What are the properties of silver $(Ag_{(n)}^{1+} \text{ or } Ag^{1+})$ and its methods of action?

- Promotes accelerated wound healing while improving cosmetic appearance on recovery (no scarring)¹
- Positive effects exerted through antimicrobial properties, reduction in wound • inflammation, and modulation of fibrogenic cytokines¹
- In human physiology, silver plays an important role. It is literally an essential trace element for the peripheral nervous system. Science has now identified receptor sites for silver in myelin neural tissue.^{2 3}
- Positive silver ions stimulates de-differentiation and redifferentiation of stem cells in • vivo, accelerating healthy regenerative events wherever there is inflammation, infection or injury.⁴
- Oligodynamic silver improves the body's internal colloidal milieu by facilitating oxidative reactions central to immunity.^{5 6 7}

What are the antimicrobial properties of silver?

Like bacteria and fungi, infectious viral organisms may have multiple susceptibilities when encountering oligodynamic Ag¹⁺. On the other hand, evidence suggests that oligodynamic Ag¹⁺ will not interfere with normal white blood cell (WBC) activity, and may even enhance WBC activity.⁸ ⁹ Feng et al.¹⁰ concluded that oligodynamic Ag¹⁺ offered profound immune benefits because of its ability to intervene with select bacteria in three key ways almost simultaneously. Central to all three is the ability of oligodynamic Aq1 to denature (dose-dependent permanent inactivation) essential microorganisms' protein and DNA:

- 1. One type of essential protein maintains the integrity of the cell's membranes and boundaries. Once the membranes become unstable, the cell begins to rupture.
- 2. Simultaneously, the smallest sizes of Ag¹⁺ may more easily penetrate the membrane pores of the bacteria. Once penetration occurs, life-essential enzyme reactions governing cell metabolism go into partial or full arrest.
- 3. As the silver further penetrates the most interior recesses of the cell, the genetic building blocks (nucleic acids) of the germs are paralyzed, ending the ability of the invaders to replicate.

How does silver eradicate bacteria, viruses and fungus?

- Aq¹⁺ at the nano and picoscale denatures the protein coat of a virus, can penetrate the cell wall of a bacteria and fungus and enter the mitochondria, binding with RNA and DNA rendering them unable to replicate (in the case of viral particles) or reproduce.
- The antiseptic activity of silver compounds results from the reaction of Aq¹⁺ with proteins of the microorganism, such as structural proteins and enzymes. Chambers et al have shown

Chembiochem. 2004 Dec 3;5(12):1686-91. Samuni A, et al. On the Cytotoxicity of Vitamin C and metal ions. Eur J Biochem. 1983;99:562.

¹ Jun Tian, Dr. et al. Topical Delivery of Silver Nanoparticles Promotes Wound Healing 31 Oct 2006 ChemMedChem Vol. 2 Issue 1, P. 129-136

 ² Gallyas, F., "Physico-Chemical Mechanism of the Argyrophil I Reaction," *Histochemistry* (1982) 74:393.
³ Gallyas, F., "Simultaneous Determination of the Amounts of Metallic and Reducible Silver in Histologic Specimens," *Histochemistry*, (1979)

^{64:77-86.}

⁴ Becker, RO, "Induced De-differentiation; A Possible Alternative to Embryonic Stem Cell Transplants." Neurorehabilitation 17 (2002):23-31. ⁵ Gan X, Liu T, Zhong J, Liu X, Li G. Effect of silver nanoparticles on the electron transfer reactivity and the catalytic activity of myoglobin

⁷ Jansson, G, Harms-Ringdahl, M, "Stimulating Effects of Mercuric- and Silver Ions on the Superoxide Anion Production in Human

Polymorphonuclear Leukocytes," Free Radic Res commun, 1993; 18(2):87-98.
Ellerman-Eriksen S, Rungby J, Morgensen SC. Autointerference in silver accumulation in microphages without affecting phagocytic,

 ⁹ Jansson G, Harms-Ringdahl M. Stimulating effects of mercuris and silver ions on the superoxide anion production in human

polymorphonuclear leukocytes. Free Radic Res Commun 1993; 18(2):87–98.
¹⁰ Feng QL, Wu J, Chen GO, et al. A mechanistic study of the antibacterial effect of silver ions on Escherichia coli and Staphylococcus aureus. J Biomed Mater Res 2000; 52: 662-8.

that the activity of a specified amount of silver is related to the concentration of Ag¹⁺ ion, which is in an unbound state, rather than to the chemical or physical nature of its source.¹¹

- With all prokaryotes, there is a destructive translocation of silver hydrosol particles through their biological membrane or cell wall. There is a destructive translocation of silver hydrosol particles across some simple eukaryotes of various fungal species. The Zeta potential of Ag_n^{1+} in the organized water molecules contributes to an electroporation event, which further destabilizes the bacterial cell wall.¹²
- Silver (Ag¹⁺) ions have been tested extensively for their antibacterial efficacy on both gram negative and gram positive bacteria.¹³
- Feng et al were able to elaborate on the changes in bacteria via x-ray microanalysis and the inactivation of DNA replication in these bacteria.¹⁴

What form or species of silver is its true active state?

