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Antibacterial Brew: Silver's NanoMagi

Silver and tea, working together on the nanoscale, can be used to "brew up" a new weapon against treatment-resistant microorganisms.

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One of the major challenges of the twenty-first century is the effective treatment of bacterial infections. In today's era of great technological advancement, this goal might seem quite trivial, as antibiotics have been known and used successfully for over 100 years. Unfortunately, their efficacy in treatment is increasingly diminishing, as microorganisms are becoming resistant to their effects. A novel solution to this global issue has been proposed in Poland – involving silver and tea extract.

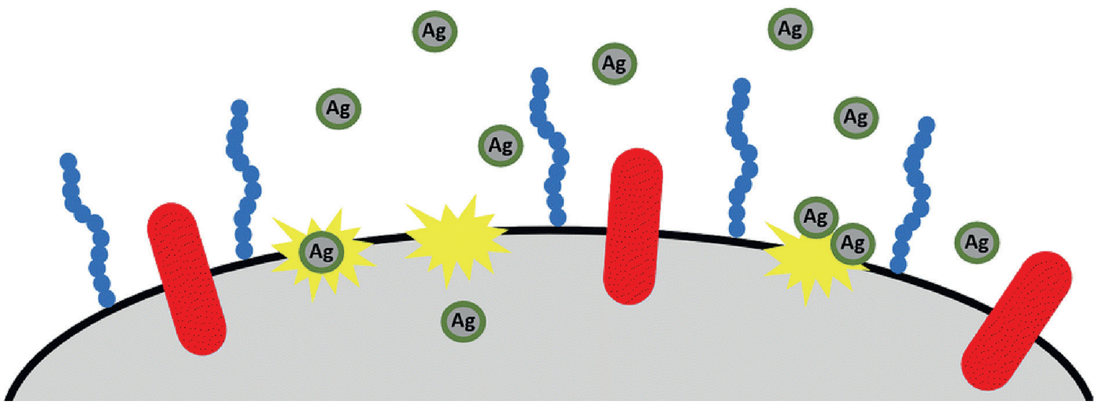
Silver nanoparticles created using tea extracts are microbes' worst nightmare

Once hailed as a panacea or cure-all, antibiotics were credited with bringing tuberculosis, typhus, and many other severe illnesses under control. The introduction of the first antibiotic, penicillin, significantly increased worldwide life expectancy. Antibiotics are only effective against bacterial infections, but their excessive use is leading to the rampant development of *antibiotic resistance*. This term encompasses a variety of cellular mechanisms that render pathogens less susceptible to treatment.

Problems with Antibiotics

Antibiotic resistance can involve modifying the drug molecule, degrading it, or changing the permeability of the bacterial cell wall, thereby inhibiting the penetration of antibiotics. Some bacteria can actively defend themselves even after the antibiotic has penetrated inside them, by expelling the drug or by developing biochemical defenses. All this makes treating patients increasingly complex or – even worse – renders antibiotic therapy ineffective and potentially fatal. The potential for such problems was foreseen decades ago by the pioneer of antibiotic therapy himself, Alexander Fleming, who warned that prolonged use of antibiotics could render them ineffective. Indeed, the WHO reports that approximately 1.27 million deaths annually are directly associated with bacterial resistance. This issue has become a severe global crisis. The escalating difficulty in treating infections has driven the scientific community to explore alternative methods to combat these tenacious bacteria. Scientists are now focusing on microorganisms that have developed resistance to all known antibiotics.

Recently, our team of scientists from the Institute of Physical Chemistry of the Polish Academy of Sciences, under the leadership of Prof. Jan Paczesny, has confronted pathogens such as bacteria from a group known as ESKAPE. The acronym derived from the names of its members: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter spp*. These are all microorganisms that



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Nanoparticles work by penetrating the bacterial cell membrane, bringing in toxic silver and polyphenols, thereby poisoning the bacterium

quickly become resistant to all available antibiotics. Scientists have identified them as primary contributors to hospital-acquired infections worldwide. Their proliferation can lead to sepsis and even cancers. The team also studied pathogenic yeasts resistant to standard medical treatments, such as *Candida auris* and *Cryptococcus neoformans* – strains that pose a threat to patients with weakened immune systems.

