Figure 1

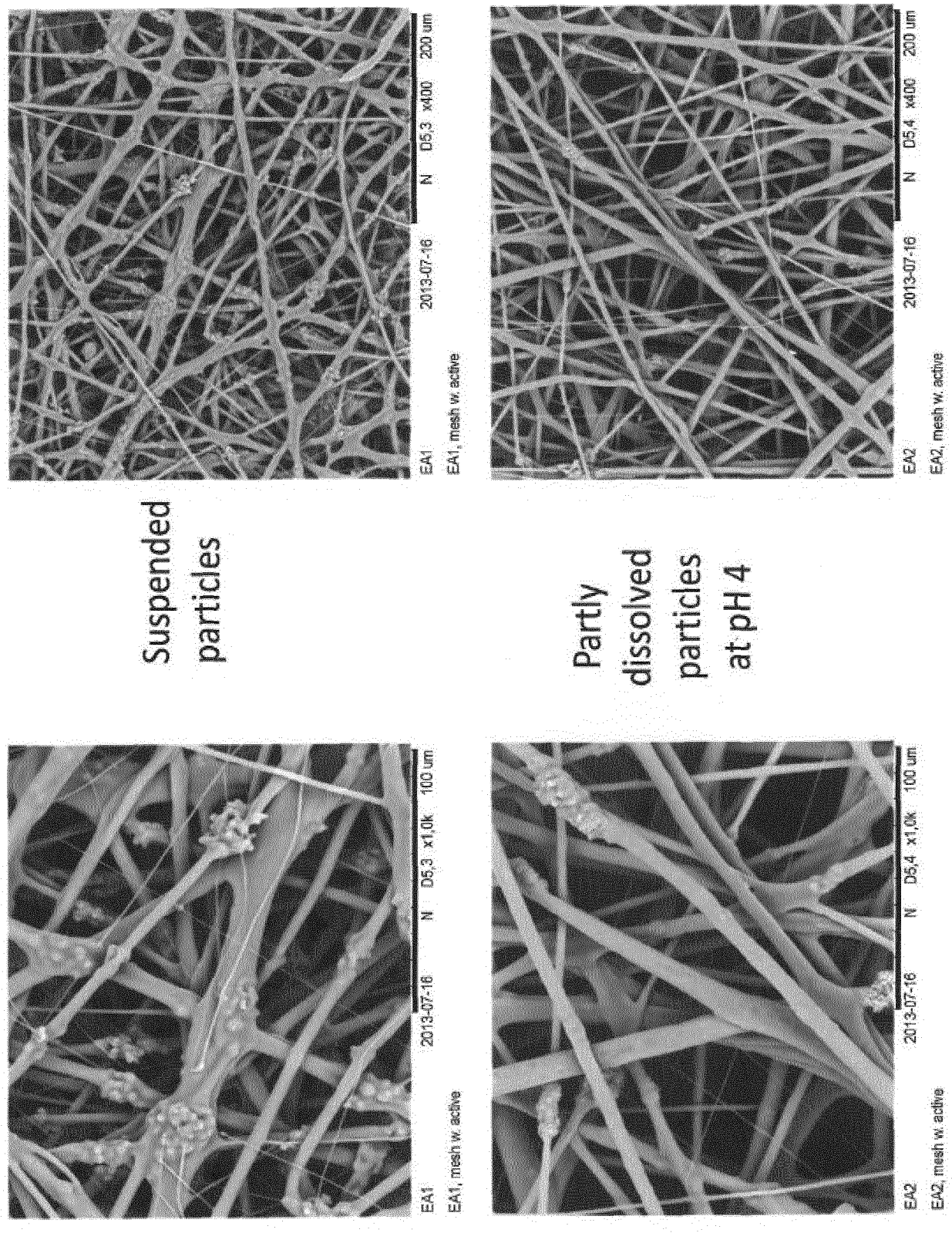

Suspended particles
Partly dissolved particles at pH 4
EA1
EA1, mesh w. active
2013-07-16
N
D5,3
x400
200 um
EA2
EA2, mesh w. active
D5,4
x1,0k
100 um

