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ORIGINAL RESEARCH

Comparison of taurolidine with 4% ethylenediaminetetraacetic acid on antimicrobial lock effectiveness: An experimental study

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Abstract

Background: Antimicrobial lock therapy is recommended for preventing and treating catheter-related bloodstream infections, but different solutions have uncertain efficacy.

Methods: Two locks, 1.35% taurolidine and 4% ethylenediaminetetraacetic acid (EDTA), were tested on *Staphylococcus epidermidis*, *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Pseudomonas aeruginosa*, multidrug-resistant *P. aeruginosa*, vancomycin-resistant *Enterococcus faecium*, *Klebsiella oxytoca* (carbapenemase producing), *K. pneumoniae* (extended-spectrum β-lactamase producing), *Candida albicans*, and *Candida glabrata*. Broviac catheter segments were incubated with these organisms and then exposed to various lock solutions. Colony-forming units (CFUs) were counted after 2, 4, and 24 h of incubation.

Results: Taurolidine showed a significant decrease in CFUs after 2 h in *S. aureus*, *S. epidermidis*, methicillin-resistant *S. aureus*, vancomycin-resistant *E. faecium*, *P. aeruginosa* (both sensitive and multidrug-resistant strains), *K. oxytoca*, *C. albicans*, and *C. glabrata*. After 4 h, significant reductions were noted in *S. aureus*, *S. epidermidis*, methicillin-resistant *S. aureus*, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, *K. pneumoniae*, *K. oxytoca*, and *C. albicans*. Taurolidine was also effective after 24 h, especially against methicillin-resistant *S. aureus* and multidrug-resistant *P. aeruginosa*. Four percent EDTA acid showed a significant reduction in CFUs after 2 h in *S. aureus*, vancomycin-resistant *E. faecium*, *P. aeruginosa*, *K. oxytoca*, *C. albicans*, and *C. glabrata*. After 4 h, reductions occurred in *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, *K. oxytoca*, and *C. albicans* and after 24 h in methicillin-resistant *S. aureus*, *P. aeruginosa*, and *K. oxytoca*.

Conclusion: Taurolidine is more effective than 4% EDTA acid in eradicating Gram-positive and Gram-negative microorganisms and fungi.

KEYWORDS

antimicrobial lock, catheter-related blood stream infection, ethylenediaminetetraacetic acid, home parenteral nutrition, taurolidine, venous catheter

CLINICAL RELEVANCY STATEMENT

Antimicrobial lock therapy is a critical strategy in preventing and treating catheter-related bloodstream infections. This study demonstrates that 1.35% taurolidine is significantly more effective than 4% ethylenediaminetetraacetic acid in eradicating a broad spectrum of Gram-positive and Gram-negative pathogens, including multidrug-resistant organisms and fungi, within clinically relevant timeframes. These findings support the superior efficacy of taurolidine lock solutions, emphasizing their potential for improving infection management in catheterized patients.

BACKGROUND

Central venous catheters, essential for long-term vascular access, are crucial for patients who need dialysis, chemotherapy, or parenteral nutrition. The most serious and common complications linked to these catheters are infections, particularly catheter-related bloodstream infections. Regrettably, catheter-related bloodstream infections frequently lead to a notable rise in mortality and significantly higher financial costs.[1] Consequently, enhancing catheter care and reducing catheter-related infections should decrease mortality rates, cut treatment costs, and shorten hospital stays.[2] These infections often occur when microbial organisms within the catheter's intraluminal biofilm migrate, leading to catheter-related bloodstream infections. Most guidelines suggest removing the catheter and administering systemic antimicrobial treatment on suspicion or confirmation of a catheter-related bloodstream infection.[3] However, clinical conditions, such as the absence of alternative venous access, bleeding disorders, or comorbidities, often prevent the removal of the device. Alternative approaches, like the use of antimicrobial lock therapy, to manage these biofilm-related infections of intravenous catheters have gained significant interest recently.[4] Antimicrobial lock solutions have been variably successful in filling the lumen of the catheter to eradicate biofilms. This method delivers very high concentrations of antimicrobial agents directly at the infection site. Nonetheless, concerns about the selection of resistant organisms, toxicity, and treatment failures have limited their widespread use in treating catheter-related bloodstream infections.

