**The Use of Silver to Increase Daptomycin Effectiveness**

Jon Liles

Biochemistry

Department of Microbiology and Molecular Genetics, Oklahoma State, OK 74078, USA

**Key Words:**

Antibiotics, Daptomycin, Bacteria, Silver Nanoparticles

**Abstract**

 Antibiotics, the ability to properly use them and their diminishing effectiveness have recently become serious concerns for many doctors and scientists. Because of their overuse, as well as many other factors, most of the antibiotics which are currently available have become less effective at fighting certain bacteria. Although this is a potentially life-threatening problem, there appear to be some viable solutions. Among these are the development of new antibiotics, which will inhibit bacteria when the older antibiotics fail, researching ways to meaningfully augment the effectiveness of many of the older antibiotics in regards to stopping diseases and, finally, restricting the misuse of antibiotics so that bacteria are far less likely to develop resistance to current antibiotics. Each of these measures are important actions for doctors and scientists to take to ensure the future effectiveness of antibiotic treatments. One method, which is now being researched using currently-available antibiotics, is the use of silver to increase their effectiveness. In one recent study, silver has been shown to increase the effectiveness of Daptomycin, which has the potential to provide success in the fight against bacterial diseases.

**Introduction**

 The successful use of antibiotics has probably been one of the biggest factors in the dramatic increase in both life expectancy and quality of life over the last 75 years. However, the effectiveness of antibiotics, which has quite literally changed the world, is increasingly threatened by their overuse and abuse. The effectiveness of virtually all antibiotics is in the process of dramatically decreasing, primarily because many forms of bacteria are developing a resistance to various antibiotics. It appears that this dangerous trend will continue unless immediate actions are taken by both scientists and doctors.

 Unfortunately, as any antibiotic is used, there is a small chance that certain bacteria will gain a defense against that particular antibiotic, and in some cases even other antibiotics, rendering them either less effective or completely useless against that strain of bacteria. Since antibiotics are so widely used in the modern world, there are plenty of opportunities for these bacteria to develop resistance against them. This often results in the situation where antibiotic treatments which used to be totally curative for many bacterial diseases have become less effective. Diseases which were once easy to cure have now become somewhat problematic.

 Of course, the main factors contributing to this antibiotic crisis are their overuse and abuse, their inappropriate use for viruses and other non-responsive diseases and finally the extremely low number of new antibiotics being developed, tested, approved and produced.[[1]](#footnote-1) [[2]](#footnote-2) These factors have combined to truly threaten the vast benefits which society has enjoyed by having access to numerous safe and relatively inexpensive antibiotics. For these reasons, a few scientists have either started to research ways to develop new types of antibiotics or to find methods to dramatically increase the effectiveness of current antibiotics. Either one of these options, and certainly both of them, taken together, could dramatically increase our ability to fight bacterial diseases.

 If these methods to develop new antibiotics or enhance the effectiveness of current antibiotics to fight bacterial diseases were to fail, then many people will begin to suffer from diseases which had previously been easily curable. This gives the need for new, as well as increased effectiveness of old antibiotics much weight and urgency. A world with fewer effective antibiotic options will be continuously worse off in terms of health, quality of life and life expectancy. For this reason, it is critical to continue to make new discoveries which more than offset the gains of antibiotic-resistant bacteria.

 One method currently being researched, which holds great promise in the fight to materially increase the effectiveness of antibiotics, is the use of silver in combination with a currently-known antibiotic. Since silver can facilitate the destruction of bacteria, the combination of silver and a specific antibiotic might be more efficient in destroying many bacterial diseases. This treatment could dramatically decrease the likelihood that the bacteria would both survive and be able to pass on its resistance to antibiotics to other bacteria.

**Recent Progress**

 One of the ways to potentially increase antibiotic effectiveness is to combine current antibiotics with silver. This may be an effective solution to the antibiotic crisis because silver is known to have bactericidal properties.[[3]](#footnote-3) The combination of an antibiotic with any element or material known to harm bacteria makes it less likely for that bacteria to either survive or develop resistance or immunity to the antibiotic. Of course, one of the potential problems with this kind of antibiotic-enhancement therapy is that silver already has well-known negative effects on human health.[[4]](#footnote-4) When silver nanoclusters were combined with Daptomycin, a well-known, current antibiotic, the combination was shown to be more effective in combating bacteria than the Daptomycin alone.[[5]](#footnote-5) This could open the door for more use of silver, and other bactericidal materials, to be used in combination with antibiotics in order to fight bacterial diseases. More research and testing, including possible ways to reduce the negative impact of silver in humans, will need to be done, not only to confirm the effectiveness of these results but, also, to determine the safety of this type of antibiotic-enhancing treatment.

