



NATURAL MEDICINE JOURNAL **RESEARCH GUIDE**

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CLINICAL APPLICATIONS OF BIOACTIVE FORMS OF SILVER HYDROSOL

A review of the safety, efficacy and practice implications for healthcare professionals

Authors: Tina Kaczor, ND, FABNO
Karolyn A. Gazella

BEFORE THERE WERE ANTIBIOTICS, there was silver. The antimicrobial and wound healing effects of silver have been embraced for more than 2,000 years. Silver has a rich history of being used by ancient civilizations, on the Civil War and World War I battlefields and even by NASA. Just as with the early use of herbal medicines, silver was used in various medical applications. Colloidal silver in particular has a 125+ year history of use in North America. Medicinal use of silver declined after the introduction of antibiotics in the early 1940s, yet silver was reintroduced in medicine for topical applications in the late 1960s. Silver's use is still prominent in wound healing in the form of topical creams and dressings, particularly for severe burns.

Silver has come a long way since ancient times. As a testament to silver's popular historical use and present-day research, there are many colloidal silver products on the market. Unfortunately, some of these products contain salts, proteins, stabilizers, or other compounds that can negatively impact silver's efficacy and safety. Research shows that there is a direct link between such impurities and toxicity.

There is a form of silver that is reliably safe and effective. Highly bioactive silver hydrosol, made using a proprietary manufacturing process, is available to healthcare professionals as a dietary supplement. Here are some distinguishing factors about this bioactive silver hydrosol:

- It is actively charged, containing >98% bioactive silver ions and nanoclusters, which are the smallest forms of silver particles.
- The smaller particle size of 0.8 nanometers allows for better absorption and elimination. *Note: Always look for third party verification of particle size.*

Parts Per Million Measurement

Parts per million (PPM) is often considered when choosing a colloidal silver product. However, from a safety and efficacy standpoint, PPM is not the only measurement to evaluate. PPM only measures weight, it does not measure particle size, which is also relevant when it comes to silver safety and efficacy. The smallest particle size (0.8 nanometers) delivers the most bioavailable product, which optimizes absorption, excretion, and overall therapeutic effects. In addition, a more bioavailable product means less silver is needed to achieve a therapeutic effect which is safer for the patient.

Using Transmission Electron Microscopy (TEM), which is often used in nanotechnology research, the images above (at 110,000x) show the difference between a highly bioactive form of silver hydrosol, which is 23 PPM versus a silver that is 70 PPM. The black blotch in the 70 PPM image indicates larger silver particles or silver bound to proteins, salts or other compounds that were in the solution. As you can see from the image, the bioactive silver particles are carried in a more pristine solution, with even dispersion and no unwanted compounds, meaning the silver is freely available and highly absorbable.

- It only has 2 ingredients: 99.999% pure silver and pharmaceutical-grade purified water.
- It is vegan and does not contain allergens, gluten, GMOs, or added salts, proteins, stabilizers, or other compounds that can disrupt the purity and efficacy of the silver.
- It is a clear liquid, indicating the complete dispersion of nanoclusters and silver ions in the solution.

Bioavailability and purity are critical factors when it comes to delivering successful clinical outcomes with silver products.

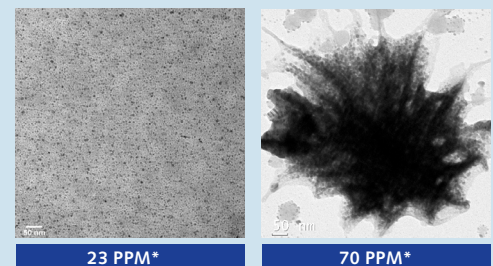
Key Clinical Applications

Much of the research on colloidal silver and forms of silver such as a bioactive silver hydrosol are *in vitro* and *in vivo*. More human clinical trials are needed.

There are three main clinical applications of bioactive silver hydrosol:

1. Antimicrobial
2. Broad spectrum immune and inflammatory modulation
3. Wound healing and tissue regeneration

The antimicrobial properties of silver ions are well known. Research demonstrates that there is a dose-dependent antimicrobial effect against several microbes including methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* (*E. coli*). According to a 2016 review published in the journal *Frontiers in Microbiology*, silver nanoparticles have been proven "effective against over 650 microorganisms including bacteria (both Gram-positive and negative), fungi, and viruses."



*Total silver concentration, not particle size measurement

The authors of a 2008 paper published in the *Digest Journal of Nanomaterials and Biostructures* point out that silver nanoparticles act as a catalyst that disables a respiratory enzyme used by many bacteria, viruses and fungi. The authors explain the silver nanoparticles cause them to “suffocate without corresponding harm occurring to human enzymes or parts of the human body chemistry.”

