13.5% of the *C. coli* strains studied utilized acetate [84]. In our study of 111 *C. coli* swine strains, it was concluded that L-lactic acid was not utilized by the *C. coli* swine strains based on the concentration of dissociated acid at the MIC_Ms [15]. However, it was clear that 83/111 (75%) of the *C. coli* swine strains tested may utilize acetic acid [15].

Salmonella spp. utilization of OAs

Salmonella must penetrate the lining of the intestinal wall to cause infection, and this invasion requires formate to act as a *Salmonella* inducing signal [85]. However, since this type of formate utilization is not connected to energy or growth production it would not be expected to affect the susceptibility of *Salmonella* to formic acid as an inhibitor. When *Salmonella enterica* serovar Typhimurium is invading a host, host inflammation drives the host cell metabolism to release L-lactate [86]. *Salmonella* then utilizes this L-lactate along with oxygen as an electron acceptor to allow further colonization of the host [86]. Since this utilization, again, is not directly funneled into energy or growth production it most likely would not affect the susceptibility of *Salmonella* to inhibition by L-lactic acid. We have previously studied the effects of four OAs (acetic, citric, L-lactic, and propionic acid) on 145 strains of *Salmonella* spp. [16]. An effect on the concentrations of L-lactic acid needed to inhibit the *Salmonella* spp. was not observed, which is in agreement with the hypothesis that the utilization of L-lactate by *Salmonella* is not funneled into energy or growth production, therefore, no increase of susceptibility should be produced.

E. coli O157:H7 utilization of OAs

An *E. coli* protective effect was observed when low concentrations (5 mM) of acetic, malic, or L-lactic acid were added to an acidic medium containing the bacterium [87]. However, when these OAs were added at higher concentrations no protective effect was observed [87]. When *E. coli* were grown in Koser's medium the bacteria utilized citrate (Koser's citrate test) [88-90], and it is known that *E. coli* will utilize citrate under certain growth conditions [91, 92]. In a long-term study of *E. coli* evolution, the most interesting adaptation was the evolution of aerobic growth on citrate [93, 94]. In our studies with *E. coli* O157:H7, the MIC_Ms for dissociated citric acid were observed at high enough concentrations suggesting citrate was utilized by the bacterial strains isolated from cattle [17].

Non-O157 STEC utilization of OAs

The literature has no information about non-O157 STECs utilizing OAs, and our studies against the four OAs tested (acetic, citric, L-lactic, and propionic acid) show no potential utilization of these acids by the different non-O157 STEC strains tested [18].

Ps. aeruginosa utilization of OAs

It is described in the literature that *Ps. aeruginosa* does utilize lactate [95, 96]. It was further proposed that an NAD-independent L-lactate dehydrogenase (L-iLDH) purified from the membrane of *Ps. stutzeri* SDM played an indispensable role by catalyzing the conversion of L-lactate into pyruvate [97]. It was then later demonstrated that *Ps. aeruginosa* has two L-lactate utilization dehydrogenases, L-iLDH encoded by *lldD* and a flavin-containing membrane-bound L-iLDH encoded by *lldA* [98]. A *lldD* and *lldA* double mutant was not able to grow in a medium when the sole carbon source

was L-lactate [98]. L-Lactate utilization by *Ps. aeruginosa* was confirmed in our study of evaluating the interactions of OAs against *Ps. aeruginosa* [19], which showed that elevated levels of dissociated L-lactic acid were required to inhibit the bacteria.

Vancomycin-resistant *E. faecium* utilization of OAs

The metabolism of citrate was studied in *E. faecalis* FAIR-E 229 in both a glucose medium and as a sole carbon source, and the results supported the idea that enterococcal strains have the ability to metabolize citrate [99]. Citrate metabolism was studied in *Enterococcus faecium* ET C9 and in *Enterococcus durans* Ov 421, and both strains were shown to utilize citrate as a sole carbon source to produce energy [100]. Also, co-metabolism of citrate and lactose was observed in a study of citrate metabolism of *E. faecium* FAIR-E 198, and in anaerobic conditions the yield of ethanol from citrate metabolism increased [101]. However, our study of 50 VRE isolated from human wastewater effluents demonstrated that the VRE tested showed no utilization of citrate for energy production or growth [20].

S. aureus utilization of OAs

A biochemical test used for identification of *S. aureus* demonstrated that the bacterium utilized citrate [102], and plasma coagulation by *S. aureus* was caused by the utilization of citrate by the bacterium [103]. *S. aureus* has evolved multiple iron transport systems to assure the supply of iron from host sources [104]. *S. aureus* utilizes citrate to produce two iron siderophores, staphyloferrin A (SA) and staphyloferrin B (SB) [76, 77]. The siderophore SA contains two molecules of citrate [105, 106], and SB contains one molecule of citrate [107]. L-Lactate can be efficiently utilized by *S. aureus* for growth [108-111]. *S. aureus* can efficiently convert L-lactate to acetate, and both L-lactate and glucose can be simultaneously utilized for growth [109, 112]. Also, when glucose concentrations become limiting, *S. aureus* can still maintain exponential growth by switching over to total aerobic metabolism where it can only utilize L-lactate [109, 112]. Our lab has demonstrated that the levels of both citric and L-lactic acid and dissociated citric and L-lactic acid are elevated when inhibiting *S. aureus* [21].

Table 1 presents a summary of the pathogenic bacteria reviewed here and the organic acids/anions utilized by those bacteria. Where possible, the enzyme systems involved are listed.

Table 1: Compilation of pathogenic bacteria and organic acids/anions utilized by the bacteria, enzymes used, and references.

Bacteria	Utilization of Organic acids/ Anions	Enzymes involved	References
Campylobacter jejuni	acetic, butyric, formic, propionic, L-lactic		14
	formate	formate dehydrogenase	78
	L-lactate	2 NAD-independent L-lactate dehydrogenases	82
Campylobacter coli	formic, lactic, propionic		83
	did not utilize lactic		15
	(some strains may use acetate)		15, 84
Salmonella	None		—
Escherichia coli	citrate		88-90
Escherichia coli O157:H7	citrate		17
Non-O157 STECs	None		—
Pseudomonas aeruginosa	lactate		19, 95, 96
	lactate → pyruvate	NAD-independent L-lactate dehydrogenase (L-iLDH)	97
	lactate → pyruvate	flavin-containing L-iLDH	98
Enterococcus faecalis FAIR-E 229	citrate		99
E. faecium ET C9 and *E. durans* Ov 421	citrate		100
Vancomycin-resistant *Enterococcus faecium*	did not utilize citrate		20
Staphylococcus aureus	citrate		102, 108-111
	uses citrate to produce two iron siderophores		76, 77
	L-lactate → acetate	lactate dehydrogenase (LDH)	109, 112
(*S. aureus* resistance to nitrosative stress)	pyruvate → α-acetolactate	α-acetolactate synthase	113

Overview for calculating ratios of the undissociated/ dissociated OAs

The calculation of the undissociated/dissociated acid ratio for the OAs can be achieved when the pH is known by using the Henderson-Hasselbalch equation [114]:

$$pH = pK_a + \log([A^-]/[HA])$$

The $pK_a = -\log_{10}$ of the acid dissociation constant (K_a), the variables in the equation are ($[A^-]$): the molar concentration of the conjugate base (or dissociated weak acid), and ($[HA]$): the molar concentration of the undissociated weak acid [114]. Upon rearrangement of the Henderson-Hasselbalch equation

the ratio of undissociated acid to the dissociated acid can be calculated [64]:

$$\text{Ratio} = [HA]/[A^-] = 1/10^{pH-pKa}$$

Therefore, when the pK_a of the OA in question and the pH of the solution are known, the ratio of the undissociated to the dissociated acid can be calculated. The published pK_a's for the OAs are as follows: acetic, butyric, citric, formic, L-lactic, and propionic acid are 4.75, 4.75, 3.14, 3.75, 3.86 and 4.87, respectively. There are three pK_as for citric acid, 3.14, 4.77, and 6.39; in all of the work reported here the first pKa = 3.14 was used for the citric acid calculations since the work is only dependent upon the dissociation of any one OH group. With measurement of the pH at all the bacterial MICs and since the molar concentrations of the OAs are known at the MICs, then the molar concentrations of the undissociated acids and dissociated acids at each MIC can be calculated by using the ratios of the undissociated/dissociated OA [14-21].

Overview of a study evaluating *Salmonella* interactions against OAs

With permission granted from the *Journal of Food Chemistry & Nanotechnology* the following three figures, figure 1 to figure 3, from the study of OAs against *Salmonella* strains from feedlot water-sprinkled cattle [16] will be used as an example to view the typical type of data that has been generated for the following eight different pathogenic bacteria discussed in this review: *C. jejuni* [14], *C. coli* [15], *Salmonella* spp. [16], *E. coli* O157:H7 [17], non-O157 STEC [18], *Ps. aeruginosa* [19], vancomycin-resistant *E. faecium* (VRE) [20], and *S. aureus* [21]. Mueller-Hinton broth was used in all studies to determine the susceptibilities of the microorganisms against the OAs tested, and in a previous study Mueller-Hinton broth was determined to not influence the results of bactericidal tests with disinfectants [115].

pH at the *Salmonella* MICs against the four OAs, acetic, citric, L-lactic and propionic acid

Figure 1 displays the graphical presentation of the pH data observed at the MIC_Ms of 145 *Salmonella* strains isolated from feedlot water-sprinkled cattle [16]. The pH data for *Salmonella* [16] are typical of the data obtained for all eight of the pathogenic bacteria discussed here. The number of strains at each MIC_M is listed next to each data point. The MIC_Ms occurred for 97.2% of the *Salmonella* strains against acetic acid at pH 5.15 and the MIC_Ms occurred for 100% of the *Salmonella* strains against propionic acid at pH 4.86 [16]. However, the MIC_Ms for 100% of the *Salmonella* strains against citric and L-lactic acid occurred at pH 4.06 and 4.25, respectively [16]. The difference between the pH values at the MIC_Ms for the same *Salmonella* strains against acetic and propionic acid compared with citric and L-lactic acid is almost a whole pH unit. This difference in pH values at the MIC_Ms for the same strains against two different OA groups shows that bacterial inhibition is not dependent on the pH at the MIC_Ms, as others have suggested [64, 70], but most likely is dependent on some other aspect of these OAs [116]. If bacterial inhibition was primarily caused by pH, then the same pH values would be expected to be observed at the MICs for the same bacteria against different OAs, but that is not what we have observed in experiments with eight different pathogenic bacteria [14-21]. Also, if pH is the only important aspect of OA inhibition of bacteria, then acid resistant pathogenic bacteria [117-120] would be an important health threat in OA acidified foods [66]. However, OA acidified food products have been safely made and used for very many years [121].

