BioInteractions

Advancing Healthcare Through Innovation™

Avert™

Surface Active Antimicrobial Coating

BioInteractions has developed the dual functional **Avert™ Surface Active Antimicrobial Coating**, specifically designed to reduce the incidence of device related infections.

Overview

Implantable medical devices are prone to suffer from bacterial colonisation, which can lead to device related infection and result in morbidity with significant mortality in certain unfavourable cases.

Device related infections are common to devices such as:

1) Central venous lines – *linked with blood stream infections*.

2) Ventilators - *linked to pneumonia-type infections*.

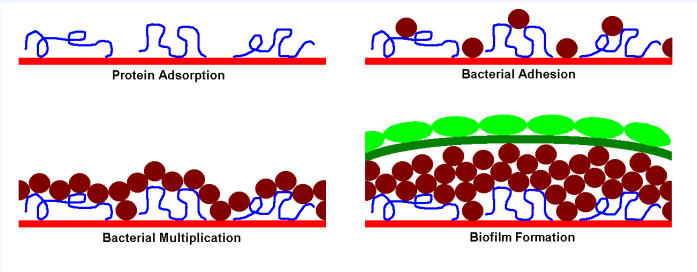
3) Catheters- *linked to blood and urinary tract infections.*

4) Vascular grafts.

The Centres for Disease Control and Prevention (CDCP) have reported that the average rate of central venous catheter associated blood stream infections is in the order of 80,000 occurrences each year in the intensive care unit (ICU). It is estimated that this costs (per infection) in the region of $34,000 to $56,000 – the average cost for caring for patients in the U.S. is believed to range from $300 million to $2 billion.

The Clinical Problem

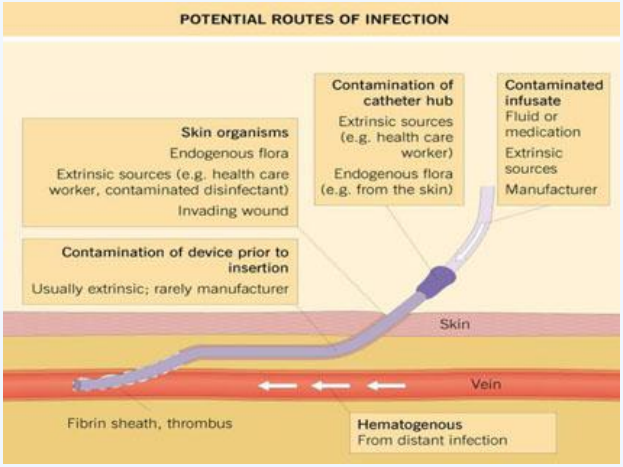
The first step towards this complex problem is the adhesion of bacteria, which can occur on the device itself or on proteins that have adsorbed onto the device. The protein layer provides a suitable breeding ground for the bacteria, leading to colonisation and biofilm formation.



The route to biofilm formation

The infecting bacteria release exopolysaccharides forming a mesh of biofilm, which covers tissue and the medical device. The bacteria contained/protected by the biofilm rapidly divide and extend along the surface of the device.

The bacteria within the biofilm can release into the blood stream and are able to bind to non-colonised surfaces, thereby spreading the infection.



Potential routes of infection.

Once a biofilm has been established it is extremely difficult for antibiotics to penetrate and a far higher dose is often required to kill a biofilm when compared with individual colonies.

Preventative Measures

There have been various attempts to develop antimicrobial coatings for medical devices, which have mainly relied on the release of active agents such as silver, antibiotics and disinfectants. These infection resistant agents have typically been adsorbed into a hydrophilic coating or impregnated into the polymer structure. Simplistically, the mechanism is the release of the agent from the surface of the device and into the bacteria, whereby inhibition or interruption of the various synthetic pathways is achieved.

BioInteractions Ltd.
Science and Technology Centre
Earley Gate, Whiteknights Road
Reading, Berkshire, RG6 6BZ
United Kingdom

T +44 (0)118 935 7000
F +44 (0)118 926 7917
E general@biointeractions.com

www.biointeractions.com

ISO 9001:2008
FS 531243

BioInteractions

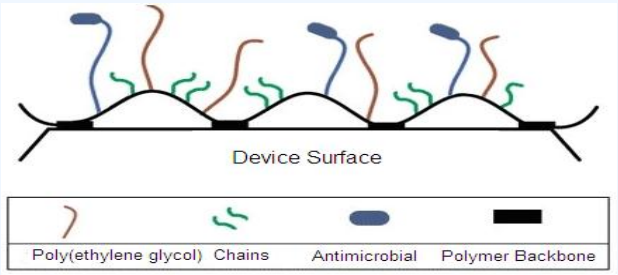
Advancing Healthcare Through Innovation™

A major constraint of these methods, for the prevention of infection, is that they lose their potency over time and therefore, their efficacy is somewhat short-lived. Another constraint is that the bulk distribution of the active ingredient is not stable and in certain cases, it is able to permeate from the device into body tissue or fluid and cause harmful side-effects.

In order to overcome these constraints, BioInteractions has developed a dual functional antimicrobial coating, the Avert™ Surface Active Antimicrobial Coating.

Avert™ Surface Active Antimicrobial Coating

Avert™ has been specifically designed to provide the best in antimicrobial technology. This is achieved through a dual functional system, which not only prevents protein deposition onto the device surface, but also provides long-term antimicrobial activity to significantly 'avert' biofilm formation.