Taurolidine, chemically known as bis-(1,1-dioxoperhydro-1,2,4-thiadiazinyl-4)-methane, is a derivative of the amino acid taurine. Since its introduction in the 1970s, initially for treating bacterial peritonitis, taurolidine has been recognized for its safety and non-toxicity at utilized dosages, with no bacterial resistance reported so far.[5] It exhibits broad-spectrum antimicrobial and antifungal properties, effective against both Gram-positive and Gram-negative bacteria, including strains resistant to methicillin and vancomycin, as well as mycobacteria and some significant fungi. Taurolidine is quickly metabolized in the human body into taurultam and methylol taurinamide, breaking down into taurine, carbon dioxide, and water. Its mechanism involves binding its hydroxymethyl group to bacterial cell walls, causing irreversible damage and hindering the bacteria's ability to adhere to human epithelial cells.[6] This action helps prevent biofilm formation inside catheters. Given these properties, taurolidine locks are especially recommended for patients experiencing recurrent catheter infections.[7]

Despite the positive and proven effects of taurolidine, there have been recent opinions suggesting that taurolidine has a limited effect against already-formed biofilm and may potentially cause liver toxicity.[8] Although these opinions are rare, there is ongoing effort to develop other antimicrobial locks.

Four percent ethylenediaminetetraacetic acid (EDTA) solution is used as an anticoagulant and antimicrobial agent in the prevention and treatment of catheter-related infections, particularly in central venous catheters. This solution helps maintain catheter patency and reduces the risk of central line-associated bloodstream infections by preventing the formation of biofilm and blood clots. EDTA is effective against a wide range of microorganisms, including Gram-positive and Gram-negative bacteria, fungi, and yeasts. The effect of EDTA lies in its ability to chelate and potentiate bacterial cell walls and destabilize the biofilm by sequestering calcium and magnesium, making them more susceptible to damage.[9]

OBJECTIVES

The aim of our work was to compare the efficacy of antimicrobial locks with EDTA and taurolidine in vitro. This comparison was made by evaluating the efficacy of individual locks through the monitoring of the decrease in colony-forming units (CFUs) over time compared with the control. It can be assumed that the faster the number of CFUs decreases over time the more effective the solution is. The results of this in vitro study hold potential for practical application in the treatment and prevention of catheter-related infections in everyday clinical practice.

METHODS

To assess the antimicrobial effectiveness of various substances, we adopted a modified version of the Andris method.[10] This method aims to simulate biofilm formation on the catheter as it likely occurs in the human body, particularly in patients with long-term central venous access, such as those receiving home parenteral nutrition. We have successfully used this method in the past.[11] Our modifications included altering the evaluation times and using various types of antibiotics at different concentrations. We tested the antimicrobial activity against several bacterial strains, including *Staphylococcus epidermidis*, *Staphylococcus aureus*, methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and *Klebsiella oxytoca*–producing carbapenemase (KLOX KPC), *Klebsiella pneumoniae*–producing extended-spectrum β-lactamase (KLPN ESBL), *Pseudomonas aeruginosa* and multidrug-resistant *P. aeruginosa* (defined as resistance to all agents in at least three of four classes: fluoroquionolones,

aminoglycosides, carbapenems, and antipseudomonal penicillins/cephalosporins), *Candida albicans*, and *Candida glabrata*.