In addition to directly killing organisms, *in vitro* studies have demonstrated that silver nanoparticles may induce cytotoxicity and a localized inflammatory response. According to a 2016 review published in the journal *Frontiers in Microbiology* this inflammatory effect is associated, in large part, with the local generation of free radicals and ensuing mitochondrial respiration in response to free radical hyperoxidation.

While localized immune response is stimulated through limited inflammation, silver nanoparticles were found “effective at decreasing inflammation in peritoneal adhesions without significant toxic effects,” as shown by Wong and colleagues in a 2009 *in vivo* study. This is in keeping with its role in supporting proper wound healing.

In vivo studies demonstrated that topical delivery of silver nanoparticles helped promote wound healing and tissue regeneration. A 2007 study published in the journal *Chem.Med.Chem* found that silver nanoparticles produced “rapid healing and improved cosmetic appearance.” This conclusion is consistent with a 2010 *in vivo* study published in *Chem.Med.Chem* where the researchers found that silver nanoparticles increased the rate of wound closure via “the promotion of proliferation and migration of keratinocytes.” The researchers also noted that the silver nanoparticles influenced the “differentiation of fibroblasts into myofibroblasts, thereby promoting wound contraction.”

In addition to these well-known applications of silver nanoparticles, recent research has looked at the connection between silver and the gut microbiome.

The Gut Microbiome

The significance of the gut microbiome to systemic health cannot be overstated. The bacterial ecosystem in the gut has far reaching health implications. Research is now confirming that the gut microbiome interacts directly with the brain and other key organs in the body, thereby influencing the health status of those organs.

Dysbiosis by definition is an imbalance of gut microbiota that can cause the tight junctions between enterocytes

Proper Packaging

A pure and highly bioactive form of silver hydrosol is best packaged in an amber glass bottle. Here's why amber glass may be preferred over plastic:

- Glass is an inorganic material that is guaranteed to be free of possible organic toxins. Plastic, on the other hand, may contain traces of plasticizers.
- Leaching has been seen in a variety of plastics over time. The longer the product remains in the plastic, the more leaching of plasticizers (i.e., BPA) can occur. There is no leaching with glass.
- The leaching of harmful chemicals can also cause instability of nanoparticles and allow the silver particles to be absorbed into the plastic and rendered unavailable to the user of the product.
- Glass does not degrade with time. Plastic, on the other hand, is subject to degradation caused by exposure to oxygen, light, heat, and humidity.
- Glass is not permeable to carbon dioxide and other gasses, which provides added protection and ensures product efficacy.

to open up and allow larger molecules (i.e., organisms, peptides, chemicals) to enter the bloodstream. This is called increased intestinal permeability, also known as “leaky gut,” and it can have many harmful health effects.

There are several factors that can cause dysbiosis, but one that is reliable is antibiotic use. The accumulation of antibiotic overuse for many decades has created antibiotic resistance in many common bacterial species, something that the Centers for Disease Control and Prevention (CDC) calls one of “the biggest public health challenges of our time.” The CDC reports that antibiotic resistance causes more than 23,000 deaths per year.

The use of highly bioactive forms of silver hydrosol is a more effective first-line defense compared to antibiotics. The authors of a 2016 review paper published in the journal *Frontiers in Microbiology* identified multiple antimicrobial mechanisms of bioactive silver including “adhesion to microbial cells, penetration inside the cells, ROS and free radical generation, and modulation of microbial signal transduction pathways.”