Figure 2

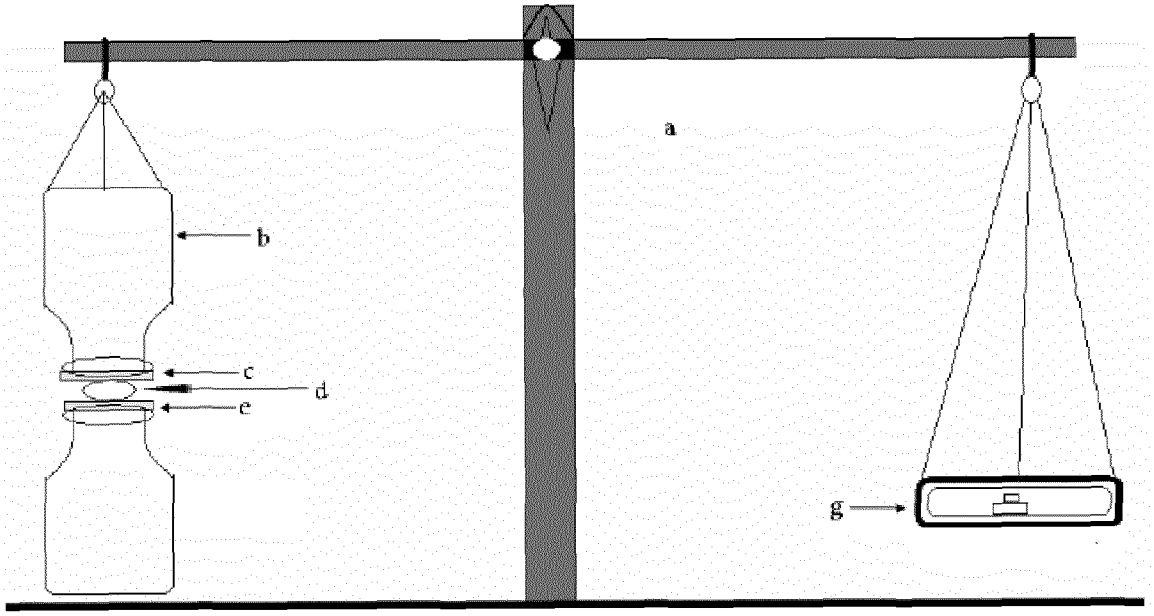


Figure 3

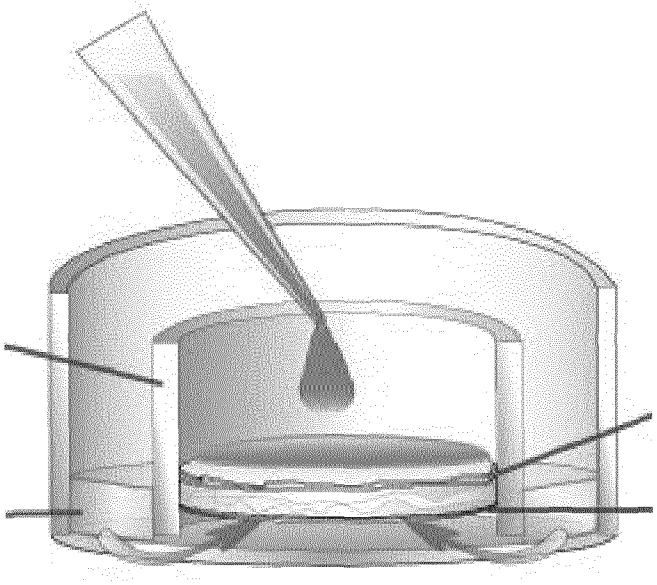

Cell culture insert
Media
Buccal human keratinocytes differentiated morphology with barrier function
Microporous membrane