Before each assay, the strains were grown aerobically for 18–24 h at 36°C in brain-heart bouillon broth (BioMerieux). An aliquot of these cultures (100 µl) was aseptically transferred to fresh brain-heart bouillon broth and grown at 36°C to reach the middle of the logarithmic phase (optical density ≈ 0.6) corresponding to 10^8 CFUs/ml. *C. albicans* and *C. glabrata* were grown in Sabouraud broth (BioMerieux) under the same conditions to reach 10^7 CFUs/ml. The turbidimetric method was used for the measurement of optical density. Tested locks were: saline (control), 1.35% taurolidine (TauroLock; Tauropharm GmbH) and 4% tetrasodium EDTA (KiteLock; Sterile Care). Centimeter-length segments of Broviac catheter were immersed into the human plasma at a temperature of 37°C during the night. Afterwards, the catheter was incubated in tryptose-soy broth (Bio-Rad), which was inoculated by a strain, at 37°C for 18–24 h. Then, segments were rinsed thrice in phosphate-buffered saline and incubated in the testing solution for 2, 4, and 24 h at 37°C. After incubation, segments were washed 10 times in phosphate-buffered saline and placed into the tryptose-soy broth and sonicated for 3 min. Then, the tryptose-soy broth was serially diluted (series of 6- to 10-fold dilution in phosphate-buffered saline for each tested concentration and strain). One hundred milliliters of each dilution in duplicate was streaked on agar plates (Mueller Hinton 2 agar, Sabouraud agar; BioMerieux). After a 24-h incubation of bacteria and a 48-h incubation of yeasts at 37°C, the number of colonies was counted and recorded for analysis. The antimicrobial effect of individual substances was evaluated by comparing the number of CFUs after the tested culture was exposed to the lock solution with the number of CFUs in the control samples (without the lock solution). All experiments were conducted in triplicate to ensure the reliability of the results.

Statistics

Results were tested for normality, and nonparametric tests were used. We compared the statistical significance (reduction in CFUs) over time after using each solution against the control. The significance of differences was determined with two-way analysis of variance and the Dunn's post hoc test. $P \le 0.05$ was considered significant. Statistically significant differences when compared other solutions to the control solution are marked with asterisks in Tables 1–3.

RESULTS

Summary results are shown in Tables 1–3. Decrease of CFUs after the administration of individual locks in different microorganisms is stated. On the completion of cultivation, a natural decrease in the number of CFUs occurs, regardless of the use of the antimicrobial lock, because of the removal of the culture medium. The efficacy of

TABLE 1 The table shows the average values of colony-forming units of Gram-positive microorganisms as a comparison of the effectiveness of tested locks in reduction of colony-forming units in time compared with the control solution (saline).

	STAU 2 h	STAU 4 h	STAU 24 h	STEP 2 h	STEP 4 h	STEP 24 h	MRSA 2 h	MRSA 4 h	MRSA 24 h	VRE 2 h	VRE 4 h	VRE 24 h
Control	6,733,333	3,383,333	446,667	5,450,000	3,353,333	143,250	8,283,333	5,250,000	4,466,667	778,333	158,633	118,500
4% EDTA	2,426,667*	1,030,000	18	2,085,000	259,000	435	5,416,667	4,066,667	112*	45,500**	84,533	2
1.35% taurolidine	341,667***	475,667*	3	227,833*	28,522***	0	202,500***	34,333***	0*	9683**	14,117	0

Note: The significance of differences was determined with two-way analysis of variance and Dunn's post hoc test. Statistically significant differences when compared with the control solution are marked with asterisks.

Abbreviations: EDTA, ethylenediaminetetraacetic acid; MRSA, methicillin-resistant *Staphylococcus aureus*; STAU, *Staphylococcus aureus*; STEP, *Staphylococcus epidermidis*; VRE, vancomycin-resistant *Enterococcus faecium*.

*$P \le 0.05$; **$P \le 0.01$; ***$P \le 0.001$.

TABLE 2 The table shows average values of colony-forming units of Gram-negative microorganisms as a comparison of effectivity of tested locks in reduction of colony-forming units in time compared with control solution (saline).

	PSAE 2 h	PSAE 4 h	PSAE 24 h	PSAE MR– 2 h	PSAE MR– 4 h	PSAE MR– 24 h	KLPN ESBL+ 2 h	KLPN ESBL+ 4 h	KLPN ESBL+ 24 h	KLOX KPC 2 h	KLOX KPC 4 h	KLOX KPC 24 h
Control	2,916,667	4,133,333	4,233,333	5,516,667	4,900,000	3,933,333	2,916,667	4,633,333	1,766,667	2,166,667	1,508,333	1,491,667
4% EDTA	201,000*	20,450***	0***	1,935,667	55,167*	0*	2,491,667	2,215,000	2180	79,000**	96,500*	0*
1.35% taurolidine	13**	0***	0***	303**	42**	0*	9583	9313*	0	6067**	1900*	0*

Note: The significance of differences was determined with two-way analysis of variance and Dunn's post hoc test. Statistically significant differences when compared with the control solution are marked with asterisks.

