

Scientific

Drug Elution: Temperature Moderated – Collision Mediated Coating

The success of the drug eluting stent (DES) in reducing restenosis exemplifies the benefits of drug delivery coatings at implant surfaces. However many challenges related to coating platforms at medical device surfaces remain. Many of the limitations associated with realizing the full potential of localized drug delivery at implant surfaces are process related. For example the high temperature methods, such as plasma spray, used to deposit well adhered bio-active ceramic coatings at the surface of press fit-orthopedic implants preclude the concurrent deposition of therapeutics and polymers that improve elution profiles. It has also been established that noscomial infections are an issue of serious concern for pacemaker and defibrillators. Currently pacemakers are coated with bio-inert polymers such as parylene but a drug-eluting pacemaker has not been developed.

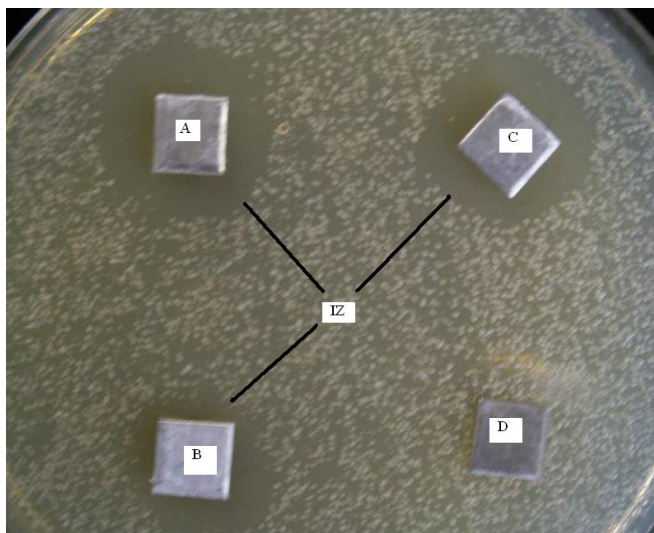


Fig. 1: Antimicrobial activity of TM-CMC deposited Hydroxyapatite/Vancomycin coatings A, B and C, demonstrating inhibition zones (IZ) as compared with the negative control, sample D.

HKPB Scientific has developed a new coating technology termed Temperature Moderated – Collision Mediated Coating (TM – CMC). HKPB believes that TM - CMC has the potential to solve biocompatibility and manufacturability issues, particularly those pertaining to drug elution, associated with coatings on medical devices. TM – CMC involves atomising a liquid based precursor coating composition to form an aerosol, which is directed to the surface of the substrate in conjunction with a stream of shot particles. The collision energy released by the impacting shot mediates the transformation of the precursor composition into a well-adhered coating in a one step process. The precursor composition can comprise polymer, solvent and therapeutic agents. No curing agents, cross linkers or other deleterious chemical agents are added to the precursor composition.

We present preliminary results that demonstrate the efficacy of TM - CMC for the formation of drug-eluting coatings. Our preliminary results demonstrate that thermally sensitive

therapeutic agents remain active and potent through the process presenting the possibility of coating a vast variety of bioactive coating compositions onto medical devices with a versatile, single-step, controllable process.

In TM – CMC it is the liquid component of the precursor composition protects the therapeutic agent from degradation as shown in fig. 1 where inhibition zones are observed around samples treated with TM – CMC relative to the negative control. In preliminary trials, see fig. 2, a drug loading comparable to that of the XIENCE V Everolimus Eluting Coronary Stent System (100 µg cm²) has been achieved.

HKPB believes that TM – CMC has many advantages which include:

- **Biocompatibility:** therapeutics can be evenly distributed throughout the coating as carrier matrix and therapeutics are concomitantly coated on the device.
- **Biocompatibility:** therapeutic and carrier matrix are not degraded using TM - CMC
- **Biocompatibility:** using TM – CMC the requirement for subsequent processing of the device is minimized reducing the opportunity for therapeutic degradation.
- **Biocompatibility:** deleterious chemicals are not included in the precursor composition.
- **Manufacturability:** single-step process reduces processing time, labour costs etc.
- **Manufacturability:** a low flow rate of precursor composition ensures minimal waste of expensive therapeutic agents.
- **Manufacturability:** TM – CMC combines two existing equipment platforms, shot peeners and atomizers that are readily automated in a manufacturing setting.

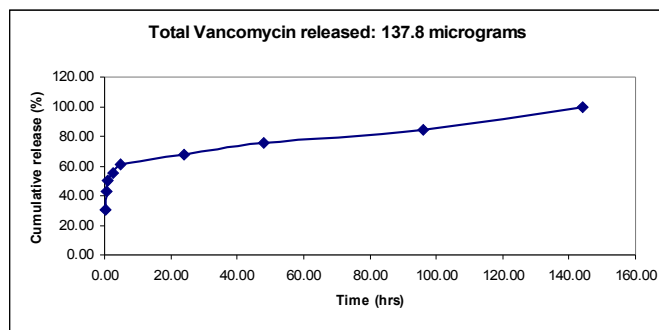


Fig. 2: Elution profile of vancomycin from the HA/Vancomycin coatings deposited with TM-CMC. Sample area is one cm square.

In summary the efficacy of a novel coating technology TM-CMC has been demonstrated: The process allows for the simultaneous deposition of therapeutics with a variety of carrier materials both in a single step. The process uses well established equipment platform allows the coating of therapeutics and other thermally sensitive materials without adversely affecting their activity.