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abstract

Research Objectives: An evaluation of the antimicrobial mechanism and efficacy of Lactic Acid, alone and in synergy with surfactants.

Methods: Assessment of studies carried out according to the EN 1276 European Standard for evaluation of bactericidal efficacy of disinfecting liquids. The EN 1276 Standard is a Quantitative Suspension Test for the assessment of the bactericidal activity of chemical antiseptics and disinfectants that evaluates how effectively the product causes a reduction in the number of viable bacterial cells of relevant test microorganisms.

Results: In absence of surfactants, Lactic Acid is especially effective against Gram-negative bacteria. Gram-positive bacteria are generally less sensitive to Lactic Acid but are rendered susceptible by surfactants. This synergy gives the combination of surfactants and Lactic Acid a broad spectrum antimicrobial activity in cleaning products. In the appropriate combination, Lactic Acid and surfactants work in symphony. Various combinations of Lactic Acid and surfactants act as broad spectrum antibacterial formulations. Other secondary ingredients, such as preservatives, chelating agents and alcohols, can boost the bactericidal action of Lactic Acid.

Conclusions: Lactic Acid is a safe, biobased and biodegradable option for antimicrobial products and formulations, with proven broad range efficacy against bacteria and viruses.

Origin and Uses of Lactic Acid

Lactic Acid is one of the earliest antibacterial substances to be harnessed by humankind. The first examples of functional chemistry in history include the fermentation of food. The most obvious and ancient example is the use of fermented milk products. For centuries people have applied the same process in preserving vegetables, sausages, cheese and silage feed production for animals. Lactic Acid bacteria are allowed to ferment and acidify these foodstuffs by producing Lactic Acid. In fermentation, Lactic Acid is the end-point of their energy metabolism. Lactic Acid is excreted to levels that inhibit competing bacteria, which happen to be the undesirable types for humans.

In plants, animals and humans, Lactic Acid, or Lactate, is also part of regular metabolism. Unlike its production in Lactic Acid bacteria metabolism, it does not represent the end-point of energy generation. It has long been believed that Lactate was a sign of fatigue during exercise, but it is now recognized as an essential intermediate in various metabolic processes [1].

In the 19th century, it was discovered that Lactic Acid is not only produced in foodstuffs, but can be accumulated in a reaction vessel known as a fermentor. Since that time, Lactic Acid fermentation has been applied industrially to produce purified Lactic Acid. The isomer of Lactic Acid standardly-obtained by fermentation is L-Lactic Acid – the body's own Lactic Acid isomer. Optimized versions of this industrial bio-

process tailored to a variety of carbohydrate feedstocks are produced commercially across the globe. As Lactic Acid is based on biological raw materials, it contributes to the capture of CO₂ from the atmosphere.

The L-Lactic Acid produced by fermentation is the starting point for the various levels of purification, tailored for various applications. At the lowest level of purification, it is used in animal fodder, in which the residues from fermentation add value as flavors and nutrients. High purity L-Lactic Acid is employed as active ingredient for antimicrobial cleaning and personal care formulations. L-Lactic Acid at the very highest levels of purification is a colorless, odorless liquid that is commonly used in cosmetics and pharmaceuticals.

Methods Antibacterial Mechanism

An evaluation of the antimicrobial mechanism and efficacy of Lactic Acid, alone and in combination with surfactants was carried out. Assessment of antimicrobial properties were made using studies carried out according to the EN 1276, European Standard for evaluation of bactericidal efficacy of disinfecting liquids. The EN 1276 Standard is a Quantitative Suspension Test for the assessment of the bactericidal activity of chemical antiseptics and disinfectants that evaluates how effectively the product causes a reduction in the number of viable bacterial cells of relevant test microorganisms.

Results

Antibacterial Mechanism

L-Lactic Acid is an organic acid and shares several features with similar sized acids. The unique combination of low acid dissociation constant (pK_a) and low hydrophobicity makes it readily miscible with water. L-Lactic Acid resides primarily in the water phase of an emulsion. This gives it an advantage over more hydrophobic organic acids, because the water phase is where bacteria also reside. It is a particularly good at “shuttling” protons, or acidity, across cell membranes. In doing so, it does rely on low pH of the environment or medium. Once inside the cell, there are four broad-acting mechanisms that inhibit the bacterial cell. These four mechanisms were reviewed insightfully by Desriac and coworkers in 2013 [2]:

1. Acid stress disrupts cell regulation on a general level.
2. Bacteria spend energy to maintain pH, by pumping out acid.
3. Bacteria change their metabolism to produce alkaline metabolites.
4. Acid stress generates free radicals that damage all cellular mechanisms.