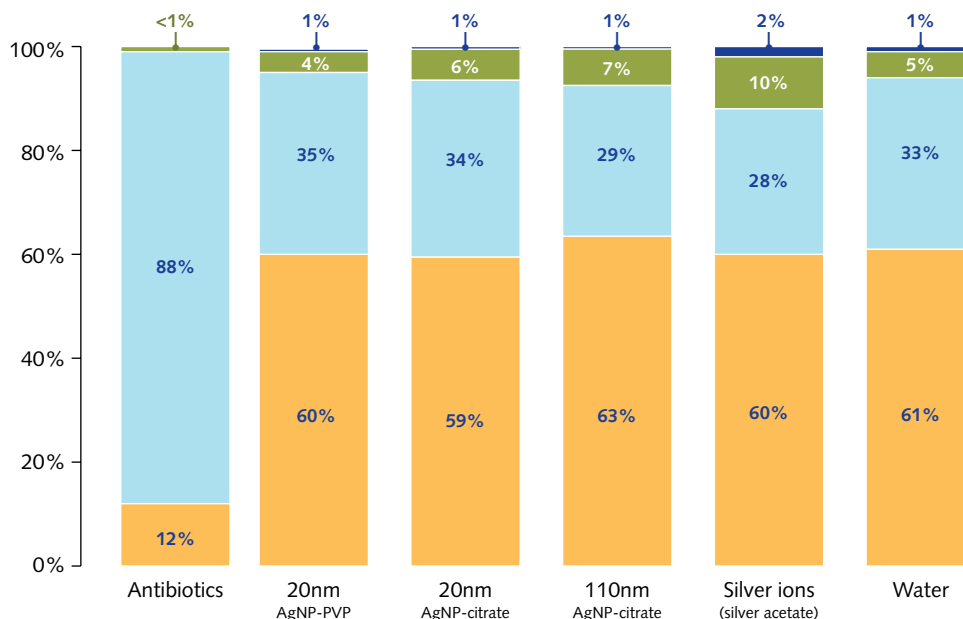
In addition to its antimicrobial activity, as illustrated by Table 1 on page 4, silver does not disrupt gut microbiome diversity compared to antibiotics and other drugs.

TABLE 1 Gut Microbiome Diversity

Silver Does Not Disrupt Gut Microbiome Diversity

- Gut microbiome diversity is not impacted by silver, even at 2,000 times the EPA and WHO Safety Limit Guidelines
- Antibiotics disrupt balance significantly (cefoperazone)

- Other
- Deferribacteres
- Firmicutes
- Bacteroidetes



Data from L.A. Wilding, et al, "Repeated dose (28-day) administration of silver nanoparticles of varied size and coating does not significantly alter the indigenous murine gut microbiome." *Nanotoxicology*, 2016, 10:5, 513-520

Research suggests that silver nanoparticles may actually help enhance gut health. A 2019 review published in the *Journal of Applied Toxicology* looked at the effects of silver nanoparticles on gut bacteria. The authors explain that silver nanoparticles positively impacted the gut microbiome in the following ways:

- Destruction of bacterial cell membranes
- Blocks protein synthesis
- Denatures enzymes
- Inhibits bacterial respiration
- Inactivates enzyme function via interaction with thiol group L-cysteine residues
- Blocks *E. coli* DNA replication

A 2017 study utilizing a mouse model of ulcerative colitis and Crohn's disease that was published in *Chemical Biology & Drug Design* showed that silver nanoparticles reduced colonic inflammation, *E. coli* and *Clostridium perfringens*. In addition, the number of *Lactobacillus* bacteria increased. The authors concluded that silver nanoparticles "...have the potential to become valuable agents for the treatment of inflammatory bowel diseases."

According to this preliminary research, silver nanoparticles do not disrupt gut microbiome diversity and may actually play a synergistic role in enhancing gut health. More research is required to confirm this effect.

Bioactive forms of silver hydrosol can also be used topically.

Topical Applications

There are pure forms of silver blended with homeopathic ingredients and an odorless gelling agent that can be used for safe, effective skin healing applications. As a first aid gel, topical homeopathic silver (Argentum Metallicum 10x, 20x, 30x) can effectively:

- Reduce pain from skin irritation
- Calm inflammation
- Fight infections
- Promote wound healing

Clinically, homeopathic bioactive forms of silver hydrosol blended into a gel can help with burning, stinging, itching, redness, bruising, blisters, minor cuts and scrapes, bug bites, and rashes. It can also help ease skin eruptions caused by acne, eczema, psoriasis, shingles or minor infections. Several studies, including a 2016 paper published in the *Journal of Applied Biomaterials & Functional Materials*, have confirmed that silver nanoparticles applied topically decrease inflammatory cytokines (TNF- α and IL12), growth factors (VEGF), and the expression of COX-2.

Silver nanoparticles have also been shown to accelerate wound healing in the case of chronic conditions such as diabetes. Research published in 2017 in the *International Journal of Biological Macromolecules* demonstrated

that silver-infused nanobiocomposites accelerated diabetic wound healing by reducing inflammation and supporting “early proliferation, collagen formation and epithelialization.”

To obtain optimal efficacy using the topical first aid gel, clean the affected area and apply a liberal consistent layer. Do not rub dry. The area should be left wet and can be unbandaged or bandaged. Repeat three times a day or as needed to relieve symptoms.