Abbreviations: EDTA, ethylenediaminetetraacetic acid; KLPN ESBL+, *Klebsiella pneumoniae*–producing extended-spectrum β-lactamase; KLOX KPC, *Klebsiella oxytoca*–producing carbapenemase; PSAE, *Pseudomonas aeruginosa*; PSAE MR–, multidrug-resistant *Pseudomonas aeruginosa*.

*$P \le 0.05$; **$P \le 0.01$; ***$P \le 0.001$.

individual locks was compared against the control to account for and eliminate this natural factor.

A statistically significant decrease in CFUs was observed after 2 h of taurolidine exposure in *S. aureus*, *S. epidermidis*, MRSA, VRE, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, KLOX KPC, *C. albicans*, and *C. glabrata*; after 4 h in *S. aureus*, *S. epidermidis*, MRSA, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, KLPN ESBL, KLOX KPC, and *C. albicans*; and after 24 h in MRSA, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, and KLOX KPC. A statistically significant decrease in CFUs was observed after 2 h of 4% EDTA exposure in *S. aureus*, VRE, *P. aeruginosa*, KLOX KPC, *C. albicans*, and *C. glabrata*; after 4 h in *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, KLOX KPC, and *C. albicans*; and after 24 h in MRSA, *P. aeruginosa*, multidrug-resistant *P. aeruginosa*, and KLOX KPC.

These results indicate that in the case of 4% EDTA with Gram-positive bacteria, a statistically significant difference compared with the control was observed after 2 h in two of the four tested bacteria, unlike taurolidine, in which an effect was observed in all four tested bacteria with higher statistical significance. After 4 h of exposure to the solutions, a difference compared with the control was observed only with taurolidine. After 24 h, no statistically significant difference compared with the control was observed with either solution.

For Gram-negative bacteria, when using 4% EDTA, a statistically significant difference compared with the control was observed after 2 h in two of four tested bacteria, unlike taurolidine, in which an effect was observed in three tested bacteria with higher statistical significance. After 4 h of exposure to the solutions, a difference was observed in three bacteria in the case of 4% EDTA and in all four bacteria with taurolidine. After 24 h, a significant difference compared with the control was observed in three of four bacteria. In the case of yeasts, the results did not differ.

DISCUSSION

The mechanisms of the antimicrobial action of taurolidine and 4% EDTA solution are different, and thus it is not surprising that their efficacy can also vary. In our in vitro experiment, we demonstrated better efficacy of antimicrobial locks with taurolidine. Currently, there are not enough controlled studies or meta-analyses available comparing the effectiveness of antimicrobial locks with taurolidine and 4% EDTA solution. Only studies that compare their efficacy indirectly can be found.[12] This paper compared the efficacy of taurolidine and 4% EDTA solution. However, this study did not conduct its own measurements but instead drew from theoretical models and the results of selected previously published studies. For example, the incidence of catheter-related bloodstream infections with taurolidine is reported as 1.23/1000 catheter days. According to the Czech Registry of Patients on Home Parenteral Nutrition, the incidence of catheter-related bloodstream infections in the Czech Republic for patients receiving home parenteral nutrition is significantly lower. In 2013, the incidence of catheter-related sepsis was reported as 0.81 per year per 1000 catheter days compared with 0.1 catheter-related sepsis incidents per

TABLE 3 The table shows average values of colony-forming units of the yeast as a comparison of the effectiveness of the tested locks in reduction of colony-forming units in time compared with control solution (saline).

	CDAL 2 h	CDAL 4 h	CDAL 24 h	CDGL 2 h	CDGL 4 h	CDGL 24 h
Control	168,333	291,667	19,333	381,667	55,667	15,333
4% EDTA	4717*	2072**	68	23,500***	3833	2702
1.35% taurolidine	2433*	1807**	0	19,000***	1983	0

Note: The significance of differences was determined with two-way analysis of variance and Dunn's post hoc test. Statistically significant differences when compared with the control solution are marked with asterisks.

Abbreviations: CDAL, *Candida albicans*; CDGL, *Candida glabrata*; EDTA, ethylenediaminetetraacetic acid.