Other researchers have shown that acetic acid and HCL inhibited enterohemorrhagic *E. coli* at different pH values, namely 5.5 and 4.25 pH, respectively, for a $\Delta = 1.25$ pH unit difference between these two acids [122]. Our laboratory observed a 1.1 pH unit difference at the MIC_Ms for 50 VRE strains against six OAs [20]. A difference of 0.98 pH unit was observed at their MIC_Ms for 175 *Ps. aeruginosa* [19], and 98% of 344 *E. coli* O157:H7 strains showed a difference of 0.56 pH unit at their MIC_Ms against three OAs [17]. A difference of 0.99 pH unit was observed for 138 non-O157 STEC strains at their MIC_Ms against four OAs [18], and 95% of 145 *Salmonella* strains had a difference of 1.1 pH unit at their MIC_Ms against four OAs [16]. A difference of 1.76 pH units was observed for 111 *C. coli* strains at their MIC_Ms against six OAs [15], and 97% of 96 *C. jejuni* strains had a difference of 1.34 pH units at their MIC_Ms against six OAs [21]. In the studies of all eight pathogenic bacteria, the lowest pH observed at bacterial inhibition was with *S. aureus*, at a pH of 3.07 [21], and the highest pH observed at bacterial inhibition was with *C. jejuni*, at a pH of 7.31 [15]. These data demonstrate that inhibition of bacteria by OAs is not dependent on pH, as had been suggested by other researchers [64, 70, 123]. Therefore, inhibition of bacteria by OAs must rely on some other aspect of OAs [21, 116].

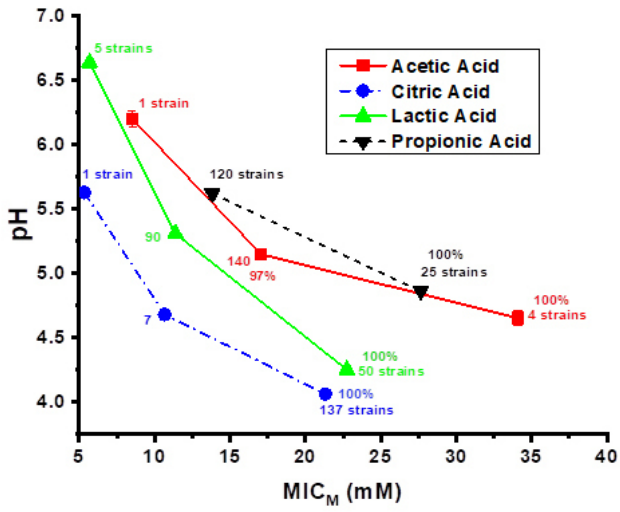

Figure 1: pH at the MIC_Ms of the 145 *Salmonella* strains in acetic, citric, lactic and propionic acids. The error bars represent the standard deviation of three pH measurements. The *Journal of Food Chemistry & Nanotechnology* granted permission to use this figure on 29 August 2020, which is found in reference [16].

The calculated molar concentrations of undissociated OAs at the *Salmonella* MIC_Ms

The undissociated OA data calculated using the

Henderson-Hasselbalch equation at the *Salmonella* MIC_Ms [16] are typical of the type of data generated for all eight studies of pathogenic bacteria against OAs [14-21]. Figure 2 shows the molar undissociated concentrations of acetic, citric, L-lactic, and propionic acids at the MIC_Ms for 145 *Salmonella* strains. The number of strains at each MIC_M is shown next to each data point. An undissociated acetic acid concentration of 19.0 mM is sufficient to inhibit all 145 *Salmonella* strains. However, an undissociated citric acid concentration of only 2.29 mM is required to inhibit these same *Salmonella* strains. The shaded band in Figure 2 indicates the difference for inhibiting the same 145 *Salmonella* strains by undissociated acetic and undissociated citric acid for a difference of Δ = 16.71 mM OA. Figure 2 shows no correlation between the *Salmonella* MIC_Ms and the different undissociated OAs. These results are consistent with the other seven studies of pathogenic bacteria against OAs [14, 15, 17-21]. For the MIC_Ms of 98.3% of 344 *E. coli* O157:H7 strains the difference in undissociated acetic and citric acid was Δ = 47.77 mM [17]. For the MIC_Ms of 98.6% of 138 non-O157 STEC strains the difference in undissociated acetic and citric acids was Δ = 14.07 mM [18]. For the MIC_Ms of 100% of 175 *Ps. aeruginosa* strains the difference in undissociated acetic (21.65 mM) and citric (2.53 mM) acids was Δ = 19.12 mM [19]. For the MIC_Ms of 100% of 50 VRE strains the difference in undissociated propionic and citric acids was Δ = 35.21 mM [20]. For the MIC_Ms of 100% of 111 *C. coli* strains the difference in undissociated acetic and citric acids was Δ = 39.91 mM [15]. For the MIC_Ms of 96 *C. jejuni* strains the difference in undissociated L-lactic and citric acid levels was Δ = 50.78 mM [14]. For the MIC_Ms of 164 *S. aureus* strains the difference in undissociated acetic and formic acid levels was Δ = 44.72 mM [21]. In the studies of all eight pathogenic bacteria, the lowest level of undissociated OA observed at bacterial inhibition was with *S. aureus*, at a concentration of 0.00006 mM [21], and the highest level of undissociated OA observed at bacterial inhibition was with *E. coli* O157:H7, at a concentration of 114.59 mM [17]. The undissociated OA levels required to inhibit these pathogenic bacteria are extremely variable, high and low, and there are no consistent values of undissociated OAs that are associated with bacterial inhibition. The extremely low undissociated OA levels are not considered reasonable concentrations for inhibiting bacteria.

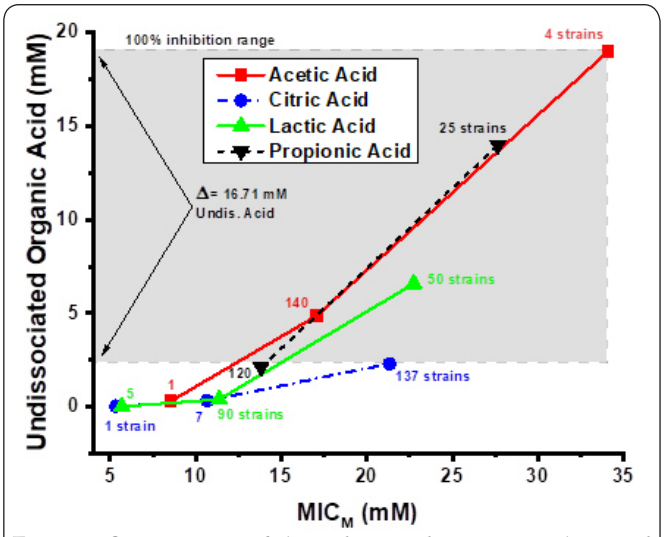

Figure 2: Concentrations of the undissociated acetic, citric, lactic and propionic acids at the MIC_Ms of the 145 *Salmonella* strains. The grey band shows a difference of 16.71 mM between the four undissociated organic acids required for inhibition of 100% of the *Salmonella* strains. The *Journal of Food Chemistry & Nanotechnology* granted permission to use this figure on 29 August 2020, which is found in reference [16].

The calculated molar concentrations of dissociated OAs at the *Salmonella* MIC_Ms

The dissociated OA data calculated using the Henderson-Hasselbalch equation at the *Salmonella* MIC_Ms [16] are typical of the type of data generated for all eight studies of pathogenic bacteria against OAs [14-21]. The dissociated OA concentrations for acetic, citric, L-lactic and propionic acids were calculated at the MIC_Ms of 145 *Salmonella* strains and the graphical presentation of the interactions of these dissociated OAs against *Salmonella* are shown in figure 3. The number of strains at each MIC_M is shown next to each data point. The shaded band in figure 3 shows the dissociated OA concentrations necessary to cause the MIC_Ms of 100% of the 145 *Salmonella* strains by all four OAs tested. Only a Δ = 5.36 mM concentration difference in dissociated acetic, citric, L-lactic, and propionic acids was observed to cause the MIC_Ms of all *Salmonella* strains. There is only a Δ = 1.43 mM concentration difference in the MIC_Ms from dissociated acetic and dissociated propionic acids for 100% of the *Salmonella* strains [16]. This narrow range of dissociated OAs needed to inhibit these 145 *Salmonella* strains is in stark contrast to the extreme variability, high and low concentration values having no consistency as seen with the undissociated OAs for inhibition of these same bacterial strains, and the wide range of pH values.

