Drug delivery to the vessel wall: Coated balloons and the role of the excipient

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BioInterface 2015
- Balloon angioplasty (POBA)
  - >4 million patients treated annually
  - Dissections
  - Elastic recoil
  - Restenosis caused by cellular proliferation
- Bare metal stents (BMS)
  - Decreased dissections and elastic recoil
  - Stent thrombosis
  - Intimal hyperplasia (leading to in-stent restenosis)
  - Not a viable option in some sites
- Drug eluting stents (DES)
  - Decreased cellular proliferation; less in-stent restenosis
  - Late stent thrombosis
- Drug coated balloons (DCB)
  - Effective treatment without long-term implant
- Angioplasty balloon coated with anti-restenotic drug
  - Paclitaxel (most common)
  - Sirolimus (in development)

- Used to treat arterial stenosis
  - Coronary
  - Peripheral

- Lack of implant favors DCB where stenting is difficult or ineffective
Durable coating retains drug during transit and upon inflation

Minimal Drug Particulates
Drug is deposited on vessel wall while unused drug is retained on the balloon
DISPOSITION OF DEVICE DRUG LOAD

Actual DCB Performance (current generation)
- Lost During Procedure
- Retained on Balloon
- Transferred to Vessel

Ideal DCB Performance (future generation)
Attributes of an Ideal DCB Coating

- Facilitate drug retention on balloon during transit
- Effectively release drug from the balloon to the target lesion site
- Provide adhesion of the drug to the vessel wall
- Drug retention upon restoration blood-flow; formation of depot for long-term release
- Facilitate drug uptake by tissue

Excipients can play an important role in achieving these attributes
Hypotheses for in-vitro drug adhesion test system

- Matrigel® coatings can mimic the denuded arterial lumen surface
- Adhesion of drug particles to Matrigel can form a model to elucidate the mechanisms of excipient-mediated drug transfer and retention in artery walls
**In vitro test model**
- Suspensions of paclitaxel alone and with excipients
- Measure deposition on to Matrigel® coated surface

**In vivo test model**
- Balloons coated with paclitaxel and excipient
- Assess
  - Drug content in tissue (pharmacokinetics)
  - Physical disposition of drug (immunostaining & visualization)
  - Biological effect (histology, CVPath)
B. Braun SeQuent Please DCB

Early-generation DCB
Crystalline paclitaxel
Iopromide (contrast) excipient
SurModics SurVeil™ DCB

Development-stage DCB
Crystalline paclitaxel
Proprietary excipient
Visualization of Ptx on Matrigel® with HCAEC cells

SurModics Excipient: nonspecific binding

Cells (dark)  Excipient (bright)

Iopromide: cell-specific binding

Cells (dark)  Excipient (bright)

Results – In vitro adhesion assays

Excipients promote increased drug adhesion to cells
SurModics excipient promotes adhesion to ECM mimic, independent of cells
Excipients promote drug deposition in the tissue
SurModics excipient trends toward higher deposition
Visualized by immunostaining 24 hours post-treatment

Excipients promote adhesion to the vessel wall
Transfer with SurModics excipient appears more robust
Results: Bioeffect in vivo

Histology from CVPath Institute
Tissue stained with Movat Pentachrome, 28-days post-treatment

Excipients lead to increased biological effect
SurModics excipient leads to more uniform biological effect

SurModics Excipient  Iopromide (B. Braun)  Uncoated (POBA)

Blue/Green Color = Drug Effect
Results: Safety response and bioeffect *in vivo*

**Primary markers of drug effect**

- **SurModics**
- **Excipient-Only**
- **B. Braun**
- **Uncoated**

**Score (0 - 4 scale)**

**Exciptents lead to increased biological effect**

**SurModics excipient trends toward stronger effect**

Scores provided by CVPath Institute.
Simple bench-top adhesion assay showed suitability for screening DCB formulations

- Drug adhesion *in vitro* showed patterns similar to those observed by staining *in vivo*
- Transfer *in vitro* trended similar to transfer *in vivo*

Excipients in general improve DCB formulations

- Increase drug transfer to ECM mimics and actual tissue
- Enhance retention of drug at treatment site
- May enhance transfer to cells (function of excipient)

SurModics excipient further enhances DCB formulations

- Significant increase in drug adhesion to ECM mimics and cell layers *in vitro*
- Increased drug transfer from a DCB *in vivo* compared to a commercially-available DCB formulation
SurModics SurVeil™ DCB

0.035” PTA platform
4–7 mm x 40–150 mm

Shaft coating
Serene™ hydrophilic coating

Proprietary PhotoLink® basecoat

Uniform drug topcoat
Paclitaxel + proprietary excipient
2 µg/mm² drug load
360° coating coverage

This product is not commercially available

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Comparison to Competitive DCBs

SurModics SurVeil DCB

Competitive DCB #1

Competitive DCB #2
SurVeil DCB Delivers More Drug than Competitive DCB

2 µg/mm²

3.5 µg/mm²
Robust Biological Drug Effect at 28 days

Competitive DCB

SurVeil DCB

POBA Control
Thank you