*$P \le 0.05$; **$P \le 0.01$; ***$P \le 0.001$.

year per 1000 catheter days in 2021. This decrease is mainly attributed to the preventive introduction of taurolidine locks.[13]

The price may also vary regionally; therefore, data comparing cost-effectiveness may not be valid worldwide. Specifically, in the Czech Republic, the cost of a 4% EDTA solution is double that of taurolidine locks; therefore, the published conclusions of this work likely do not correspond to our conditions. Based on our results and specific to our country, we assess taurolidine locks as a more effective and currently cheaper solution compared with 4% EDTA solution locks. However, results may vary across different countries.

Our results confirm the difference in the efficacy of the various solutions on different microorganisms. This difference can be attributed to the distinct mechanisms of action. EDTA is primarily effective against Gram-negative bacteria and, in some cases, Gram-positive bacteria probably for several reasons related to its chemical properties and mechanism of action. EDTA is a chelating agent, which means it can bind metal ions, such as calcium, magnesium, and iron. These ions are essential for the stability of bacterial cell walls and membranes. Gram-negative bacteria have an outer membrane containing lipopolysaccharides stabilized by divalent cations (eg, Ca^{2+} and Mg^{2+}).[14] When EDTA chelates these cations, it destabilizes the outer membrane, leading to increased permeability and subsequent damage to the bacterial cell wall. Gram-negative bacteria have a more complex cell wall with an outer membrane that is more sensitive to destabilization on loss of divalent cations. This increases the permeability of the cell wall, which can lead to leakage of intracellular contents and cell death. In contrast, Gram-positive bacteria have a thick peptidoglycan layer that is less dependent on divalent cations for stability than the outer membrane of Gram-negative bacteria.

This means that EDTA may not be as effective against all Gram-positive bacteria, as our data also show. However, in the longer term, EDTA disrupts the cell wall sufficiently to inhibit their growth or kill them. This is also evident from our data, as the differences between the solutions diminish over time. EDTA can also act synergistically with other antimicrobial agents. By destabilizing the cell wall and increasing permeability, it can allow better penetration of antibiotics or other antimicrobial agents into the bacterial cell, thereby enhancing their effectiveness.

Taurolidine has direct bactericidal effect, which means it actively kills bacteria. It acts quickly by disrupting bacterial cell walls and membranes, leading to their death. In contrast, EDTA primarily acts as a chelating agent that inhibits bacterial growth. Additionally, EDTA can disrupt biofilm, which is a structure formed by bacteria to protect against adverse conditions. By chelating metal ions that stabilize extracellular polymeric substances in the biofilm, EDTA can help prevent formation and facilitate the breakdown of existing biofilm.

On the other hand, taurolidine's effectiveness against biofilm lies in several of its properties and mechanisms of action. Taurolidine disrupts the biofilm structure by interfering with the bacteria's adhesion processes, preventing them from attaching to surfaces and forming biofilm.[15] Without the ability to create a solid structure, it is harder for bacteria to survive and protect themselves from the immune system, antibiotics, or other antimicrobial agents. Taurolidine can also inhibit the synthesis of the polymeric substances forming the biofilm, which weakens the overall structure and facilitates its breakdown.[16] Therefore, a combination of these solutions might be interesting and useful in both prevention and treatment in clinical practice.[17]

CONCLUSIONS

The antimicrobial application of locks is effective in prevention and treatment against Gram-positive bacteria, Gram-negative bacteria, and yeast. From our results, it is evident that, compared with a 4% EDTA solution, taurolidine has a faster and stronger onset of action. However, both types of locks are effective and can be used in the prevention and treatment of catheter-related infections.

AUTHOR CONTRIBUTIONS

Jakub Visek contributed to the methodology, original draft, investigation, conceptualization, project administration, formal analysis, review and editing, and visualization. Lenka Ryskova contributed to the investigation, methodology, and review and editing. Petra Cesakova contributed to the investigation. Jana Stanclova contributed to the investigation. Marie Vajrychova contributed to the formal analysis and review and editing. Vladimir Blaha contributed to the supervision, resources, and review.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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REFERENCES