The narrow range of dissociated OAs needed to inhibit 100% of the *Salmonella* strains is very similar to the inhibition ranges observed for the other seven pathogenic bacteria against OAs [14, 15, 17-21]. A difference of Δ = 5.44 mM dissociated OAs was observed at the MIC_Ms of 98.3% of the 344 *E. coli* O157:H7 strains against acetic, citric, L-lactic, and propionic acid [17]. A difference of Δ = 6.19 mM dissociated OAs was observed at the MIC_Ms of 100% of 138 non-O157 STEC strains against acetic, citric, L-lactic, and propionic acids [18]. A difference of Δ = 6.34 mM dissociated acetic and citric acids was observed at the MIC_Ms of 100% of 175 *Ps. aeruginosa* strains [19]. Only a difference of Δ = 3.1 mM dissociated OAs was observed at the MIC_Ms of 100% of 50 VRE strains against acetic, butyric, citric, formic, L-lactic, and propionic acids [20]. A difference of Δ = 11.92 mM dissociated butyric, citric, and L-lactic acids was observed at the MIC_Ms of 100% of 111 *C. coli* strains [15]. A difference of Δ = 4.47 mM dissociated acetic, butyric, citric, and propionic acids was observed at the MIC_Ms of 97–100% of 96 *C. jejuni* strains [14]. A difference of Δ = 6.11 mM OAs was observed at the MIC_Ms of 100% of 164 *S. aureus* strains against acetic, butyric, formic, and propionic acids [21]. The narrow ranges of dissociated OAs observed for bacterial inhibition are consistent for both Gram-positive and Gram-negative pathogens.

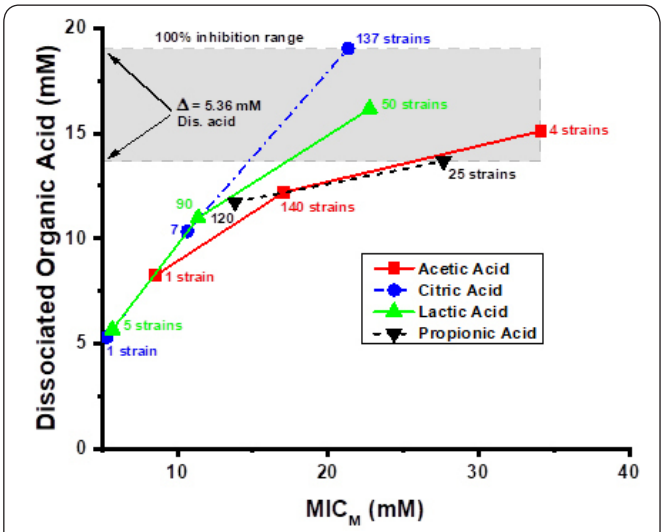

Figure 3: Concentrations of the dissociated acetic, citric, lactic and propionic acids at the MIC$_M$s of the 145 *Salmonella* strains. The grey band shows a difference of 5.36 mM between the levels of all dissociated organic acids, acetic, citric, lactic and propionic acids required for disinfection of 100% of the *Salmonella* strains. The *Journal of Food Chemistry & Nanotechnology* granted permission to use this figure on 29 August 2020, which is found in reference [16].

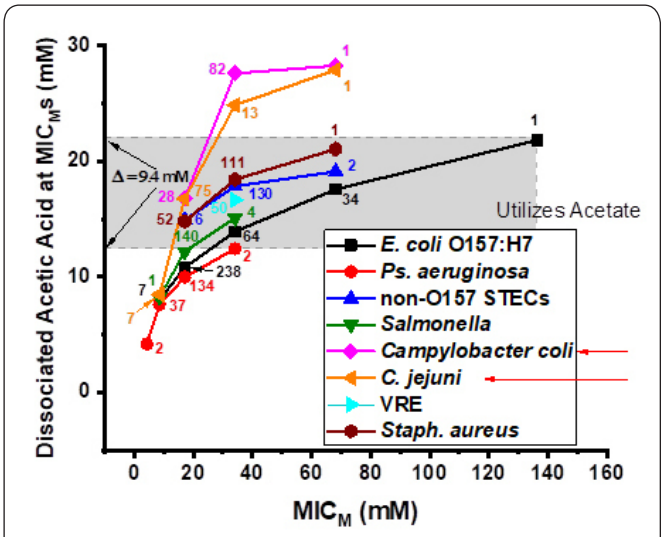

Figure 4: The dissociated acetic acid concentrations are shown at the MIC$_M$s for all pathogenic bacteria studied with the bacterial inhibition of 100% of the strains for *Escherichia coli* O157:H7, *Pseudomonas aeruginosa*, non-O157 STECs, *Salmonella*, VRE, and *Staphylococcus aureus* occurring between 12.45 and 21.83 mM, Δ = 9.38 mM dissociated organic acids. A red arrow is pointing to the bacteria that utilize acetic acid; *C. coli* and *C. jejuni*.

Comparison of dissociated OA inhibition among all eight pathogens

In this section we will look at each individual OA's effects on all the pathogens studied against that OA. The graphical presentation of the interactions of six OAs (acetic, formic, propionic, citric, L-lactic, and butyric acids) against the pathogenic bacteria studied are shown in figures 4-9. These figures were generated by analyzing and combining the data presented in papers published on OA inhibition of each individual organism, *C. jejuni*, *C. coli*, *Salmonella*, *E. coli* O157:H7, non-O157 STECs, *Ps. aeruginosa*, VRE, and *S. aureus* [14-21]. These figures showing the comparison of interactions of pathogens with OAs have not been previously published.

Dissociated acetic acid inhibition of pathogenic bacteria

The interactions of various dissociated acetic acid concentrations at the MIC$_M$s of the pathogenic bacteria, *E. coli* O157:H7 [17], *Ps. aeruginosa* [19], non-O157 STECs [18], *Salmonella* [16], *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21] are presented graphically in figure 4. The number of strains at each MIC$_M$ is shown next to each data point. Acetate is utilized by both *C. coli* and *C. jejuni*, thereby forcing the elevation of the acetic acid levels required to inhibit these two bacteria. The red arrows in figure 4 indicate that these two bacteria utilize acetate. In a study by Elharrif and Mégraud, 13.5% of the *C. coli* swine strains studied utilized acetate [84]. But in a study at our laboratory, it was clear that 83/111 *C. coli* swine strains (75%) may be utilizing acetate [15]. *C. jejuni* uses acetate as an energy source [79, 81]. Dissociated acetic acid causes the inhibition of 100% of the other six pathogens that reside within the highlighted box in figure 4 from 12.45 mM against *Ps. aeruginosa* to 21.83 mM against *E. coli* O157:H7. Therefore, a concentration of 21.83 mM dissociated acetic acid will inhibit the six bacteria as seen in figure 4, but not the two bacteria that utilize acetate, *C. coli* and *C. jejuni*.

Dissociated formic acid inhibition of pathogenic bacteria

We have evaluated the interactions of formic acid against the following four different pathogenic bacteria: *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21]. The interactions of dissociated formic acid with these four bacteria are shown in figure 5. The number of strains at each MIC$_M$ is shown next to each data point. It is clear that 100% of the 50 VRE strains studied were inhibited at the dissociated formic acid concentration of 19.76 mM [20], and 100% of the 164 *S. aureus* strains studied were inhibited by 19.81 mM dissociated formic acid [21]. However, both *C. coli* and *C. jejuni* show high levels of dissociated formic acid necessary for inhibition

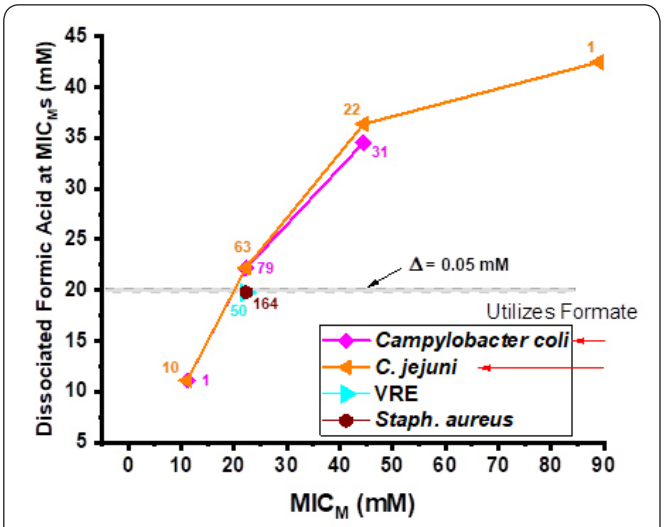

Figure 5: The dissociated formic acid concentrations are shown at the MIC$_M$s for the pathogenic bacteria studied with the bacterial inhibition of 100% of the strains VRE and *Staphylococcus aureus* occurring between 19.76 and 19.81 mM, respectively, which is a Δ = 0.05 mM dissociated organic acids. A red arrow is pointing to the bacteria that utilize formic acid; *C. coli* and *C. jejuni*.

of the bacteria. These two bacteria utilize formic acid. Wagley and coworkers demonstrated that *C. coli* utilizes formic acid [83], and we confirmed that high levels of formic acid were needed to inhibit *C. coli* in a study of *C. coli* against OAs [15]. *C. jejuni* uses a multi-subunit formate dehydrogenase to metabolize formate [78]. This formate metabolism leads to chemoattraction by *C. jejuni* for formate and then respiration; therefore, *C. jejuni* uses formate as a primary energy source [79, 80]. The two bacteria (VRE [20] and *S. aureus* [21]) that do not utilize formate are inhibited by a concentration of 19.81 mM dissociated formic acid.