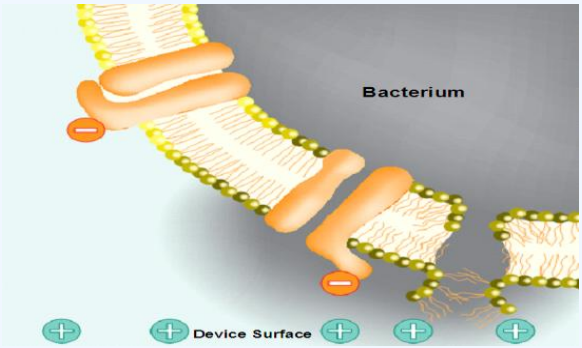
Schematic representation of Avert™.

The prevention of protein (and platelet) adhesion onto the device surface is achieved through the incorporation of highly hydrophilic, non-thrombogenic, poly(ethylene glycol) (PEG) functionalities. By minimising the adhesion of proteins, the breeding ground on which bacteria can grow is also minimised, thereby reducing the chance for bacterial colonisation. In addition, PEG moieties reduce platelet activation, thus minimising the chance of thrombus formation.

The active antimicrobial component of Avert™ is based on a biguanide functionality, which has long been employed for such applications and has been clinically tested. This active agent is stable and non-leaching and as such, is not flushed away from the surface of the device during use. This property of Avert™ is highly advantageous when compared to coatings that release the active agent, as long-term efficacy is maintained, whilst avoiding any adverse systemic reactions.

The antimicrobial activity is based on a 'contact-kill' mechanism, which results from excess positive charge.

As micro-organisms attempt to colonise on the device surface, the highly polarised coating causes the destruction of the lipid bilayer in the colonising cell, thereby leading to cell death.



Schematic representation of Avert™ mechanism of action.

This bifunctional approach to preventing biofilm formation ultimately reduces device related infections, a result that has been demonstrated on central venous catheters.

Performance Evaluation

It is imperative that the antimicrobial agent on the medical device has a broad spectrum of efficacy in order to prevent device related infections. This is becoming increasingly important as bacterial strains are progressively adapting to antibiotic treatment and becoming more resistant.

Studies on Avert™ have demonstrated a vast spectrum of efficacy against a number of different bacterial strains, including gram-positive, gram-negative (*Pseudomonas*

BioInteractions Ltd.
Science and Technology Centre
Earley Gate, Whiteknights Road
Reading, Berkshire, RG6 6BZ
United Kingdom

T +44 (0)118 935 7000
F +44 (0)118 926 7917
E general@biointeractions.com

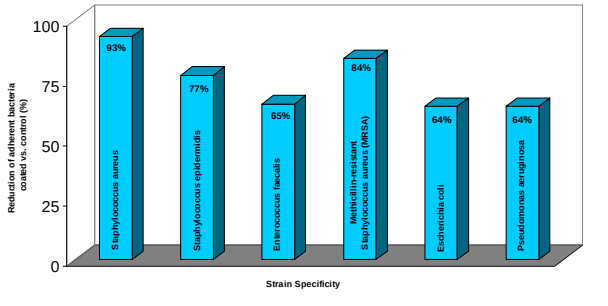
www.biointeractions.com

ISO 9001:2008
FS 531243

BioInteractions

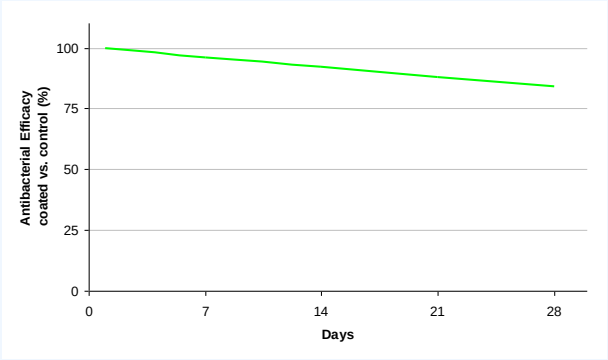
Advancing Healthcare Through Innovation™

aeruginosa, *Escherichia coli*) and more specifically MRSA (methicillin-resistant *Staphylococcus aureus*).



Spectrum of activity for Avert™.

In addition to a broad spectrum of efficacy, Avert™ has also demonstrated long term protection against bacterial colonisation, with less than a 20% reduction in activity after 4 weeks.



The efficacy of Avert™ is maintained for more than 4 weeks.

The coating process developed allows for both external and internal surfaces of a device to be coated, e.g. catheter, therefore increasing the overall efficacy of the device. In addition, a range of medical devices (substrates) can be coated in a cost-effective manner. The hydrophilic nature of the coating promotes laminar flow, making it ideally suited for catheter applications.

Summary

The Avert™ Surface Active Antimicrobial Coating provides a bifunctional approach to preventing device related infections. The non-thrombogenic component prevents protein/platelet deposition and platelet activation and the antimicrobial system offers a broad spectrum of efficacy against a range of bacterial strains.

The stable, non-leaching active component provides superior long-term protection against infection, without the risk of any adverse systemic reactions.

The contact-kill mechanism significantly reduces bacterial colonisation and biofilm formation.

BioInteractions has established license agreements with major medical device manufacturers for the Avert™ coating, which include B. Braun.

We are committed to the advancement of healthcare through innovation and welcome interest in the Avert™ Surface Active Antimicrobial Coating.

BioInteractions Ltd.
Science and Technology Centre
Earley Gate, Whiteknights Road
Reading, Berkshire, RG6 6BZ
United Kingdom

T +44 (0)118 935 7000
F +44 (0)118 926 7917
E general@biointeractions.com

www.biointeractions.com

ISO 9001:2008
FS 531243