Positive silver ions $(Ag^{1+} or Ag_n^{1+})$ are the only active state of silver for use within the body. Acél¹⁵ was perhaps the first to observe that the oligodynamic action of silver was due to liberated Ag¹⁺ as opposed to metallic (neutral) Ag. Eichorn *et al*¹⁶ emphasized that the charge significantly facilitates electron displacement. The Ag¹⁺ structure of silver hydrosol has been shown to have the greatest antimicrobial activity at or near the picoscalar level¹⁷ due to the fact that it enjoys the greatest surface presentation ($\sim 6 \text{km}^2 \text{ per gram Ag}$).¹⁸

Why is Particle Charge important in the action of silver hydrosol?

The term oligodynamic is only applicable to extremely low concentrations of metal ions (Ag¹⁺). Ace 1¹⁹ was perhaps the first to observe that the oligodynamic action of silver was due to liberated Ag¹⁺ as opposed to metallic (neutral) Ag. Eichorn et al.²⁰ emphasized that the charge significantly facilitates electron displacement. The oligodynamic metal charge effectively yanks electrons away from a molecule, in essence weakening the molecular bond and rendering it susceptible to cleavage. Goetz²¹ observed that silver is microcidal only if it is in the ionic state, and this was later characterized further by Rochart and Uzdins²² [59] who observed that cells selectively bond only with Aq¹⁺.

What is the metabolic pathway of elimination?

The normal physiologic pathway in humans and animals for the metabolism and elimination of ingested silver occurs in phase II liver glutathione conjugation, which leads to normal excretion as solid waste through the colon.²³

¹⁴ Clement JL, Jarrett PS. Antibacterial Silver. Metal Based Drugs, ed. By Frank Shaw, III, August 17th-20th, 1994; 1(5-6):472 ¹⁵ Acel D, Biochem Z, 1920; 112: 23-32. In: Russell, AD, Path, FR, Hugo, WB, Antimicrobial Activity and Action of Silver. Prog Med Chem,

¹¹ Chambers CW, Proctor CM, Kahler PW. Bactericidal effect of low concentrations of silver. J.Am. Wat. Wks. Ass. 1962; 54:208-216. ¹² Rentz, EJ., Pathogens: A Global Solution, Section: Colloidal Charged Particle Description: Zeta potential, Med. Ref. Txtbk., LOC

TXu001146453, Oct. 2003.
¹³ Feng *et al.* A Mechanistic Study of the Antibacterial Effect of Silver Ions on Escherichia coli and Staphylococcus aureus. *J Biomed Mater Res*, 2000 March: 52:662-8

 <sup>1994; 31:353.
&</sup>lt;sup>16</sup> Eichorn GL *et al.* Interaction of metal ions with biological systems with special reference to silver and gold. Proceedings of the First International Conference on Gold and Silver in Medicine, Bethesda, MD, 13-14 May. Washington, DC: The Silver Institute, 1987, 4.

Morones JR, et al. The bactericidal effects of silver nanoparticles. Nanotechnology. 2005;16:2346-53.

¹⁸ Goetz A, Tracy RL, Harris FS. Oligodyanmic Effect of Silver. Chapter 16. In: Silver in Industry, edited by L. Addicks, Reinhold Publishing Corp., NY, 1940; p.402. ¹⁹ Ace 1 D, Biochem Z 1920; 112: 23–32.

²⁰ Eichorn GL et al. Interaction of metal ions with biological systems, with special reference to silver

and gold. Proceedings of the First International Conference on Gold and Silver in Medicine,

Bethesda, MD, 13–14 May. Washington, DC: The Silver Institute, 1987, 4. ²¹ Goetz A. Water sanitation with silver. J Am Water Works Assoc 1943; 35: 579.

²² Rochart C, Uzdins K. Katadyn (silver preparation): clinical application. Schweiz Med Wochenschr

^{1947; 77: 1100–4.} ²³ Rentz EJ. Viral Pathogens and Severe Acute Respiratory Syndrome: Oligodynamic Ag+ for Direct Immune Intervention. *Journal of* Nutritional and Environmental Medicine (June 2003) 13(2), 109-118