Dissociated propionic acid inhibition of pathogenic bacteria

The interactions of dissociated propionic acid concentrations at the MIC_Ms of the pathogenic bacteria, *E. coli* O157:H7 [17], non-O157 STECs [18], *Salmonella* [16], *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21] were obtained from each of these studies and are graphically compared in figure 6. The number of strains at each MIC_M is shown next to each data point. Dissociated propionic acid inhibited 100% of the five pathogenic bacteria, *E. coli* O157:H7, non-O157 STECs, *Salmonella*, VRE, and *S. aureus* against OAs within a narrow concentration range from 13.67 mM (*Salmonella* [16]) to 18.18 mM (VRE [20]). Therefore, a dissociated propionic acid concentration of 18.18 mM will inhibit 100% of the *E. coli* O157:H7, non-O157 STECs, *Salmonella*, VRE, and *S. aureus* strains. The remaining two bacteria, *C. coli* [15] and *C. jejuni* [14], required high levels of propionic acid for inhibition of these bacteria (figure 6). These two pathogens utilize propionic acid, and the red arrows in figure 6 indicate that these two bacteria utilize propionate. Wagley and coworkers demonstrated that *C. coli* utilizes propionic acid [83], and we confirmed that high levels of propionic acid were needed to inhibit *C. coli* in the study of *C. coli* against OAs [15]. It was demonstrated that *C. jejuni* utilizes propionic acid as an energy source [81]. Based on the high levels of propionic acid required to inhibit *C. jejuni* in a study of *C. jejuni* against OAs, it was hypothesized that *C. jejuni* must utilize propionic acid [14].

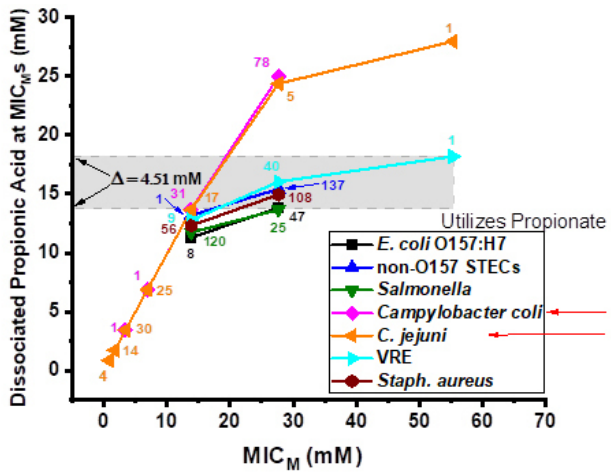

Figure 6: The dissociated propionic acid concentrations are shown at the MIC_Ms for pathogenic bacteria studied with the bacterial inhibition of 100% of the strains, *Escherichia coli* O157:H7, non-O157 STECs, *Salmonella*, VRE, and *Staphylococcus aureus* occurring between 13.67 and 18.18 mM, Δ = 4.51 mM dissociated organic acids. A red arrow is pointing to the bacteria that utilize propionic acid; *C. coli* and *C. jejuni.*

Dissociated citric acid inhibition of pathogenic bacteria

Figure 7 shows the interactions of dissociated citric acid concentrations at the MIC_Ms of the eight pathogenic bacteria, *E. coli* O157:H7 [17], *Ps. aeruginosa* [19], non-O157 STECs [18], *Salmonella* [16], *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21] from eight different bacterial studies against OAs. The number of strains at each MIC_M is shown next to each data point. The shaded area from 10.64 mM (*C. coli* [15]) to 20.39 mM (*C. jejuni* [14]) or Δ = 9.75 mM dissociated OAs is the difference in dissociated OAs required to inhibit the six bacteria known to not utilize OAs in some way. However, five of these bacteria, *Ps. aeruginosa*, non-O157 STECs, *Salmonella*, *C. jejuni*, and VRE were inhibited by the interaction of dissociated citric acid over a narrow concentration range from 18.79 mM (*Ps. aeruginosa* [19]) to 20.39 mM (*C. jejuni* [14]) or Δ = 1.6 mM. It is discussed in the literature that *Enterococcus faecalis* FAIR-E 229 [99] and *E. faecium* ET C9 and *E. durans* Ov 421 [100] can utilize citrate as a sole energy source. However, our VRE data shown in figure 7 suggests that VRE most likely do not utilize citrate [20]. The data in figure 7 clearly show, in general, the bacteria that do not utilize citric acid are inhibited very uniformly and consistently by dissociated citric acid. The red arrows in figure 7 indicate that *S aureus* utilizes citrate and that some strains of *E. coli* O157:H7 also may utilize citrate.

It is known that *E. coli* will utilize citrate under certain growth conditions [91, 92], and an interesting result from an evolutionary study showed that *E. coli* could evolve to use citrate under aerobic growth conditions [93, 94]. In a study of

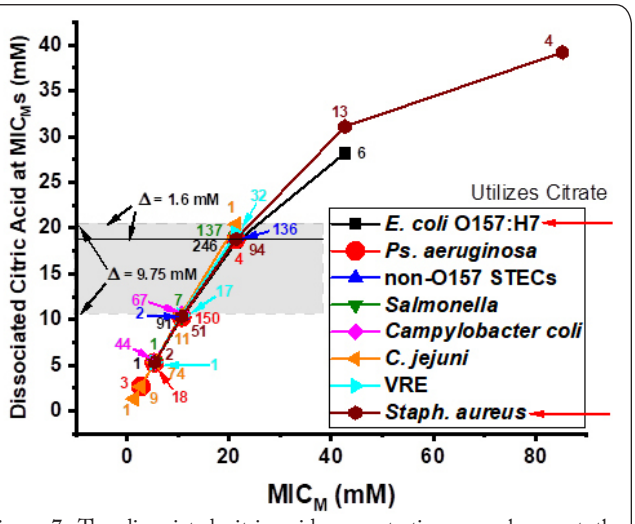

Figure 7: The dissociated citric acid concentrations are shown at the MIC_Ms for all *pathogenic bacteria* studied with the bacterial inhibition of 100% of the strains, *Pseudomonas aeruginosa*, non-O157 STECs, *Salmonella*, *Campylobacter coli*, *C. jejuni*, and VRE occurring between 10.64 and 20.39 mM, Δ = 9.75 mM dissociated organic acids. However, a 100% of *Ps. aeruginosa*, non-O157 STEC, *Salmonella*, *C. jejuni*, and VRE were inhibited between the dissociated organic acid concentrations of 18.79 and 20.39 mM, Δ = 1.6 mM. A red arrow is pointing to the bacteria that utilize citric acid; Staphylococcus aureus, and this data suggests *Escherichia coli* O157:H7 utilizes citrate.

E. coli O157:H7 against OAs, the dissociated citric acid levels needed to inhibit some strains appeared high and suggest that *E. coli* O157:H7 may utilize citric acid in some way [17].

A biochemical test used for the identification of *S. aureus* demonstrated that this bacterium utilized citrate [102]. Multiple iron transport systems have evolved in *S. aureus* to allow the bacteria to obtain iron from a host [104]. Citrate is utilized by *S. aureus* to produce two different iron chelating siderophores, staphyloferrin A (SA) and staphyloferrin B (SB) [76, 77]. Two molecules of citrate are contained in the siderophore SA [105, 106], and one molecule is contained in siderophore SB [107].

Dissociated L-lactic acid inhibition of pathogenic bacteria

The interactions of dissociated L-lactic acid concentrations at the MIC_Ms of the pathogenic bacteria, *E. coli* O157:H7 [17], *Ps. aeruginosa* [19], non-O157 STECs [18], *Salmonella* [16], *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21] were obtained from each of these bacterial studies and are graphically compared in figure 8. The number of strains at each MIC_M is shown next to each data point. The five pathogens *E. coli* O157:H7, non-O157 STECs, *Salmonella*, *C. coli*, and VRE were inhibited by dissociated L-lactic acid over a concentration range from 12.93 mM (non-O157 STECs [18]) to 22.23 mM (*E. coli* O157:H7 [17]), or Δ = 9.3 mM of dissociated OAs. Therefore, a dissociated L-lactic acid concentration of 22.23 mM will inhibit all five of these bacteria, but this concentration would not be sufficient to inhibit the other three bacteria, *Ps. aeruginosa*, *C. jejuni*, and *S. aureus*, that utilize L-lactic acid. *C. coli* was shown by Wagley et al. to utilize lactic acid [83], but *C. coli* strains from swine shown in figure 8 did not utilize L-lactic acid in studies with OAs conducted in our laboratory [15].

Gao and coworkers demonstrated that *Ps. aeruginosa* utilizes lactate [95, 96]. It was shown that an NAD-independent L-iLDH purified from *Ps. stutzeri* SDM catalyzed the conversion of L-lactate to pyruvate [97]. Wang and coworkers then discovered that *Ps. aeruginosa* has two dehydrogenases, an L-iLDH encoded by the gene *lldD* and a membrane bound dehydrogenase encoded by the gene *lldA* [98].

C. jejuni has been shown to utilize L-lactic acid as an energy source [81, 82]. This utilization is mediated through two NAD-independent L-LDHs. One L-LDH enzyme contains a non-iron-sulfur, and the other L-LDH enzyme contains a flavin and an iron-sulfur [82]. In our studies of OAs against *C. jejuni*, the elevated concentration of dissociated L-lactic acid needed for inhibition of the bacteria suggested that L-lactic acid was well utilized by *C. jejuni* [14].

S. aureus can efficiently convert L-lactate to acetate, and then both L-lactate and glucose can simultaneously be utilized for growth [109]. *S. aureus* can maintain an exponential growth phase when glucose concentrations become limiting by switching to total aerobic metabolism where it solely utilizes L-lactate [109]. In our OA studies against *S. aureus*, the levels of dissociated L-lactic acid needed to inhibit the bacteria were wide ranged as seen in figure 8 [21].