During short exposures that lead directly to inactivation of bacteria, some of these mechanisms are more relevant than others. In standardized testing of the antimicrobial quality of cleaning products, exposures can be as brief as 30 seconds. In this time frame, bacteria cannot respond by adapting their structure or their metabolism for survival. The sudden severe acid stress leads to an unmitigated shock of oxidative stress, while any survival

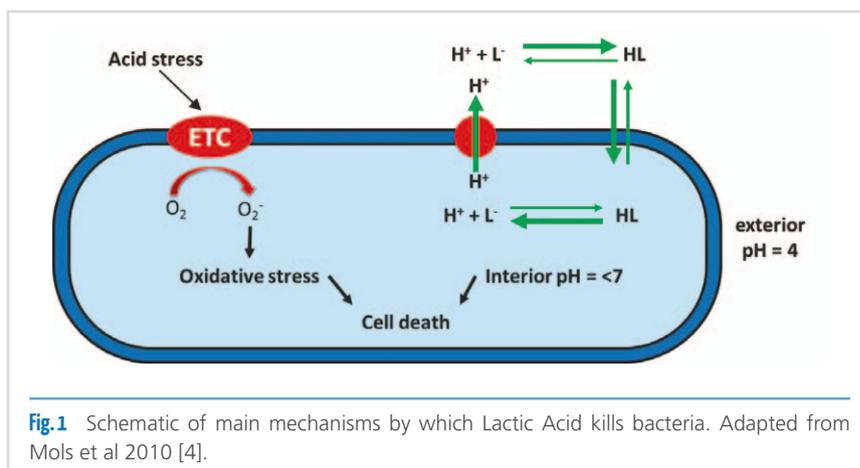


Fig.1 Schematic of main mechanisms by which Lactic Acid kills bacteria. Adapted from Mols et al 2010 [4].

mechanisms are suppressed by the low intracellular pH (Fig. 1) In this respect, Lactic Acid is very different from some synthetic antimicrobials that can rely on singular mechanisms to kill bacteria. No single adaptation could render a bacterium resistant.

The generation of the oxidative stress occurs at the cell membrane, due to the malfunctioning of the Electron Transport Chain. When exposed to cleaning products, the bacterial membranes are already destabilized. They are rendered more fluid by the presence of surfactants to result in a more effective inactivation [3].

Lactic Acid is effective against Gram-negative bacteria in the absence of surfactants. Gram-positive bacteria are generally less sensitive to Lactic Acid, but are rendered susceptible by surfactants. This cascade of antibacterial effects gives the combination of surfactants and Lactic Acid a broad spectrum activity in cleaning products.

Activity in HPC Formulations Against Bacteria and Viruses

Surfactants alone can already exert some pressure on bacteria. In the appropriate combination, Lactic Acid and surfactants will work in symphony (Tab. 1 & 2). Various

Lactic Acid and Surfactant (5 min):	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>E. hirae</i>	<i>S. aureus</i>
3% Lactic Acid, pH 3	>5.0	>5.0	<1.0	<1.0
1% SLS, pH 3	>5.0	>5.0	<1.0	>5.0
1% SLS, 1% Lactic Acid, pH 3	>5.0	>5.0	>5.0	>5.0
1% SLS, pH 4	<1.0	<1.0	<1.0	<1.0
1% SLS, 1% Lactic Acid, pH 4	>5.0	>5.0	>5.0	>5.0
Hard Surface Cleaner (1 min):				
1.0% SLS, 0.5% APG, pH4.0	<1.0	<1.0	<1.0	<1.0
1.0% SLS, 0.5% APG, 0.75% Lactic Acid, pH4.0	>5.0	>5.0	>5.0	>5.0
Manual Dish Formulation:				
8% SLES, 4% SLS, 1.5% Lactic Acid, pH3.5*	>5.0	>5.0	>5.0	>5.0

Tab.1 Antimicrobial efficacy of Lactic Acid alone and in combination with surfactants. Values represent bacterial kill expressed as log 10 reductions in Colony Forming Units. Methods according to EN1276 at one to 5 minute exposures.

combinations of Lactic Acid and surfactants act as broad spectrum antibacterial formulations. This is best understood from the perspective that surfactants can weaken the bacterial cell membrane. Many of the molecular events that lead to bacterial inactivation by organic acid action involve the cell membrane. A bacterium with previously weakened membrane function is more susceptible to acid shock. This membrane-fluidizing effect is not often bactericidal. It still requires a potent antibacterial organic acid to achieve sufficient efficacy.

