PREDNISOLONE ACETATE-ELUTING NOVEL BIODEGRADABLE VASCULAR STENTS FOR IMPLANTATION

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Coronary Artery Disease (CAD)

- CAD is the leading cause of death in the Western World for men and women.

- CAD is narrowing of the small blood vessels that supply blood and oxygen to the heart (coronary arteries).

- Coronary disease usually results from the build-up of fatty material and lesions called plaque.
Atherosclerosis

• Atherosclerosis is an intimal disease which fatty material collects along the walls of arteries.

• *stenosis*

• As the coronary arteries narrow, the flow of blood to the heart can slow or stop.
Treatment

• For overcome this problem Percutaneous Transluminal Coronary Angioplasty (PTCA) was introduced in the last period of 70’s and has become a common method for treating coronary arterial stenosis.

• A balloon is used to open narrowed or blocked blood vessels of the heart coronary arteries
• PTCA with a balloon has a major limitation called **restenosis** which is the maladaptive response of the coronary artery to injury and characterized by re-narrowing of the artery after the angioplasty.

• Restenosis can be described currently as consisting of two components: first called “elastic recoil” and the second component called “neointimal hyperplasia”
Stents

• Stent is a small, metal tube that is inserted permanently into an artery.

• Acts as a scaffold, remaining in place permanently to help keep the artery open.
• Restenosis rates in patients who have stents implanted are 20–40%.

**In-Stent restenosis**

Metallic bare stents - Not Enough
Drug Eluting Stents (DES)

• DES provide both mechanical scaffolding and local delivery of a pharmacological agent.

• DES reduced the in-stent restenosis rates

• The need of a stent? Safety?

• Biodegradable Polymeric Stents
Aim

• Prednisolone Acetate (PA) – model drug

• Biodegradable Stent Formulations;
  - PA was incorporated into the film based polymeric biodegradable stents to provide controlled local release of the drug during the mechanical support phase
  - Also PA containing spray-dried chitosan microspheres were incorporated into the stents
Chitosan Microspheres

- $2^2$ Factorial design was used and 8 microsphere formulations were developed and characterized.

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Polymer Type</th>
<th>Polymer Concentration (%)</th>
<th>Targeted Encapsulation Amount (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL0,5PA10</td>
<td>Low $M_w$</td>
<td>0,5</td>
<td>10</td>
</tr>
<tr>
<td>CM1PA20</td>
<td>Medium $M_w$</td>
<td>1</td>
<td>20</td>
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</table>
Mean Particle Size: $10.41 \pm 0.03 \, \mu m$

In vitro release time: 11 Days

(100% Cumulative PA Release)
Preparation of Biodegradable Polymeric Stents

- PLGA (75:25)
- PLGA (50:50)

Solution-Casting Method

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<th>PA or Microspheres</th>
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<tbody>
<tr>
<td>S1</td>
<td>PLGA (75:25)</td>
<td>PA Incorporated</td>
</tr>
<tr>
<td>S2</td>
<td>PLGA (75:25)</td>
<td>Microsphere Incorporated</td>
</tr>
<tr>
<td>S3</td>
<td>PLGA (50:50)</td>
<td>PA Incorporated</td>
</tr>
<tr>
<td>S4</td>
<td>PLGA (50:50)</td>
<td>Microsphere Incorporated</td>
</tr>
</tbody>
</table>
PLGA + PEG 4000
Dichloromethane
+ 4°C
Prednisolone acetate/
Microspheres
Surface and Morphology of the Stents

PA incorporated (a) and PA containing chitosan microspheres incorporated (b) PLGA (75:25) stents, PA incorporated (c) and PA containing chitosan microspheres incorporated (d) PLGA (50:50) stents
The polymer wall thickness was

- 136.5 ± 5 µm - PLGA (75:25) stents
- 109 ± 8 µm - PLGA (50:50) stents
PLGA (75:25) stents

(a) PA incorporated

(b) PA containing chitosan microspheres incorporated
PA incorporated (a)  PA containing chitosan microspheres incorporated (b)

PLGA (50:50) stents
In Vitro Release

- 2 mL of 0.5% (w/v) sodium lauryl sulfate and 0.05% (w/v) sodium azide containing Phosphate Buffered Saline (PBS) pH 7.4

- The stents were shaken in Eppendorf tubes in a horizontal shaker at 50 rpm, at 37°C
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Conclusion

• By using biodegradable PLGA (75:25) and PLGA (50:50) polymers, cardiovascular stents were manufactured and characterized.

• Different release profiles were obtained with using different polymers.
• The released amount of PA from the PLGA (50:50) stents (with PA only or PA containing microspheres) was always higher.

• PA release from the stents which contain chitosan microspheres was slower than the only PA incorporated ones. Adding microspheres instead of drug only, was extended the release.

• The stents formulated with PLGA (75:25) polymers were considered to be more promising.
Thank You

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