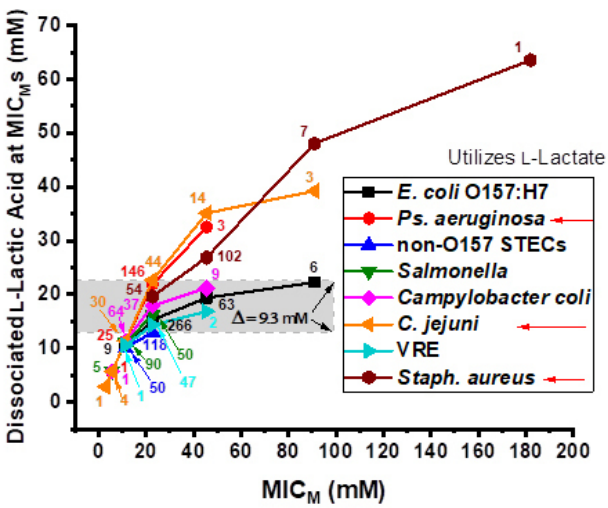

Figure 8: The dissociated L-lactic acid concentrations are shown at the MIC_Ms for all pathogenic bacteria studied with the bacterial inhibition of 100% of the strains for *Escherichia coli* O157:H7, non-O157 STECs, *Salmonella*, *Campylobacter coli*, and VRE occurring between 12.93 and 22.23 mM, Δ = 9.3 mM dissociated organic acids. A red arrow is pointing to the bacteria that utilize L-lactic acid (L-lactate); *Pseudomonas aeruginosa*, *C. jejuni*, and *Staphylococcus aureus*.

Dissociated butyric acid inhibition of pathogenic bacteria

The interaction of dissociated butyric acid concentrations at the MIC_Ms of the four pathogenic bacteria, *C. coli* [15], *C. jejuni* [14], VRE [20], and *S. aureus* [21] were obtained from each of these bacterial studies and are graphically compared in figure 9. The number of strains at each MIC_M is shown next to each data point. The three pathogens *C. coli*, VRE, and *S. aureus* were inhibited by dissociated butyric acid over a concentration range from 18.75 mM (*S. aureus* [21]) to 22.56 mM (*C. coli* [15]), or Δ = 3.81 mM dissociated OAs as shown by the highlighted grey band in figure 9. Therefore,

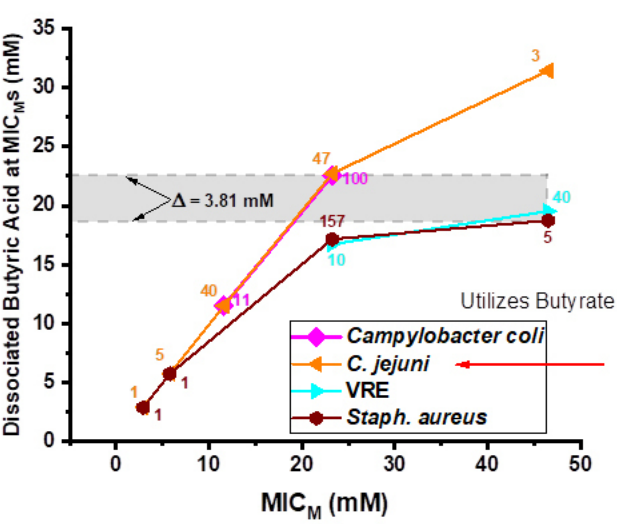

Figure 9: The dissociated butyric acid concentrations are shown at the MIC_Ms for the pathogenic bacteria studied with the bacterial inhibition of 100% of the *Staphylococcus aureus* and *Campylobacter coli* strains occurring between 18.75 and 22.56 mM, respectively, which is a Δ = 3.81 mM dissociated organic acids. A red arrow is pointing to *C. jejuni*, which utilizes butyric acid.

a dissociated butyric acid concentration of 22.56 mM will inhibit *C. coli*, VRE, and *S. aureus* but would not be sufficient to inhibit *C. jejuni* strains, which have been shown to utilize butyric acid [79, 81].

Conclusion

It has been shown in eight studies of OAs against pathogenic bacteria that the inhibition of the bacterial strains studied were not solely dependent on pH or the concentration of undissociated organic acids [14-21]. However, both Gram-negative and Gram-positive bacteria were consistently inhibited by a narrow range of dissociated OA concentrations as observed in this review by the interactions of the dissociated OAs against these pathogenic bacteria. The reviewed studies were conducted from 2013-2020, and clearly show that a dissociated OA level of acetic, formic, propionic, citric, L-lactic, and butyric acids with dissociated acid levels of 21.83, 19.81, 18.18, 20.39, 22.23, and 22.56 mM for a Δ = 4.38 mM will inhibit 100% of the strains studied from all eight bacterial species studied in these reviewed works. Therefore, bacterial inhibition by dissociated OAs required only a narrow range of 4.38 mM in contrast to pH which required a range of 3.07–7.31 pH units and undissociated OAs which required a range of 0.00006–114.59 mM. However, when a bacterium utilizes an OA, the levels of that OA will be required to be significantly increased to inhibit the bacterium. It has been abundantly clear by the research community that intracellular accumulation of anions is a primary reason for inhibition of bacteria by OAs. Until now, the mechanism of action of OAs has not been understood. Researchers have agreed that the inhibition of bacteria is not dependent on pH, and we have shown in the studies discussed in this review that both pH and the undissociated OAs do not correlate with the inhibition of bacteria [14-21]. However, the aspect of OAs that does correlate with inhibition is the concentrations of dissociated OAs at the MIC_Ms, as has been clearly shown in this review [14-21]. Strategies to control foodborne pathogens on the farm and in the processing plant by OA applications should be planned in conjunction with utilizing the inhibitory dissociated OA concentrations.

Conflict of Interest

The author declares no conflict of interest.

Acknowledgements

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References

1. WHO. 2017. WHO publishes list of bacteria for which new antibiotics are urgently needed. https://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed (Accessed on: September 08, 2020).
2. WHO. 2017. WHO names 12 bacteria that pose the greatest threat to human health. https://www.theguardian.com/society/2017/feb/27/world-health-organisation-12-antibiotic-resistant-bacteria-threat-human-health (Accessed on: September 14, 2020).
3. European Commission. 2016. The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2015. *EFSA J* 14(12): 4634. https://doi.org/10.2903/j.efsa.2016.4634
4. Scallan E, Hoekstra RM, Angulo FJ, Tauxe RV, Widdowson M-A, et al. 2011. Foodborne illness acquired in the United States—major pathogens. *Emerg Infect Dis* 17(1): 7-15. https://doi.org/10.3201/eid1701.P11101
5. Affhan S, Dachang W, Xin Y, Shang D. 2015. Lactic acid bacteria protect human intestinal epithelial cells from *Staphylococcus aureus* and *Pseudomonas aeruginosa* infections. *Gen Mol Res* 14(4): 17044-17058. https://doi.org/10.4238/2015.December.16.5
6. Centers for Disease Control and Prevention (CDC). 2019. *Pseudomonas aeruginosa* in healthcare settings. https://www.cdc.gov/hai/organisms/pseudomonas.html (Accessed on: January 25, 2021).
7. Kluytmans J, van Belkum A, Verbrugh H. 1997. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 10(3): 505-520. https://doi.org/10.1128/CMR.10.3.505
8. Gould IM. 2009. Antibiotics, skin and soft tissue infection and methicillin-resistant *Staphylococcus aureus*: cause and effect. *Int J Antimicrob Agents* 34(Suppl. 1): S8-S11. https://doi.org/10.1016/S0924-8579(09)70542-4
9. Kluytmans J, van Leeuwen W, Goessens W, Hollis R, Messer S, et al. 1995. Food-initiated outbreak of methicillin-resistant *Staphylococcus aureus* analyzed by pheno- and genotyping. *J Clin Microbiol* 33(5): 1121-1128. https://doi.org/10.1128/jcm.33.5.1121-1128.1995
10. Porco FV, Visconte EB. 1995. *Pseudomonas aeruginosa* as a cause of infectious diarrhea successfully treated with oral ciprofloxacin. *Ann Pharmacother* 29(11): 1122-1123. https://doi.org/10.1177/106002809502901110
11. Chuang C-H, Janapatle RP, Wang Y-H, Chang H-J, Huang Y-C, et al. 2017. *Pseudomonas aeruginosa*-associated diarrheal diseases in children. *Pediatr Infect Dis J* 36(12): 1119-1123. https://doi.org/10.1097/INF.0000000000001567
12. Jones TF, Kellum ME, Porter SS, Bell M, Schaffner W. 2002. An outbreak of community-acquired foodborne illness caused by methicillin-resistant *Staphylococcus aureus*. *Emerg Infect Dis* 8(1): 82-84. https://doi.org/10.3201/eid0801.010174
13. Azimirad M, Dezfulian A, Alebouyeh M, Esfehani RB, Shahrokh S, et al. 2017. Infection with enterotoxigenic *Staphylococcus aureus* as a concern in patients with gastroenteritis. *J Glob Antimicrob Resist* 9: 111-114. https://doi.org/10.1016/j.jgar.2017.02.009
14. Beier RC, Byrd JA, Caldwell D, Andrews K, Crippen TL, et al. 2019. Inhibition and interactions of *Campylobacter jejuni* from broiler chicken houses with organic acids. *Microorganisms* 7(8): 223. https://doi.org/10.3390/microorganisms7080223
15. Beier RC, Harvey RB, Hernandez CA, Hume ME, Andrews K, et al. 2018. Interactions of organic acids with *Campylobacter coli* from swine. *PLoS ONE* 13(8): e0202100. https://doi.org/10.1371/journal.pone.0202100
16. Beier RC, Callaway TR, Andrews K, Poole TL, Crippen TL, et al. 2017. Interactions of organic acids with *Salmonella* strains from feedlot water-sprinkled cattle. *J Food Chem Nanotechnol* 3(2): 60-66. https://doi.org/10.17756/jfcn.2017-038

17. Beier RC, Poole TL, Brichta-Harhay DM, Anderson RC, Bischoff KM, et al. 2013. Disinfectant and antibiotic susceptibility profiles of *Escherichia coli* O157:H7 strains from cattle carcasses, feces, and hides and ground beef from the United States. *J Food Prot* 76(1): 6-17. https://doi.org/10.4315/0362-028X.JFP-12-253

18. Beier RC, Franz E, Bono JL, Mandrell RE, Fratamico PM, et al. 2016. Disinfectant and antimicrobial susceptibility profiles of the big six non-O157 Shiga toxin-producing *Escherichia coli* strains from food animals and humans. *J Food Prot* 79(8): 1355-1370. https://doi.org/10.4315/0362-028X.JFP-15-600

