The Science of Oligon

Vantex
Whitepaper 01
Science of Oligon

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Introduction

The U.S. Centers for Disease Control's *Study on the Efficacy of Nosocomial Infection Control* researched nosocomial infections (NI) over a ten-year period from 1975 to 1985 and found a 7% incidence of NIs among all U.S. hospital admissions.[1] A ten-year trend analysis (1980–1990) reported a tripling in the incidence during that period. In 1998, the CDC reported that the trend of increasing nosocomial infection rates has continued unabated. In the United States, approximately two million patients per year develop nosocomial infections.[1,2] More than three million patients annually contract NIs in Europe.

Of the four most common types of nosocomial infections (bloodstream, surgical site, respiratory tract and urinary tract) all except surgical site infection are generally caused by some sort of catheter or other tube-like invasive medical device.[1,2] The risk of infection correlates with the length of time a device is left in place and the number of times the extracorporal end is exposed, handled, punctured or disconnected from lines. Infection risk is considered minimal for devices in place less than three days. Beyond three days, however, the risk rises considerably, and for patients such as those receiving cancer or nutritional therapy, requiring chronic dialysis, or permanently incontinent or bedridden patients, infection rates range as high as 60%.[3,4] Moreover, although infections can be caused by microbial colonization on either the device's outer or inner surface, the longer a device remains in the body, the greater the relative risk associated with the inner surface.

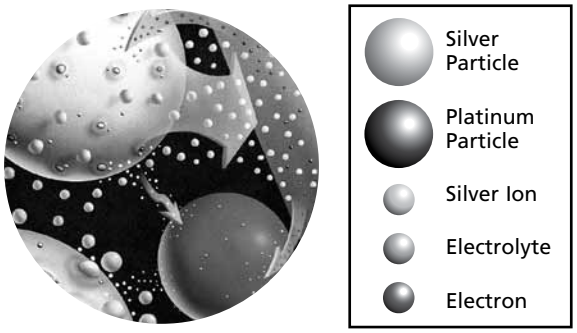
"In the United States, approximately two million patients per year develop nosocomial infections." [1,2]

Since medical device infection complications such as bacteremia (bacteria in the bloodstream) have significant morbidity and mortality and can cost from $6,000 to as much as $40,000 per patient to treat, the benefit of having medical devices which resist infection is clear.[2,5,6] One method of creating such devices would be to make them out of polymers which themselves are antimicrobial. Oligodynamic iontophoretic polymers hold forth this promise. These polymers can provide resistance to microbial colonization on and surrounding devices by releasing minute amounts of antimicrobial metal ions directly from the material.

History and Antimicrobial Benefits of Silver

Materials, and in particular metals, that are antimicrobial in minute amounts are called oligodynamic. One of the most potent of these is silver, and the antimicrobial form is silver ions. The microbicidal effects involve both altering the function of the cell membrane and linking to the cell's DNA, disrupting cell reproduction. The bactericidal action of silver ions is effective against a broad spectrum of bacteria, including the common strains which cause infection and the more virulent antibiotic-resistant strains.[7] Silver ions have also been shown to be fungicidal. Moreover, when silver ions are used in the minute concentrations required to kill or stem the growth of bacteria and fungi, they have not shown any detrimental effect on normal mammalian cells.[11]

Silver has been in medical use for decades and was used in systemic drugs before the advent of antibiotics. Today, silver is used routinely in antibacterial salves, such as silver sulfadiazine, and silver nitrate is put into the eyes of newborns to prevent infection. Several medical devices which use either silver nitrate or metallic silver are currently on the market.



Body fluids interact with silver and platinum particles in the material, causing a release of silver ions.

The most notable of these are a long-term, tunneled central venous catheter, two wound dressings and a urinary drainage catheter. Clinical studies support lower infection rates with these products compared to their non-antimicrobial counterparts. However, the silver technologies of these products have two competing drawbacks. Either the silver ions are released rapidly for only a short period of time, making the technology unsuitable for a product implanted for more than a few days, or only a very small amount of silver ions are released from a metallic silver coating, significantly limiting the potential effectiveness.

What Is Oligodynamic Iontophoresis and How Is It Effective?

One research path from the 1970s onward has been directed toward improving the utility of oligodynamic metals by electrically injecting the metal ions into solution. This process, known as oligodynamic iontophoresis, has been shown to reduce bacterial colonization fifteen to one-hundred fold in benchtop and animal experiments.[8-12] For example, if two electrodes made of silver are introduced into a conductive medium and an electrical potential is applied across the electrodes, silver ions are driven into solution, creating the microbicidal effect. The current required to safely drive a sufficient amount of silver ions into solution to control microbial growth is in the range of 1 to 400 microAmperes. This current range does not cause localized cell necrosis and it is below the sensory or pain threshold.

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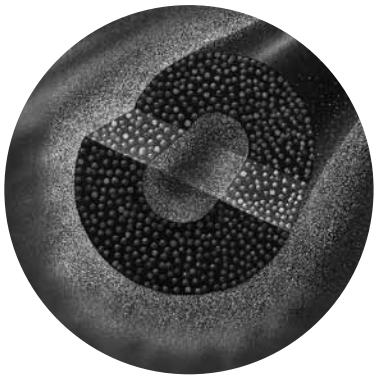
If two dissimilar metal electrodes, such as silver and platinum, are placed in a conductive fluid, no applied electric potential or current is required to release the silver ions. The dissimilar metals provide the necessary potential by classic oxidation-reduction reactions. The silver ions are released, as opposed to the platinum, because the silver is lower on the electrochemical potential scale. Common uses of this phenomenon include standard battery chemistry, "sacrificial electrodes" on boat hulls to prevent the rusting of propeller parts, and electroless metal plating. So-called iontophoretic polymers are designed to release silver ions when wet with body fluids by combining silver and platinum powders in the polymer composition. When the composite material is placed in contact with or immersed in a fluid that is electrolytic, such as saline, blood, drug preparations or urine, the metal powders become an array of small electrodes. Specifically, each metal powder granule embedded in the base material that makes contact with the electrolytic fluid becomes either an anode or a cathode.

One additional component is needed to allow the reactions to continue and the silver ions to be released over the long term. In order that no charge buildup occur on the metal powders in the polymer, an electrically conductive path between the silver and platinum particles needs to be established. This is done by also adding carbon to the polymer compound, so as to make the polymer conductive. The amount of carbon, metal powders, their ratios, their particle sizes and the permeability of the polymer composition all contribute to determining the rate of the silver ion release from the material and the longevity of the effect. For polymers used in medical devices, these parameters are adjusted to make the material a safe and effective antimicrobial for the length of the intended use of the device.[13]



Cross section of catheter shows active release of silver ions from all catheter surfaces and into the surrounding environment, providing antimicrobial protection.

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Antimicrobial activity on the Oligon surface and inner lumens of the catheter during handling and placement has been demonstrated through *in vitro* testing against organisms commonly associated with nosocomial infections. The activity of the antimicrobial agents is localized at the catheter surfaces and is not intended for treatment of systemic infections.

In vitro testing demonstrated that the Oligon material provided broad spectrum effectiveness (≥ 3 log reduction from initial concentration within 48 hours) against the organisms tested: *Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae, Enterococcus faecalis, Candida albicans, Escherichia coli, Serratia marcescens, Acinetobacter calcoaceticus, Corynebacterium diptheriae, Enterobacter aerogenes, GMRSa* and *Pseudomonas aeruginosa*. The impact of Oligon material on infection rates has not been demonstrated.

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