

An In Depth History of Silver

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Historic Perspectives on Clinical Use and Efficacy of Silver

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Prior Civilizations

Since ancient times silver has been highly regarded as a versatile healing tool. In ancient Greece, Rome, Phoenicia, and Macedonia, silver was used extensively to control infections and spoilage. Hippocrates, the “Father of Medicine,” taught that silver healed wounds and controlled disease. Around 400 B.C. he listed as a singular treatment for ulcers “the flowers of silver alone, in the finest powder.” Herodotus describes how the King of Persia carried with him boiled water in silver flagons to prevent sickness. In 69 B.C., silver nitrate was described in the contemporary pharmacopoeia.

The popularity of medicinal silver especially arose throughout the Middle East from 702 A.D. through 980 A.D. where it was widely used and esteemed for blood purification, heart conditions, and used to control halitosis. Paracelsus (circa 1520) extensively used silver medicinally, and later Caradanus, Pareus, and Sala also used it. For example, Angelus Sala used silver nitrate to successfully treat chorea, and tabes dorsalis (syphilis). These crude and inferior forms of silver were reported by Sala to rarely cause the bluish-hue skin discoloration (argyria) due to overuse. It is widely thought that during the Middle Ages silver utensils and goblets contributed a bluish-hue to the skin-tone of the upper class, resulting in the term “blue-bloods.” Plausibly, “born with a silver spoon in his mouth” was coined during that time for the same reason, as an attribute for describing the good fortune of being healthy more than being wealthy. Blue-bloods were noted to have been afforded a measure of protection from the rampant plagues common to Europe in those centuries.

During the wars with Napoleon, the armies of Tsar Alexander used water casks lined with silver to clean drinking water from rivers and streams. This practice by the Imperial Russian army was continued through World War I and by some units in the Soviet Army in World War II. Raulin recorded the first description of the water cleansing effect by silver in 1869. He observed that *Aspergillus Niger* could not grow in silver vessels.

Modern Research using the Scientific Method

In 1861, Thomas Graham found that certain solutions would pass through a membrane and others would not. He found a stable, intermediate state of matter, and was able to describe it. Graham’s discovery was that substances could enter a solution in such a manner that they exhibit characteristics that are quite different from those of a true solution. He applied the term “colloidal” (from kolla = glue) to this intermediate state, as glue, gelatin, and related substances were the most obvious to him as being in this unique state. The Swiss botanist von Nageli recorded one of the amazing discoveries of the nineteenth century in 1869. Von Nageli coined the term “oligodynamic” to describe the microbiocidal properties of a metal hydrosol (e.g. copper, silver and tin) at minute concentrations. , In 1884, Crede introduced the use of 1% silver nitrate for the prevention of ophthalmia neonatorum. By 1897, silver nitrate began to be used in America to prevent blindness in newborns and is still used today. , By 1910,

Henry Crookes had documented that certain metals, when in a colloidal state, had strong germicidal action, but were harmless to human beings. The oligodynamic concept has motivated the development of many antimicrobial processes and products. One of the water purification developments that took place in 1928 was the development of katadyn silver, described as a porous metallic, spongy mesh that attempts to maximize surface area. This silver meshwork also contains a small quantity of gold or palladium. Katadyn silver has been used inside flasks, storage containers and with water filters. During the last century, advances in pharmacological manufacturing methods sought to harness this time-valued strategy expressed in nearly all silver formulations. Yet early manufacturing methods rarely created high quality, homogenous oligodynamic Ag⁺. Nevertheless, more than 96 different silver medicinals (many used intravenously) were in use prior to 1939, as documented by The Council on Pharmacy and Chemistry of the American Medical Association. A project begun at the State University of New York by Robert Becker and associates involved a silver nylon product in the early 1970's. This project was originally instigated in order to find an electromagnetic shield. Instead, it led to the revolutionary discoveries by Becker of silver's unique antimicrobial properties, and his discovery that silver ions could induce fibrocytes to dedifferentiate into stem cells and back again. One of Becker's research associates, A. Bart Flick, continued work in this area for professional and commercial applications. As a result, Flick has filed patents in 1994, 1996 and 2000 for silver-based wound dressings that are far superior to anything that has ever been available before. He has also obtained approval for these dressings from the US Food and Drug Administration. Because of the success of these silver dressings, many other medical product manufacturers have filed for their own parallel products. In the early 1970's silver topical salves, such as silver sulfadiazine, provided superior control and prophylaxis in severe burn cases. Today, multiple drug resistant (MDR) microbes are challenging this formulation's effectiveness, but we shall review how state-of-the-art silver protocols and formulations offer superior protection against microbial strategies for acquiring resistance. To date, absolute microbial resistance to medicinal silver has not been scientifically established. Several studies indicated that some bacterial species have physiological mechanisms that circumnavigate silver's toxicity. Although it is clear that some pathogens have mechanisms to survive exposure to silver, these mechanisms are limited when compared to higher life forms. Herein lie all the clues necessary to identify strategic silver therapeutics that pathogens are unlikely to survive. It is probable that pathogens lack sufficient defense mechanisms to circumvent the toxic effects of silver ions when oligodynamic silver is delivered in sufficient, physiologically compatible quantities. In fact, the "apparent" resistance of microbes to silver was mistakenly made by many who failed to notice and identify: (a) insufficient oligodynamic Ag⁺ particle concentrations, (b) inadequate protocols, or (c) improper procedures. Reports that multiple-drug-resistant (MDR) pathogens (i.e., MRSA and *Acinetobacter* spp.) were truly resistant to silver proved to be erroneous. Grier stated, "Some so-called Ag⁺ resistant microorganisms may result from an apparent neutralization of the metal's inhibitory action or other assay artifacts. These include the presence of chelators such as several amino acids, constituents of hard water, different buffers, light, incubation temperature, and particularly, soluble components of trypticase soy agar (TSA) and tryptose glucose extract agar (TGE)."