19. Beier RC, Foley SL, Davidson MK, White DG, McDermott PF, et al. 2014. Characterization of antibiotic and disinfectant susceptibility profiles among *Pseudomonas aeruginosa* veterinary isolates recovered during 1994–2003. *J Appl Microbiol* 118(2): 326-342. https://doi.org/10.1111/jam.12707

20. Beier RC, Harvey RB, Poole TL, Hume ME, Crippen TL, et al. 2018. Interactions of organic acids with vancomycin-resistant *Enterococcus faecium* isolated from community wastewater in Texas. *J Appl Microbiol* 126(2): 480-488. https://doi.org/10.1111/jam.14145

21. Beier RC, Andrews K, Poole TL, Harvey RB, Crippen TL, et al. 2020. Interactions of organic acids with *Staphylococcus aureus* and MRSA strains from swine mandibular lymph node tissue, commercial pork sausage meat and feces. *Int J Microbiol Biotechnol* 5(4): 165-183. https://doi.org/10.11648/j.ijmb.20200504.12

22. Wachsmuth IK, Sparling PH, Barrett TJ, Potter ME. 1997. Enterohemorrhagic *Escherichia coli* in the United States. *FEMS Immunol Med Microbiol* 18(4): 233-239. https://doi.org/10.1111/j.1574-695X.1997. tb01051.x

23. Hinton M, Linton AH. 1988. Control of *Salmonella* infections in broiler chickens by the acid treatment of their feed. *Vet Record* 123(16): 416-421. https://doi.org/10.1136/vr.123.16.416

24. Cox NA, McHan F, Bailey JS, Shotts EB. 1994. Effect of butyric or lactic acid on the *in vivo* colonization of *Salmonella typhimurium*. *J Appl Poult Res* 3(4): 315-318. https://doi.org/10.1093/japr/3.4.315

25. Berchieri A Jr, Barrow PA. 1996. Reduction in incidence of experimental fowl typhoid by incorporation of a commercial formic acid preparation (Bio-Add) into poultry feed. *Poult Sci* 75(3): 339-341. https://doi.org/10.3382/ps.0750339

26. Carrique-Mas JJ, Bedford S, Davies RH. 2007. Organic acid and formaldehyde treatment of animal feeds to control *Salmonella*: efficacy and masking during culture. *J Appl Microbiol* 103(1): 88-96. https://doi.org/10.1111/j.1365-2672.2006.03233.x

27. Byrd JA, Hargis BM, Caldwell DJ, Bailey RH, Herron KL, et al. 2001. Effect of lactic acid administration in the drinking water during pre-slaughter feed withdrawal on *Salmonella* and *Campylobacter* contamination of broilers. *Poult Sci* 80(3): 278-283. https://doi.org/10.1093/ps/80.3.278

28. Chaveerach P, Keuzenkamp DA, Lipman LJA, Van Knapen F. 2004. Effect of organic acids in drinking water for young broilers on *Campylobacter* infection, volatile fatty acid production, gut microflora and histological cell changes. *Poult Sci* 83(3): 330-334. https://doi.org/10.1093/ps/83.3.330

29. Menconi A, Kuttappan VA, Hernandez-Velasco X, Urbano T, Matté F, et al. 2014. Evaluation of commercially available organic acid product on body weight loss, carcass yield, and meat quality during preslaughter feed withdrawal in broiler chickens: a poultry welfare and economic perspective. *Poult Sci* 93(2): 448-455. https://doi.org/10.3382/ps.2013-03444

30. Ravindran V, Kornegay ET. 1993. Acidification of weaner pig diets: a review. *J Sci Food Agric* 62(4): 313-322. https://doi.org/10.1002/jsfa.2740620402

31. Walsh MC, Sholly DM, Hinson RB, Saddoris KL, Sutton AL, et al. 2007. Effects of water and diet acidification with and without antibiotics on weanling pig growth and microbial shedding. *J Anim Sci* 85(7): 1799-1808. https://doi.org/10.2527/jas.2006-049

32. Jacela JY, DeRouchey JM, Tokach MD, Goodband RD, Nelssen JL, et al. 2009. Feed additives for swine: fact sheets – acidifiers and antibiotics. *J Swine Health Prod* 17(5): 270-275. https://doi.org/10.4148/2378-5977.7071

33. Tung CM, Pettigrew JE. 2006. A critical review of acidifiers. National Pork Board. http://www.porkorg/research/critical-review-of-acidifier (Accessed on: September 16, 2020).

34. Epling LK, Carpenter JA, Blankenship LC. 1993. Prevalence of *Campylobacter* spp. and *Salmonella* spp. on pork carcasses and the reduction effected by spraying with lactic acid. *J Food Prot* 56(6): 536-537. https://doi.org/10.4315/0362-028X-56.6.536

35. Reynolds AE Jr. 2005. Utilization of spray wash with organic acids (peroxyacetic acid and lactic acid) and chlorinated wash in combination, utilizing direct application methods, for pathogen reduction on pork and beef carcasses in small and very small meat processing plants (revised 8/24/2005). http://www.fsis.usda.gov/wps/wcm/connect/acc8bddb-eb64-4ea2-82eb-565cf337691a/New_Technology_C29_Summary_FY2003.pdf?MOD=AJPERES (Accessed on: September 17, 2020).

36. Castillo C, Benedito JL, Méndez J, Pereira V, López-Alonso M, et al. 2004. Organic acids as a substitute for monensin in diets for beef cattle. *Anim Feed Sci Technol* 115(1-2): 101-116. https://doi.org/10.1016/j.anifeedsci.2004.02.001

37. Meat industry services. 2006. Organic acids. (Accessed on: September 17, 2020).

38. Castillo A, Lucia LM, Roberson DB, Stevenson TH, Mercado I, et al. 2001. Lactic acid sprays reduce bacterial pathogens on cold beef carcass surfaces and in subsequently produced ground beef. *J Food Prot* 64(1): 58-62. https://doi.org/10.4315/0362-028X-64.1.58

39. Departments of Pennsylvania State University, Texas Tech University, and Washington State University. 2005. Antimicrobial spray treatments for red meat carcasses processed in very small meat establishments. https://meathaccp.wisc.edu/validation/assets/acid_spray_intervention_booklet_from_Penn_State_2005.pdf (Accessed on: September 17, 2020).

40. McCarty KA, Sullivan GA, Burson DE. 2017. Organic acids and applications used for reduction of *E. coli* on beef shoulder clods used for ground beef. https://beef.unl.edu/documents/2017-beef-report/201739-Organic-Acids-and-Applications-used-for-Reduction-of-E-coli-on-Beef-shoulder-Clods-used-for-Ground-Beef.pdf (Accessed on: February 16, 2021).

41. Birk T, Grønlund AC, Christensen BB, Knøchel S, Lohse K, et al. 2010. Effect of organic acids and marination ingredients on the survival of *Campylobacter jejuni* on meat. *J Food Prot* 73(2): 258-265. https://doi.org/10.4315/0362-028x-73.2.258

42. Hinton MH, Corry JEL. 1999. The decontamination of carcass meat. In: Richardson RI, Mead GC (eds) Poultry meat science. CABI Publishing, Oxford, UK, pp 285-295.

43. Dickson JS, Hardin MD, Acuff GR. 1996. Organic acid rinses. In: Microbiology intervention methods. Proceedings of the 49th Annual Reciprocal Meat Conference, American Meat Science Association, pp 129-131. (Accessed on: 18 September 2020).

44. Raftari M, Jalilian FA, Abdulamir AS, Son R, Sekawi Z, et al. 2009. Effect of organic acids on *Escherichia coli* O157:H7 and *Staphylococcus aureus* contaminated meat. *Open Microbiol J* 3: 121-127. https://doi.org/10.2174/1874285800903010121

45. Raftari M, Aziz JF, Abdulamir AS, Ghafurian S, Radu S, et al. 2011. Optimized antibacterial measures against *Escherichia coli* O157:H7 and *Staphylococcus aureus*. *Afr J Microbiol Res* 5(20): 3113-3121. https://doi.org/10.5897/AJMR10.099

46. Mani-López E, Garci HS, López-Malo A. 2012. Organic acids as antimicrobials to control *Salmonella* in meat and poultry products. *Food Res Int* 45(2): 713-721. https://doi.org/10.1016/j.foodres.2011.04.043

47. Dickson JS, Acuff GR. 2017. Maintaining the safety and quality of

beef carcass meat. In: Acuff GR, Dickson JS (eds) Ensuring safety and quality in the production of beef. Burleigh Dodds Science Publishing, Sawston, Cambridge, UK. https://lib.dr.iastate.edu/cgi/viewcontent.cgi?article=1354&context=ans_pubs (Accessed on: 18 September 2020).