Particularly low levels of surfactants already work synergistically to obtain cost effective formulations. High levels of surfactants in cleaning products can somewhat reduce the efficacy of antibacterial components, in part due to increasing the viscosity of the formulation. This calls for more thorough design of products where high surfactant levels and higher viscosity are needed but it can be overcome through formulation. Other secondary ingredients like preservatives, chelating agents and alcohols, can boost the bactericidal action of Lactic Acid. These synergies are generally best understood as adding additional sabotage to the life processes of microbes, rendering them more vulnerable to the action of the main antimicrobial of the formulation.

Lactic Acid also has antiviral properties. Assessment of antiviral properties was made using studies carried out according to the EN 14476 European Standard for evaluation of virucidal efficacy of disinfecting liquids. Particularly enveloped viruses are sensitive to deactivation by Lactic Acid exposure. This is not due to oxidative stress as it is in bacteria, but does involve a biological membrane. In the case of enveloped virus particles, the membrane can also be disrupted and the proteins inside disabled, or denatured by the Lactic Acid.

Commercial Application

In absence of surfactants, Lactic Acid is especially effective against Gram-negative bacteria. In the food and feed industries, this makes Lactic Acid an appealing solution for *E. coli* and *Salmonella T.* problems. Gram-positive bacteria can be tackled with combinations of Lactic Acid and surfactants. This synergy gives the combination of surfactants and Lac-

tic Acid a broad spectrum antimicrobial activity in cleaning products.

In products with relatively low surfactant levels the synergy with Lactic Acid is not only functional, but also economical. Prime examples of such synergy can be found in antibacterial hard surface cleaning formulations, where low levels of anionic surfactants and Lactic Acid can make for very cost-effective antibacterial and antiviral efficacy.

Quality Aspects

In short-chain organic acids, odor or color can be an issue in application. Lactic Acid is produced through fermentation. Food grade or technical grade varieties can be suitable for formulations that make use of perfumes and dyes. For more sensitive formulations ultra-pure grades are available that enable formulations to rely on Lactic Acid for antimicrobial claims or preservation, while promoting the fact that they are fragrance-free. In creams and ointments, Lactic Acid is often used at high levels for its moisturization and anti-aging properties. Although not discussed here, the low base odor of ultra-pure grades is also often required for such functionalities. Extensively purified grades of Lactic Acid tend to lose all color, as well and have a watery clear appearance.

Safety and Regulation

L-Lactic Acid is in the approval process under the European Biocidal Products Regulation. For use in human hygiene (PT1), disinfectants (PT2), veterinary hygiene (PT3), food and feed area disinfection (PT4), and preservation (PT6) approval is expected soon. In the US PURAC® Sanilac Lactic Acid is registered at the Environmental Protection Agency (EPA) as an antimicrobial and biochemical pesticide under the FIFRA framework and carries the "designed for Environment" label. In addition, Sanilac has a GRAS (Generally Recognized As Safe) status. These broad sets of approved registrations are based upon proven antimicrobial efficacy data and are enabled by the completely safe nature of this molecule. Lactate and Lactic Acid are part of the chemistry of living cells of humans, animals, plants and bacteria. It comes from nature and can safely return to nature.

Lactic Acid and Surfactant:	<i>H. simp-lex 1</i>	<i>H1N1</i>	<i>HIV</i>	<i>Hepatitis B</i>	<i>Noro</i>	<i>Rhino</i>
3% Lactic Acid, pH 2	>4.0	>3.0	not tested	not tested	not tested	not tested
1.5% SLS, 3% Lactic Acid, pH 3	>4.0	>3.0	>4.0	>3.0	>4.0	>4.0
1% SLS, 3% Lactic Acid, pH 5	>4.0	>3.0	>4.0	>3.0	>4.0	>4.0

Tab. 2 Antimicrobial efficacy of Lactic Acid alone and in combination with surfactants. Values represent virus kill expressed as log 10 reductions in Cells. Methods according to EN14776 at 5 minute exposures.

Conclusion

The demand for safe, environmentally friendly and effective antimicrobials is growing with mounting pressure against many traditional antimicrobials. Lactic acid is a safe, biobased and biodegradable option for antimicrobial products with proven broad range efficacy against bacteria and various viruses. Incorporation of ingredients such as surfactants, preservatives, chelating agents and alcohols are proven to complement the antimicrobial efficacy of Lactic Acid in cleaner, disinfectant and personal care applications. Natural, safe and effective, Lactic Acid is used today in everything from antimicrobial and descaling solutions to solvents and buffering applications.

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