Technical White Paper: Antimicrobial Activity of Silver **V1.0 - September 2005**

The antimicrobial activity of silver has been recognised by clinicians for over 100 years (Ref 1). In addition, reports suggest that hygienic benefits have been associated with the use of silver for considerably longer. Records show that Hippocrates recognised the role of silver in the prevention of disease and accounts exist that suggest that the romans stored wine in silver vessels to prevent spoilage (Ref 2). However, it is only in the last few decades that the mode of action of silver as an antimicrobial agent has been studied with any rigour (*eg* Ref 3).

Metallic silver is relatively unreactive however, when exposed to aqueous environments some ionic silver (Ag^+) is released. Certain salts (*eg* silver nitrate) are readily soluble in water and have been exploited as antiseptic agents for many decades (Ref. 1). The generation of silver ions can also be achieved through ion exchange using complexes of silver with other inorganic materials (*eg* silver - zeolite complexes; Ref. 4). Silver nano-particles have also been demonstrated to exhibit antimicrobial properties both against bacteria (Ref 5) and viruses (Ref 6) with close attachment of the nano-particles themselves with the microbial cells / virus particles being demonstrated with activity being size dependent (Ref 7). Despite this, the principle activity of silver is as a results of the production of silver ions within an aqueous matrix (Ref 8). This therefore implies that for silver to have an antimicrobial effect, free water must be present.

Silver ions interact with a number of components of both bacterial, protozoal and fungal cells. Toxicity to microbial cells is exhibited at very low concentrations with masses within the range of a few fg $cell^{-1}$ being associated with bactericidal activity (Ref 9). The kinetics of kill vary depending on the source of silver ions with silver derived from ion exchange processes demonstrating delayed activity compared with that derived from soluble salts (Ref 9). Activity appears to increase with temperature and pH (Ref 9). Studies have demonstrated that silver ions interact with sulfydryl (-SH) groups of proteins as well as the bases of DNA leading either to the inhibition of respiratory processes (Ref 10) or DNA unwinding (Ref 11). Inhibition of cell division and damage to bacterial cell envelopes is also recorded (Ref 12) and interaction with hydrogen bonding processes has been demonstrated to occur (Ref 13). Interruption of cell wall synthesis resulting in loss of essential nutrients has been shown to occur in yeasts (Ref 14) and may well occur in other fungi. Antiviral activity of silver ions has been recorded and interaction with -SH groups has been implicated in the mode of action (Ref 15). The association of silver nano-particles with the envelope of certain viruses has been suggested to prevent them from being infective (Ref 6). Much of the research into the mechanism of action of silver ions has been associated with its use as a therapeutic agent especially as a topical dressing on burns. The concentration employed in and released from treated articles is significantly lower than in these applications (Ref 9). Under such conditions it has been suggested that in many cases the concentration of silver ions available following hydration of the surface of a treated article is too low to produce antimicrobial activity associated with many of the mechanisms described above. However, silver ions have been demonstrated to interact with the proteins and possibly phospholipids associated with the proton pump of bacterial membranes. This results in a collapse of the membrane proton gradient causing a disruption of many of the mechanisms of cellular metabolism and hence cell death (Ref 16).

Silver ions clearly do not possess a single mode of action. They interact with a wide range of molecular processes within microorganisms resulting in a range of effects from inhibition of growth, loss of infectivity to cell death. The mechanism depends on both the concentration of silver ions present and the sensitivity of the microbial species to silver. Contact time, temperature, pH and the presence of free water all impact on both the rate and extent of antimicrobial activity. However, the spectrum of activity is very wide and the development of resistance relatively low, especially in clinical situations (Ref 17).

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