48. Leeson S, Namkung H, Antongiovanni M, Lee EH. 2005. Effect of butyric acid on the performance and carcass yield of broiler chickens. *Poult Sci* 84(9): 1418-1422. https://doi.org/10.1093/ps/84.9.1418
49. Tomar K, Kumar R, Yadav SP, Sahu DS, Roy D, et al. 2020. Effect of feeding organic acid on blood biochemical parameters in commercial broiler. *Int J Chem Stud* 8(6): 260-262. https://doi.org/10.22271/chemi.2020.v8.i6d.10779
50. Cruess WV, Richert PH. 1929. Effect of hydrogen ion concentration on the toxicity of sodium benzoate to microorganisms. *J Bacteriol* 17(5): 363-371. https://doi.org/10.1128/JB.17.5.363-371.1929
51. Cruess WV, Irish JH. 1932. Further observations on the relation of pH value to toxicity of preservatives to microorganisms. *J Bacteriol* 23(2): 163-166. https://doi.org/10.1128/JB.23.2.163-166.1932
52. Hoffman C, Schweitzer TR, Dalby G. 1941. Fungistatic properties of antiseptics and related compounds: effect of pH. *Ind Eng Chem* 33(6): 749-751. https://doi.org/10.1021/ie50378a016
53. Simon EW, Blackman GE. 1949. The significance of hydrogen-ion concentration in the study of toxicity. In proceedings of the Symposia of the Society for Experimental Biology III. 61(2): 253-265. https://doi.org/10.2307/1537011
54. von Schelhorn M. 1950. Untersuchungen über konservierungsmittel. IV. Wirksamkeit verschiedener konservierungsmittel bei unterschiedlichen pH-werten. *Dtsch Lebensmitt Rundsch* 46: 151-153. ISSN/ISBN: 0012-0413
55. Oka S. 1960. Studies on transfer of antiseptics to microbes and their toxic effect. Part I. Accumulation of acid antiseptics in yeast cells. *Bull Chem Soc Jpn* 24(1): 59-65. https://doi.org/10.1080/03758397.1960.10857632
56. Eklund T. 1983. The antimicrobial effect of dissociated and undissociated sorbic acid at different pH levels. *J Appl bacteriol* 54(3): 383-389. https://doi.org/10.1111/j.1365-2672.1983.tb02632.x
57. Rehm H-J, Lukas E-M. 1963. Zur kenntnis der antimikrobiellen wirkung der sorbinsäure auf mikroorganismen. *Zentralbl Bakteriol Parasitenkd Infektionskr Hyg* 117: 306-318.
58. Sheu CW, Salomon D, Simmons JL, Sreevalsan T, Freese E. 1975. Inhibitory effects of lipophilic acids and related compounds on bacteria and mammalian cells. *Antimicrob Agents Chemother* 7(3): 349-363. https://doi.org/10.1128/AAC.7.3.349
59. Andersson RE, Bodin HG, Snygg BG. 1980. The effect of some preservatives on growth, lipase production and lipase activity of *Pseudomonas fluorescens*. *Chem, Mikrobiol, Technol Lebensm* 6: 161-164.
60. Reinhard L, Radler F. 1981. Die wirkung von sorbinsäure auf *Saccharomyces cerevisiae*. II. Adsorption, desorption und abbau von sorbinsäure. *Z Lebensm Unters Forsch* 172(5): 382-388. https://doi.org/10.1007/BF01028099
61. Eklund T. 1985. Inhibition of microbial growth at different pH levels by benzoic and propionic acids and esters of *p*-hydroxybenzoic acid. *Int J Food Microbiol* 2(3): 159-167. https://doi.org/10.1016/0168-1605(85)90035-2
62. Minor TE, Marth EH. 1970. Growth of *Staphylococcus aureus* in acidified pasteurized milk. *J Milk Food Technol* 33(11): 516-520. https://doi.org/10.4315/0022-2747-33.11.516
63. Sofos JN, Busta FF. 1981. Antimicrobial activity of sorbate. *J Food Prot* 44(8): 614-622. https://doi.org/10.4315/0362-028X-44.8.614
64. Blocher JC, Busta FF, Sofos JN. 1982. Influence of potassium sorbate and pH on ten strains of type A and B *Clostridium botulinum*. *J Food Sci* 47(6): 2028-2032. https://doi.org/10.1111/j.1365-2621.1982.tb12938.x
65. Ray B, Sandine WE. 1992. Acetic, propionic, and lactic acids of starter culture bacteria as biopreservatives. In: Ray B, Daeschel M (eds) Food biopreservatives of microbial origin, CRC press, Inc., Boca Raton, FL, pp 103-136.
66. Breidt F Jr, Hayes JS, McFeeters RF. 2004. Independent effects of acetic acid and pH on survival of *Escherichia coli* in simulated acidified pickle products. *J Food Prot* 67(1): 12-18. https://doi.org/10.4315/0362-028x-67.1.12
67. Leeson S. 2007. Balancing science versus societal issues in poultry nutrition. *CAB Rev Perspect Agric Vet Sci Nutr Nat Resour* 2(71): 071. https://doi.org/10.1079/PAVSNNR20072071
68. Ghosh HK, Halder G, Samanta G, Koley S. 2008. Effect of dietary supplementation of organic acid and mannan oligosaccharide on the plasma minerals and carcass traits of Japanese quail (*Coturnix coturnix japonica*). *Res J Vet Sci* 1(1): 44-49. https://doi.org/10.3923/rjvs.2008.44.49
69. Van Deun K, Haesebrouch F, Van Immerseel F, Ducatelle R, Pasmans F. 2008. Short-chain fatty acids and L-lactate as feed additives to control *Campylobacter jejuni* infections in broilers. *Avian Pathol* 37(4): 379-383. https://doi.org/10.1080/03079450802216603
70. Ricke SC. 2003. Perspectives on the use of organic acids and short chain fatty acids as antimicrobials. *Poult Sci* 82(4): 632-639. https://doi.org/10.1093/ps/82.4.632
71. Carpenter CE, Broadbent JR. 2009. External concentration of organic acid anions and pH: key independent variables for studying how organic acids inhibit growth of bacteria in mildly acidic foods. *J Food Sci* 74(1): R12-R15. doi: 10.1111/j.1750-3841.2008.00994.x
72. Presser KA, Ross T, Ratkowsky DA. 1998. Modelling the growth limits (growth/no growth interface) of *Escherichia coli* as a function of temperature, pH, lactic acid concentration, and water activity. *Appl Environ Microbiol* 64(5): 1773-1779. https://doi.org/10.1128/AEM.64.5.1773-1779.1998
73. Bushell FML, Tonner PD, Jabbari S, Schmid AK, Lund PA. 2019. Synergistic impacts of organic acids and pH on growth of *Pseudomonas aeruginosa*: a comparison of parametric and Bayesian non-parametric methods to model growth. *Front Microbiol* 9: 3196. https://doi.org/10.3389/fmicb.2018.03196
74. Cherrington CA, Hinton M, Mead GC, Chopra I. 1991. Organic acid: chemistry, antibacterial activity and practical applications. *Adv Microb Physiol* 32: 87-108. https://doi.org/10.1016/S0065-2911(08)60006-5
75. Van Immerseel F, Russell JB, Flythe MD, Gantois I, Timbermont L, et al. 2006. The use of organic acids to combat *Salmonella* in poultry: a mechanistic explanation of the efficacy. *Avian Pathol* 35(3): 182-188. https://doi.org/10.1080/03079450600711045
76. Kobylarz MJ, Grigg JC, Sheldon JR, Heinrichs DE, Murphy MEP. 2014. SbnG, a citrate synthase in *Staphylococcus aureus*: a new fold on an old enzyme. *J Biol Chem* 289(49): 33797-33807. https://doi.org/10.1074/jbc.M114.603175
77. Sheldon JR, Marolda CL, Heinrichs DE. 2014. TCA cycle activity in *Staphylococcus aureus* is essential for iron-regulated syntheses of staphyloferrin A, but not staphyloferrin B: the benefit of a second citrate synthase. *Mol Microbiol* 92(4): 824-839. https://doi.org/10.1111/mmi.12593
78. Shaw FL, Mulholland F, Le Gall G, Porcelli I, Hart DJ, et al. 2012. Selenium-dependent biogenesis of formate dehydrogenase in *Campylobacter jejuni* is controlled by the *fdhTU* accessory genes. *J Bacteriol* 194(15): 3814-3823. https://doi.org/10.1128/JB.06586-11
79. Wright JA, Grant AJ, Hurd D, Harrison M, Harrison M, et al. 2009. Metabolite and transcriptome analysis of *Campylobacter jejuni in vitro* growth reveals a stationary-phase physiological switch. *Microbiology* (Reading) 155(Pt 1): 80-94. https://doi.org/10.1099/mic.0.021790-0
80. Kassem II, Candelero-Rueda RA, Esseili KA, Rajashekara G. 2017. Formate simultaneously reduces oxidase activity and enhances respiration in *Campylobacter jejuni*. *Sci Rep* 6: 40117. https://doi.

org/10.1038/srep40117

81. Luethy PM, Huynh S, Ribardo DA, Winter SE, Parker CT, et al. 2017. Microbiota-derived short-chain fatty acids modulate expression of *Campylobacter jejuni* determinants required for commensalism and virulence. *mBio* 8(3): e00407-e00417. https://doi.org/10.1128/mBio.00407-17

82. Thomas MT, Shepherd M, Poole RK, van Vliet AHM, Kelly DJ, et al. 2011. Two respiratory enzyme systems in *Campylobacter jejuni* NCTC 11168 contribute to growth on L-lactate. *Environ Microbiol* 13(1): 48-61. https://doi.org/10.1111/j.1462-2920.2010.02307.x

83. Wagley S, Newcombe J, Laing E, Yusuf E, Sambles CM, et al. 2014. Differences in carbon source utilization distinguish *Campylobacter jejuni* from *Campylobacter coli*. *BMC Microbiol* 14: 262. https://doi.org/10.1186/s12866-014-0262-y

84. Elharrif Z, Mégraud F. 1986. Characterization of thermophilic *Campylobacter*. I. Carbon-substrate utilization tests. *Curr Microbiol* 13(3): 117-122. https://doi.org/10.1007/BF01568505

85. Huang Y, Suyemoto M, Garner CD, Cicconi KM, Altier C. 2008. Formate acts as a diffusible signal to induce *Salmonella* invasion. *J Bacteriol* 190(12): 4233-4241. https://doi.org/10.1128/JB.00205-08

86. Gillis CC, Winter MG, Chanin RB, Zhu W, Spiga L, et al. 2019. Host-derived metabolites modulate transcription of *Salmonella* genes involved in L-lactate utilization during gut colonization. *Infect Immun* 87(4): e00773-18. https://doi.org/10.1128/IAI.00773-18

87. Bjornsdottir K, Breidt F Jr, McFeeters RF. 2006. Protective effects of organic acids on survival of *Escherichia coli* O157:H7 in acidic environments. *Appl Environ Microbiol* 72(1): 660-664. https://doi.org/10.1128/AEM.72.1.660-664.2006

88. Koser SA. 1924. Correlation of citrate utilization by members of the colon-aerogenes group with other differential characteristics and with habitat. *J Bacteriol* 9(1): 59-77. https://doi.org/10.1128/JB.9.1.59-77.1924

89. Koser SA. 1924. Differential tests for colon-aerogenes group in relation to sanitary quality of water. *J Infect Dis* 35(1): 14-22. https://doi.org/10.1093/infdis/35.1.14

90. Koser SA. 1924. A new differential test for members of the colon group of bacteria. *J Am Water Works Assoc* 12(2): 200-205.