1. Tacconelli E, Smith G, Hieke K, Lafuma A, Bastide P. Epidemiology, medical outcomes and costs of catheter-related bloodstream infections in intensive care units of four European countries: literature- and registry-based estimates. *J Hosp Infect*. 2009;72(2):97-103. doi:10.1016/j.jhin.2008.12.012
2. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. 2011;52(9):e162-e193. doi:10.1093/cid/cir257
3. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49(1):1-45. doi:10.1086/599376
4. Justo JA, Bookstaver PB. Antibiotic lock therapy: review of technique and logistical challenges. *Infect Drug Resist*. 2014;7:343-363. doi:10.2147/IDR.S51388
5. Gudiol C, Nicolae S, Royo-Cebrecos C, et al. Administration of taurolidine-citrate lock solution for prevention of central venous catheter infection in adult neutropenic haematological patients: a randomised, double-blinded, placebo-controlled trial (TAURCAT). *Trials*. 2018;19(1):264. doi:10.1186/s13063-018-2647-y
6. Torres-Viera C, Thauvin-Eliopoulos C, Souli M, et al. Activities of taurolidine in vitro and in experimental enterococcal endocarditis. *Antimicrob Agents Chemother*. 2000;44(6):1720-1724. doi:10.1128/AAC.44.6.1720-1724.2000
7. Vernon-Roberts A, Lopez RN, Frampton CM, Day AS. Meta-analysis of the efficacy of taurolidine in reducing catheter-related bloodstream infections for patients receiving parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2022;46(7):1535-1552. doi:10.1002/jpen.2363
8. Hill J, Garner R. Efficacy of 4% tetrasodium ethylenediaminetetraacetic acid (T-EDTA) catheter lock solution in home parenteral nutrition patients: a quality improvement evaluation. *J Vasc Access*. 2021;22(4):533-539. doi:10.1177/1129729820946916
9. Liu F, Hansra S, Crockford G, et al. Tetrasodium EDTA is effective at eradicating biofilms formed by clinically relevant microorganisms from patients' central venous catheters. *mSphere*. 2018;3(6):e00525-18. doi:10.1128/mSphere.00525-18
10. Andris D. Elimination of intraluminal colonization by antibiotic lock in silicone vascular catheters. *Nutrition*. 1998;14(5):427-432. doi:10.1016/s0899-9007(98)00013-6
11. Visek J, Ryskova L, Machacova A, Marikova M, Blaha V. In vitro comparison of the effectiveness of various antimicrobial locks with taurolidine in the treatment and prevention of catheter-related bloodstream infections in patients receiving parenteral nutrition. *Nutrition*. 2023;114:112115. doi:10.1016/j.nut.2023.112115
12. Gattini D, Yan H, Belza C, Avitzur Y, Wales PW. Cost-utility analysis of 4% tetrasodium ethylenediaminetetraacetic acid, taurolidine, and heparin lock to prevent central line-associated bloodstream infections in children with intestinal failure. *JPEN J Parenter Enteral Nutr*. 2024;48(1):47-56. doi:10.1002/jpen.2551
13. Koudelková K, Waldauf P, Wohl P, et al. The Czech Home Parenteral Nutrition Registry REDNUP: comprehensive analysis of adult patients' data. *Ann Nutr Metab*. 2024;80(3):143-152. doi:10.1159/000538232
14. Clifton LA, Skoda MWA, Le Brun AP, et al. Effect of divalent cation removal on the structure of Gram-negative bacterial outer membrane models. *Langmuir*. 2015;31(1):404-412. doi:10.1021/la504407v
15. Caruso F, Darnowski JW, Opazo C, et al. Taurolidine antiadhesive properties on interaction with *E. coli*; its transformation in biological environment and interaction with bacteria cell wall. *PLoS One*. 2010;5(1):e8927. doi:10.1371/journal.pone.0008927
16. Handrup MM, Fuursted K, Funch P, Møller JK, Schrøder H. Biofilm formation in long-term central venous catheters in children with cancer: a randomized controlled open-labelled trial of taurolidine versus heparin. *APMIS*. 2012;120(10):794-801. doi:10.1111/j.1600-0463.2012.02910.x
17. Colombari B, Alfano G, Gamberini C, Cappelli G, Blasi E. EDTA and taurolidine affect *Pseudomonas aeruginosa* virulence *in vitro*-impairment of secretory profile and biofilm production onto peritoneal dialysis catheters. *Microbiol Spectr*. 2021;9(3):e0104721. doi:10.1128/Spectrum.01047-21

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