**Discussion**

 The early results of this study are promising because they appear to show that silver nanoclusters increase Daptomycin’s bacterial inhibition. There are, obviously, several critically important questions which still need to be answered about this phenomenon.

 One critically important issue is the effect of ingested silver on human health. Even if the combination of Daptomycin and silver increases the effectiveness of bacterial inhibition, the ability for the combination to be used for human treatment will require that it be done in a way which has no or at least minimal negative side effects. Silver has well-known negative health effects when ingested or absorbed by humans which might be the biggest barrier to its use as an antibiotic-enhancing material. It will obviously be necessary to show that in whatever form the silver is used, to enhance the effectiveness of any antibiotic, it will not cause more harm than good to the people we are trying to help. This is a very important issue to consider because even a small dosage of any material can have a devastating effect on that person’s future health.

 Another question to be answered is whether silver’s effectiveness will be altered when used in combination with antibiotic besides Daptomycin or against bacteria not included in the study. The versatility of a treatment option is of critical importance to its usefulness. If the proven outcomes only exist in very specific, limited circumstances, then this discovery will be far less valuable in the quest to increase overall antibiotic effectiveness. This might even mean that silver’s use is not economically feasible. And, the cost of using silver to enhance a variety of antibiotics is another factor to consider. Silver is a rare and precious metal, so it is possible that the cost of using it on any meaningfully large scale might be too expensive to be practical.

 An extremely positive potential aspect of this method of antibiotic-enhancing treatment might be its effectiveness with various antibiotics which have already been developed. Like virtually all other drugs, the necessary research, development, testing and production of a new antibiotic is very expensive and time-consuming, and this would mean that less research and investment would be necessary when compared to developing a completely new antibiotic.

 The use of silver to enhance the effectiveness of antibiotics is a very interesting concept, if it can be made to be effective while not inordinately dangerous or expensive. If it could be shown to work on a large scale, it might revolutionize the way we fight disease and help end the increasingly common bacterial resistance to antibiotics. More research into the possible benefits and drawbacks of the use of silver to enhance the effectiveness of antibiotics needs to be conducted to allow us a better understanding of the potential of this form of antibiotic-enhancing treatment.

**References**

1. Ventola, C. Lee. “The Antibiotic Resistance Crisis: Part 1: Causes and Threats.” *Pharmacy and Therapeutics* 40.4 (2015): 277–283. Print.

2. Gould, Ian M., and Abhijit M. Bal. “New Antibiotic Agents in the Pipeline and How They Can Help Overcome Microbial Resistance.” *Virulence* 4.2 (2013): 185–191. *PMC*. Web. 7 Feb. 2018.

3. Ester Falletta, Massimo Bonini, Emiliano Fratini, Antonella Lo Nostro, Giovanna Pesavento, Alessio Becheri, Pierandrea Lo Nostro, Patrizia Canton, and Piero Baglioni

*The Journal of Physical Chemistry C* 2008 *112* (31), 11758-11766

4. Braydich-Stolle, Laura, et al. “In Vitro Cytotoxicity of Nanoparticles in Mammalian Germline Stem Cells.” Toxicological Sciences, vol. 88, no. 2, 2005, pp. 412–419.

5. Zheng, Kaiyuan, et al. “Antimicrobial Cluster Bombs: Silver Nanoclusters Packed with Daptomycin.” ACS Nano, vol. 10, no. 8, 2016, pp. 7934–7942.

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/ [↑](#footnote-ref-1)
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3654619/ [↑](#footnote-ref-2)
3. <https://pubs-acs-org.argo.library.okstate.edu/doi/abs/10.1021/jp8035814> [↑](#footnote-ref-3)
4. https://www-ncbi-nlm-nih-gov.argo.library.okstate.edu/pmc/articles/PMC2911231/ [↑](#footnote-ref-4)
5. <https://pubs-acs-org.argo.library.okstate.edu/doi/ipdf/10.1021/acsnano.6b03862> [↑](#footnote-ref-5)