Safety and Dosage

When it comes to silver safety, most clinicians are concerned about the development of Argyria, a benign cutaneous blue skin discoloration. It’s important to note that there has never been a case of Argyria reported in connection with the use of a pure, low concentration, bioactive form of silver hydrosol. This is primarily due to the purity and small particle size of this specific form of silver. Small particle size also means less silver is required to deliver a safe therapeutic effect. A bioactive silver hydrosol with only 23 mcg of silver per mL offers a minuscule dose, especially when considering that the

reported Argyria cases include consumption of hundreds of fold higher doses of silver over long periods of time.

In addition, *in vivo* research also illustrates that silver is efficiently excreted from the body. This is especially true with silver nanoparticles because of the small particle size.

According to a 2011 *in vivo* study published in the journal *Particle and Fibre Toxicology*, the researchers found that “The absolute silver concentrations in the organs were generally lower after administration of AgNPs (silver nanoparticles) than after administration of AgAc (silver acetate).” This study found that the silver was primarily excreted through the feces versus urine. Similar results were published in 2016 in the journal *Nanotoxicology* which found that an acute oral dose of silver nanoparticles was predominantly excreted through the feces without any tissue accumulation or toxicity.

EPA guidelines indicate that the safe daily oral reference dose (RfD) for silver is 350 mcg per day. Table 2 illustrates that even at 6,000 times the EPA daily RfD, silver

TABLE 2 Safety of Silver in Pure Forms

Study	No Observed Adverse Events?	# of times EPA daily RfD (5 µg/kg)	mg silver / kg body weight	tsp/day, @23ppm	gal/day, @23ppm
1 tsp of 23ppm Silver Hydrosol	✓	0.33	0.0016	1	0.005
Morishita, et al, 2016, “low” dose ^[1]	✓	300	1.5	913	1
Xue, et al, 2012, “low” dose ^[2]	✓	1,500	7.5	4,565	6
Loeschner, et al, 2011, “low” dose ^[3]	✓	1,860	9.3	5,661	7
Wilding, et al, 2016 ^[4]	✓	2,000	10	6,087	8
Morishita, et al, 2016, “high” dose ^[1]	✓	2,000	10	6,087	8
Loeschner, et al, 2011, “high” dose ^[3]	✓	2,520	12.6	7,670	10
Kim, et al, 2008, “low” dose ^[5]	✓	6,000	30	18,261	24
Xue, et al, 2012, “mid” dose ^[2]	✓	6,000	30	18,261	24
Xue, et al, 2012, “high” dose ^[2]	lung & liver inflammation	24,000	120	73,043	95
Kim, et al, 2008, “high” dose ^[5]	elevated liver enzymes	60,000	300	182,609	238

*Note: Silvers in these studies were of highest purity (e.g., pharmaceutical grade water).

Safety can differ when impurities are present.

The water will become toxic before silver adverse events are observed with high purity 23 ppm silver.

[1] Morishita Y, et al. Distribution of silver nanoparticles to breast milk and their biological effects on breast-fed offspring mice. *ACS Nano*. 2016.

[2] Xue Y, et al. Acute toxic effects and gender-related biokinetics of silver nanoparticles following an intravenous injection in mice. *Journal of Applied Toxicology*. 2012. 32(11): 890-899.

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[5] Kim YS, et al. Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. *Inhal Toxicol*. 2008. 20(6):575-83.

nanoparticles are safe with no adverse events observed. Note that the silver used in these safety studies was the pure nanoparticle form. Safety results of impure silver products on the market may be different from these results.

Regarding dosage, the standard recommendation for a 10ppm bioactive form of silver hydrosol is as follows:

- Maintenance = 1 tsp held under the tongue for 30 seconds and then swallow, once per day
- Immune-Building = same as maintenance, three times per day
- Long-Term Immune Support = same as maintenance, five times per day
- Short-Term Immune Support = same as maintenance, seven times per day

A highly bioactive form of silver hydrosol has broad clinical applications and can be an effective tool for integrative practitioners. Care should be taken when choosing a silver product.

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About the Author

Tina Kaczor, ND, FABNO, is editor-in-chief of *Natural Medicine Journal* and the creator of Round Table Cancer Care. She is a naturopathic physician board certified in naturopathic oncology. She received her naturopathic doctorate from National University of Natural Medicine and completed her residency at Cancer Treatment Centers of America.



Karolyn A. Gazella is publisher of *Natural Medicine Journal* and has been writing and publishing integrative health information since 1992. She is the co-creator of the iTHRIVE cancer survivorship wellness plan and the author or co-author of several books. She also co-hosts the Five to Thrive Live weekly radio show on the Cancer Support Network, also available on iHeart Radio and Spotify.



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