An unexpected duo

In search of new solutions for treating infections by problematic pathogens, scientists have turned to nanotechnology.

We have developed hybrid nanoparticles that combine silver with biologically active compounds derived from tea leaves. Whence this unexpected combination? Silver has been known for its antibacterial and antifungal properties for centuries. The Greek historian Herodotus, born back in 484 BC, described how the Persian king took water with him on a military expedition in silver vessels. In modern times, silver's microbicidal properties were scientifically confirmed by the French chemist Jules Raulin in the late nineteenth century. On the other hand, plant extracts, rich in organic compounds such as polyphenols, are extensively used in cosmetics and pharmaceuticals for their high antioxidant efficacy, which involves neutralizing harmful oxygen molecules in cells. Among the numerous plants with such potential, we chose to focus on a very ubiquitous one, used to brew one of the most common beverages in the world: the tea plant.

To produce the most effective hybrid nanoparticles, we tried experimented with three different, well-known teas – black, red, and green. During the chemical synthesis, the tea played multiple roles; it helped precipitate the nanoparticles from the solution and stabilized them to prevent aggregation into larger clumps. Moreover, using tea as a reducing agent makes the synthesis environmentally sustainable, and so it can aptly be described as "green" chemistry. The chemical composition varied with the type of tea, resulting in nanostructures ranging in size from 34 to 65 nm.

Initially, these hybrid nanoparticles were tested against a variety of microorganisms, including both Gram-negative and Gram-positive bacteria. Specific targets were *E. coli*, commonly found in the human large intestine, and *E. faecium*, another gut bacterium. Given the differences in the cell surface structures of these bacteria, it was hypothesized that the nanoparticles would affect them differently. But in both instances, the nanoparticles did effectively inhibit bacterial proliferation.

Remarkable effectiveness

After successful initial tests, it was time to evaluate the susceptibility of the target pathogens. We found that just three hours after exposure to a small amount of nanoparticles, the numbers of *S. aureus* (golden staph) bacteria dropped by 55%, while for *E. cloacae*, the decrease was as much as 90%. Intriguingly, silver alone was ineffective against yeasts; however, the hybrid nanoparticles incorporating tea did demonstrate fungicidal properties, reducing the numbers of *C. auris* by 80 percent and *C. neoformans*, resistant to many pharmaceuticals, by 90 percent.

The efficacy of these hybrid nanoparticles is enhanced by the biologically active compounds from the extracts, including phenols and isoflavonoids, particularly antioxidants like epigallocatechin (EGC) and epigallocatechin gallate (EGCG). Utilizing these extracts also allows less silver to be used, making the nanoparticles not only more effective than traditional antibiotics but also more cost-effective to produce.

The nanoparticles developed by our team hold promise for applications beyond medicine, such as in agriculture to replace harmful chemicals used to combat crop pathogens, or in wound dressings that protect against both Gram-negative and Gram-positive bacteria. This research, however, is just the beginning of exploring their potential uses.

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Silver nanoparticles (G-TeaNPs) synthesized in green tea extract. Clearly visible is the dark core of the nanoparticles, made of silver, and the surrounding organic matter (mostly polyphenols from tea). Image created using transmission electron microscopy (TEM)

Further reading:

Raza S., Wdowiak M., Grotek M., Adamkiewicz W., Nikiforow K., Mente P., Paczesny J., Enhancing the antimicrobial activity of silver nanoparticles against ESKAPE bacteria and emerging fungal pathogens by using tea extracts, *Nanoscale Advances* 2023, vol. 5. doi.org/10.1039/ D3NA00220A