With the advent of antibiotic therapy, medicinal silver products fell largely into disuse (circa 1940 - 1945), with the notable exceptions of topical silver salves and neonatal eye drop preparations. These

salves advanced the science of “silver salt-derived” Ag + delivery and effectiveness in the mid 1960’s. Then, during the mid-1970’s, several papers were published that utilized electrically activated silver probes as delivery systems for targeted oligodynamic Ag + strategies. The interest in such strategies continues to grow to the present, with high efficacy being obtained for viral vectors such as HIV, and resistant bone and dental infection. Sufficient defense capacity to mitigate morbidity clearly exists in higher organisms, including humans (with the exception of medically benign argyria). Zhao and Stevens state that, “With the rise of antibiotic-resistant bacteria, silver is re-emerging as a modern medicine because all pathogenic organisms have failed to develop an immunity to it (Ag +).”

In Vitro Studies

The medical literature of the early 20th century regarding silver provides an important cautionary lesson from the past. Previous scientists, who were either supporters or detractors of silver medicinals, typically expressed equivocal knowledge and misapplied context because they failed to recognize silver speciation. This fault undermined their definitive knowledge about silver. Correct and in-context discernment of silver’s Therapeutic Threshold remains elusive to most investigators even today. This “box” perception about silver will continue to lose its limitations as technology continues to prove itself outside of that box in the coming decades.

Clinical reports on silver medicinals began to flood into the various medical journals worldwide at the start of the last century. Initially, the Journal of the American Medical Association took a negative position. But within 11 years, a true revolution in medical practice with silver medicinals occurred that did not subside until the U.S. government’s purchase of the patent rights to penicillin (circa 1940). Throughout this time period (1920 through 1942), JAMA articles were replete with oral (per os) and intravenous clinical reports of the efficacy and side effects of silver medicinals. In tandem with research in America, Great Britain published prominently in such respected journals as The Lancet and the British Medical Journal. Perhaps the first definitive attempt to comprehensively evaluate the efficacy and variety of silver medicinals was published by the Department of Pharmacology of the Medical School of Western Reserve University, Cleveland, circa 1923. In terms of efficacy, this landmark study arguably established “silver nitrate” as the benchmark for all silver medicinals. Unfortunately, the excitement this study produced simultaneously placed at risk subgroups of patients susceptible to symptoms of argyria. Had the technology then existed to create vast surface areas with “pure hydrosols of oligodynamic Ag +” not only would such products have revealed their greater potency over that of silver nitrate; but also, argyric thresholds would have been nearly impossible to attain during any course of therapy. Oligodynamic (picoscale) surface area enables maximal exposure of silver particles in the least amount of volume, thus achieving potency several orders of magnitude over suspensions of much higher ppm silver speciations (which necessarily manifest inferior surface area exposures). In other words, technology today can produce smaller quantities of silver that are vastly more potent than was ever historically possible. The result is a dramatic elucidation of the Therapeutic Index, resulting in unprecedented safety, efficacy, and dimension to protocol parameters. For example, beginning in 1970 at the University of Wisconsin, under contract from NASA to determine the biocidal effects of silver, researchers were able to determine that lethal effects of silver ions could be reliably reproduced at concentrations of only 250-ppb when exposed to infectious agents over two hours or less in vitro. These researchers even found that even 50-ppb over four hours or less achieved a significant biocidal effect.

The University study with laboratory-produced silver ions worked extremely well, although the extinction times were long. Follow-on investigations of these early silver medicinals failed to exert adequate lethal effects upon antibiotic resistant infectious organisms. However, as technology advanced, these highly resistant organisms were again found to succumb to the lethal effects of new silver medicinals. Additionally, extinction times proved to be dramatically lessening.

In Vivo Studies

At the height of its popularity (from 1900 through 1940), a fair estimate of humans given intravenous silver medicinals worldwide exceeded several million. The sheer scale of its utilization defined and confirmed silver medicinals as effective anti-microbials. During my training as a medical student, I had an opportunity to witness several of my elder attending physicians using various silver formulas in their clinical practice. It was fascinating to me that silver medicinals were widely used by one generation of clinicians, yet this therapeutic approach simply ended by my generation. Why? In terms of safety and efficacy, was there a justification for abandonment of this approach? One recent and noteworthy in vivo study published in the Journal of Clinical Ultrasound (2000) reported on a protocol involving puncture, aspiration, injection, and re-aspiration (PAIR) with silver nitrate directly into hepatic hydatid cysts with beneficial long-term results. Other preliminary evidence in vivo suggests that both hepatitis-C virus (HCV) and HIV, and other viral vectors, as well as in vitro studies on herpes, and the worst bacterial scourges (i.e., antibiotic resistant disease vectors) may become events of the past via the judicious and strategic use of a state-of-the-art silver medicinal and delivery system. Antimicrobial coatings for the inside and outside of medical catheters using silver have been developed for latex, polyurethane and Teflon devices. These silver coatings are very effective at blocking bacteria, such as E coli and S aureus, from entering the body along a catheter pathway.