91. Ruchhoft CC, Kallas JG, Chinn B, Coulter EW. 1931. Coli-aerogenes differentiation in water analysis. II. The biochemical differential tests and their interpretation. *J Bacteriol* 22(2): 125-181. https://doi.org/10.1128/jb.22.2.125-181.1931

92. Vaughn RH, Osborne JT, Wedding GT, Tabachnick J, Beisel CG, et al. 1950. The utilization of citrate by *Escherichia coli*. *J Bact* 60(2): 119-127. https://doi.org/10.1128/jb.60.2.119-127.1950

93. Blount ZD, Borland CZ, Lenski RE. 2008. Historical contingency and the evolution of a key innovation in an experimental population of *Escherichia coli*. *Proc Natl Acad Sci USA* 105(23): 7899-7906. https://doi.org/10.1073/pnas.0803151105

94. Blount ZD, Barrick JE, Davidson CJ, Lenski RE. 2012. Genomic analysis of a key innovation in an experimental *Escherichia coli* population. *Nature* 489(7417): 513-518. https://doi.org/10.1038/nature11514

95. Gao C, Hu C, Zheng Z, Ma C, Jiang T, et al. 2012. Lactate utilization is regulated by the FadR-type regulator LldR in *Pseudomonas aeruginosa*. *J Bacteriol* 194(10): 2687-2692. https://doi.org/10.1128/jb.06579-11

96. Gao C, Hu C, Ma C, Su F, Yu H, et al. 2012. Genome sequence of the lactate-utilizing *Pseudomonas aeruginosa* strain XMG. *J Bacteriol* 194(17): 4751-4752. https://doi.org/10.1128/JB.00943-12

97. Gao C, Jiang T, Dou P, Ma C, Li L, et al. 2012. NAD-Independent L-lactate dehydrogenase is required for L-lactate utilization in *Pseudomonas stutzeri* SDM. *PLoS ONE* 7(5): e36519. https://doi.org/10.1371/journal.pone.0036519

98. Wang Y, Xiao D, Liu Q, Zhang Y, Hu C, et al. 2018. Two NAD-independent L-lactate dehydrogenases drive L-lactate utilization in *Pseudomonas aeruginosa* PA01. *Environ microbiol Rep* 10(5): 569-575. https://doi.org/10.1111/1758-2229.12666

99. Sarantinopoulos P, Kalantzopoulos G, Tsakalidou E. 2001. Citrate metabolism by *Enterococcus faecalis* FAIR-E 229. *Appl Environ Microbiol* 67(12): 5482-5487. https://doi.org/10.1128/AEM.67.12.5482-5487.2001

100. Cabral ME, Abeijón Mukdsi MC, Medina de Figueroa RB, González SN. 2007. Citrate metabolism by *Enterococcus faecium* and *Enterococcus durans* isolated from goat's and ewe's milk: influence of glucose and lactose. *Can J Microbiol* 53(5): 607-615. https://doi.org/10.1139/W07-011

101. De Vuyst L, Vaningelgem F, Ghijsels V, Tsakalidou E, Leroy F. 2011. New insights into the citrate metabolism of *Enterococcus faecium* FAIR-E 198 and its possible impact on the production of fermented dairy products. *Int Dairy J* 21(9): 580-585. https://doi.org/10.1016/j.idairyj.2011.03.009

102. Aryal S. 2020. Biochemical test of *Staphylococcus aureus*. https://microbenotes.com/biochemical-test-of-staphylococcus-aureus/ (Accessed on: October 02, 2020).

103. Bayliss BG, Hall ER. 1965. Plasma coagulation by organisms other than *Staphylococcus aureus*. *J Bacteriol* 89(1): 101-105. https://doi.org/10.1128/jb.89.1.101-105.1965

104. Hammer ND, Skaar EP. 2011. Molecular mechanisms of *Staphylococcus aureus* iron acquisition. *Annu Rev Microbiol* 65: 129-147. https://doi.org/10.1146/annurev-micro-090110-102851

105. Beasley FC, Vinés ED, Grigg JC, Zheng Q, Liu S, et al. 2009. Characterization of staphyloferrin A biosynthetic and transport mutants in *Staphylococcus aureus*. *Mol Microbiol* 72(4): 947-963. https://doi.org/10.1111/j.1365-2958.2009.06698.x

106. Cotton JL, Tao J, Balibar CJ. 2009. Identification and characterization of the *Staphylococcus aureus* gene cluster coding for Staphyloferrin A. *Biochemistry* 48(5): 1025-1035. https://doi.org/10.1021/bi801844c

107. Cheung J, Beasley FC, Liu S, Lajoie GA, Heinrichs DE. 2009. Molecular characterization of staphyloferrin B biosynthesis in *Staphylococcus aureus*. *Mol Microbiol* 74(3): 594-608. https://doi.org/10.1111/j.1365-2958.2009.06880.x

108. Fuller JR, Vitko NP, Perkowski EF, Scott E, Khatri D, et al. 2011. Identification of a lactate-quinone oxidoreductase in *Staphylococcus aureus* that is essential for virulence. *Front Cell Infect Microbiol* 1: 19. https://doi.org/10.3389/fcimb.2011.00019

109. Ferreira MT, Manso AS, Gaspar P, Pinho MG, Neves AR. 2013. Effect of oxygen on glucose metabolism: utilization of lactate in *Staphylococcus aureus* as revealed by *in vivo* NMR studies. *PLoS ONE* 8(3): e58277. https://doi.org/10.1371/journal.pone.0058277

110. Hara T, Matsui H, Shimizu H. 2014. Suppression of microbial metabolic pathways inhibits the generation of the human body odor component diacetyl by *Staphylococcus* spp. *PLoS ONE* 9(11): e111833. https://doi.org/10.1371/journal.pone.0111833

111. Jiang T, Gao C, Ma C, Xu P. 2014. Microbial lactate utilization: enzymes, pathogenesis, and regulation. *Trends Microbiol* 22(10): 589-599. https://doi.org/10.1016/j.tim.2014.05.008

112. Yamada T, Carlsson J. 1975. Regulation of lactate dehydrogenase and change of fermentation products in streptococci. *J Bacteriol* 124(1): 55-61. https://doi.org/10.1128/jb.124.1.55-61.1975

113. Carvalho SM, de Jong A, Kloosterman TG, Kuipers OP, Saraiva LM. 2017. The *Staphylococcus aureus* α-acetolactate synthase ALS confers resistance to nitrosative stress. *Front Microbiol* 8: 1273. https://doi.org/10.3389/fmicb.2017.01273

114. Helmenstine AM. 2019. Henderson-Hasselbalch equation and example. http://chemistry.about.com/od/acidsbase1/a/hendersonhasselbalch.htm (Accessed on: 21 October 2020).

115. Langsrud S, Sundheim G. 1998. Factors influencing a suspension test method for antimicrobial activity of disinfectants. *J Appl Microbiol* 85(6): 1006-1012. https://doi.org/10.1111/j.1365-2672.1998.tb05265.x

116. Hirshfield IN, Terzulli S, O'Byrne C. 2003. Weak organic acids: a panoply of effects on bacteria. *Sci Prog* 86(Pt 4): 245-269. https://doi.org/10.3184/003685003783238626

117. Gahan CG, O'Driscoll B, Hill C. 1996. Acid adaptation of *Listeria monocytogenes* can enhance survival in acidic foods and during milk fermentation. *Appl Environ Microbiol* 62(9): 3128-3132. https://doi.org/10.1128/AEM.62.9.3128-3132.1996

118. Castanie-Cornet M-P, Penfound TA, Smith D, Elliott JF, Foster JW. 1999. Control of acid resistance in *Escherichia coli*. *J Bacteriol* 181(11): 3525-3535. https://doi.org/10.1128/jb.181.11.3525-3535.1999

119. Shaheen BW, Miller ME, Oyarzabal OA. 2007. *In vitro* survival at low pH and acid adaptation response of *Campylobacter jejuni* and *Campylobacter coli*. *J Food Saf* 27(3): 326-343. https://doi.org/10.1111/j.1745-4565.2007.00083.x

120. Varsaki A, Murphy C, Barczynska A, Jordan K, Carroll C. 2015. The acid adaptive tolerance response in *Campylobacter jejuni* induces a global response, as suggested by proteomics and microarrays. *Microb Biotechnol* 8(6): 974-988. https://doi.org/10.1111/1751-7915.12302

121. Smittle RB. 2000. Microbiological safety of mayonnaise, salad dressings, and sauces produced in the United States: a review. *J Food Prot* 63(8): 1144-1153. https://doi.org/10.4315/0362-028X-63.8.1144

122. McKellar RC, Knight KP. 1999. Growth and survival of various strains of enterohemorrhagic *Escherichia coli* in hydrochloric and acetic acid. *J Food Prot* 62(12): 460-464. https://doi.org/10.4315/0362-028x-62.12.1466

123. Blocker JC, Busta FF. 1981. Antimicrobial activity of sorbate. *J Food Prot* 44(8): 614-622. https://doi.org/10.4315/0362-028X-44.8.614