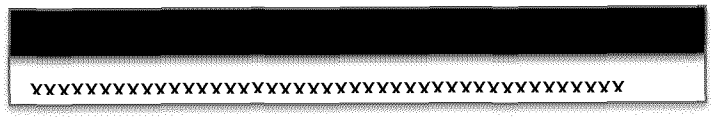
Figure 4

Different release geometry from different sheets



Drug + Bioadhesive + Hydrophilic polymer

Conventional sheet – Bidirectional drug release



Water-impermeable spun or coating

Drug + Bioadhesive + Hydrophilic polymer

Bilayer sheet – Undirectional drug release



Water-impermeable spun or coating

Drug + Hydrophilic polymer

Bioadhesive layer

Triple sheet – unidirectional drug release



Drug + Hydrophilic polymer

Bioadhesive layer

Bilayer sheet – Bidirectional release

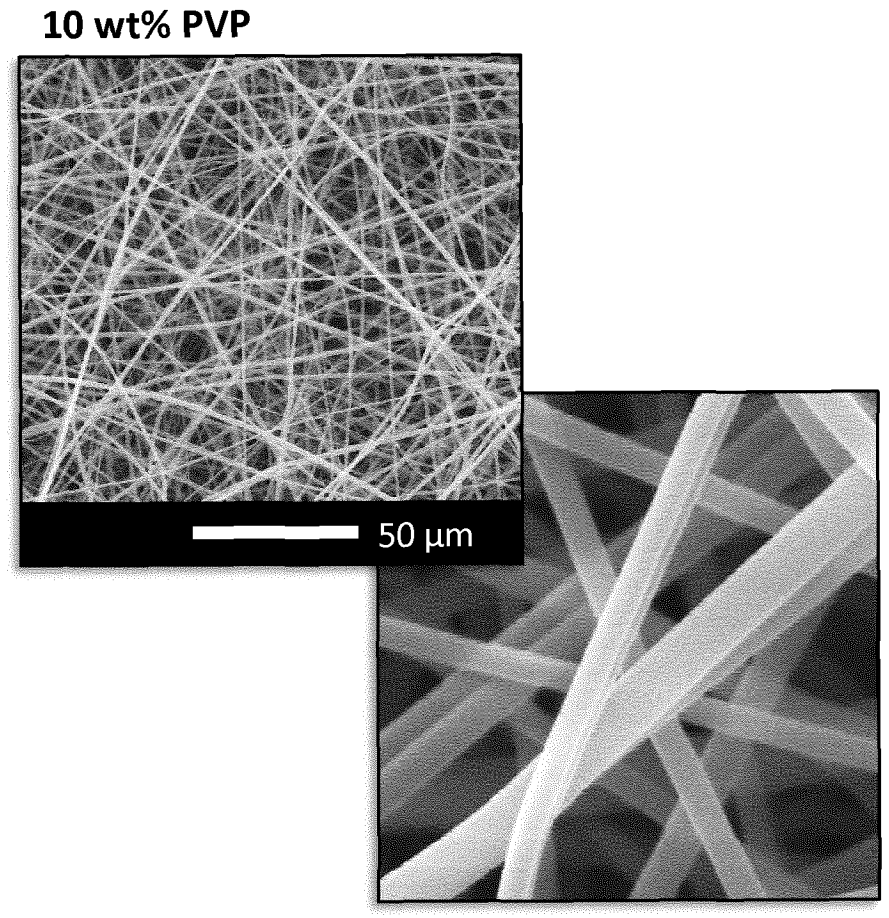
# Fabrication of drug-delivery layer

## Optimisation of electrospinning method

<u>Manufacturing method</u>

Based on protocol:

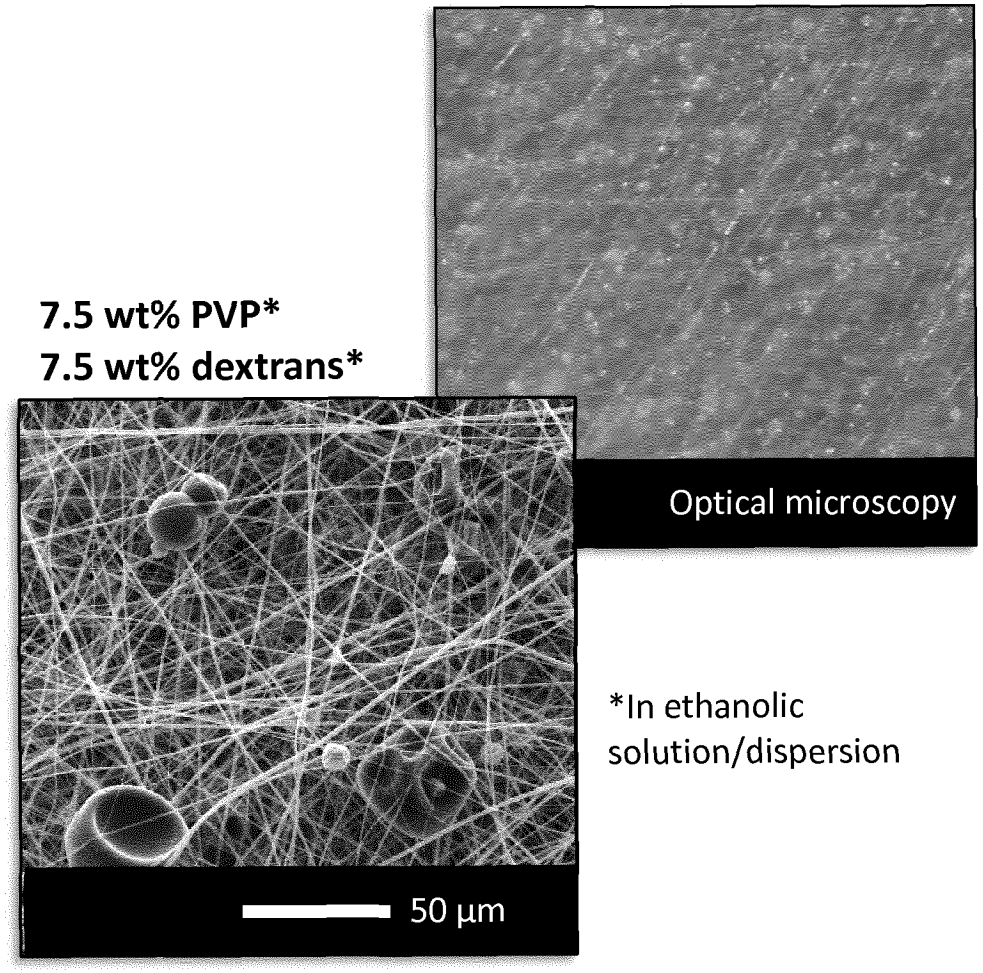
- 10 wt% PVP (Kollidon 90F, BASF) in ethanol
- Solution volume = 2 mL
- Distance = 17 cm
- Voltage = 14 kV
- Flow rate = 10 ml $h^{-1}$
- 20 gauge needle
- Ambient temperature and



# Fabrication of drug-delivery layer

## Addition of dextrans to composition

- 0-15 wt% of dextrans added to PVP solution
- Various Mw
  - ✓T500 = 500,000
  - ✓T2000 = 2,000,000
  - ✓Mixture of both
- Variable particle size
  - ✓<45 µm particle size




*In ethanolic solution/dispersion

Figure 7

# Fabrication of drug-delivery layer

## Fabrication of dyed materials

- Alcian blue 8GX (Merck)
  - ✓To observe gel in bioadhesion studies
  - ✓Powdered
  - ✓Dissolves in ethanol

- Demonstrates potential of electrospun materials to encapsulate and deliver dissolved substances
  - ✓Ethanol-soluble drugs

**10 wt% PVP + 1 w/v % alcian blue in ethanol solution**

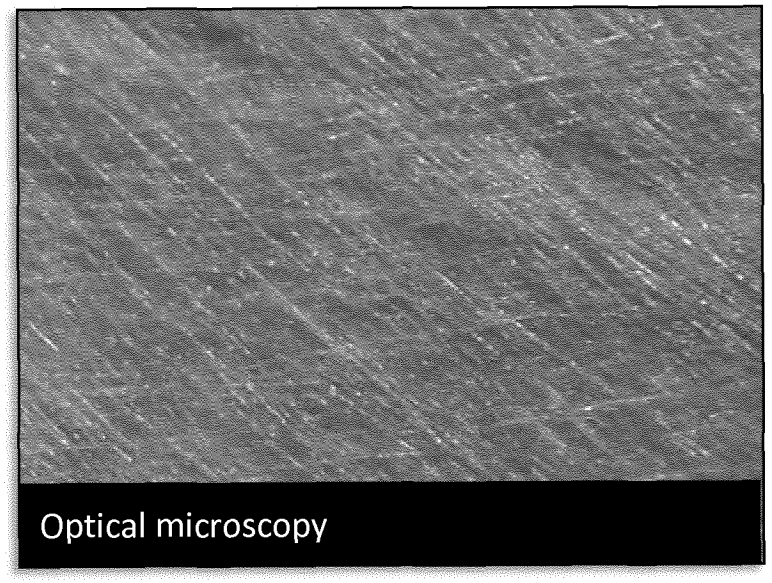


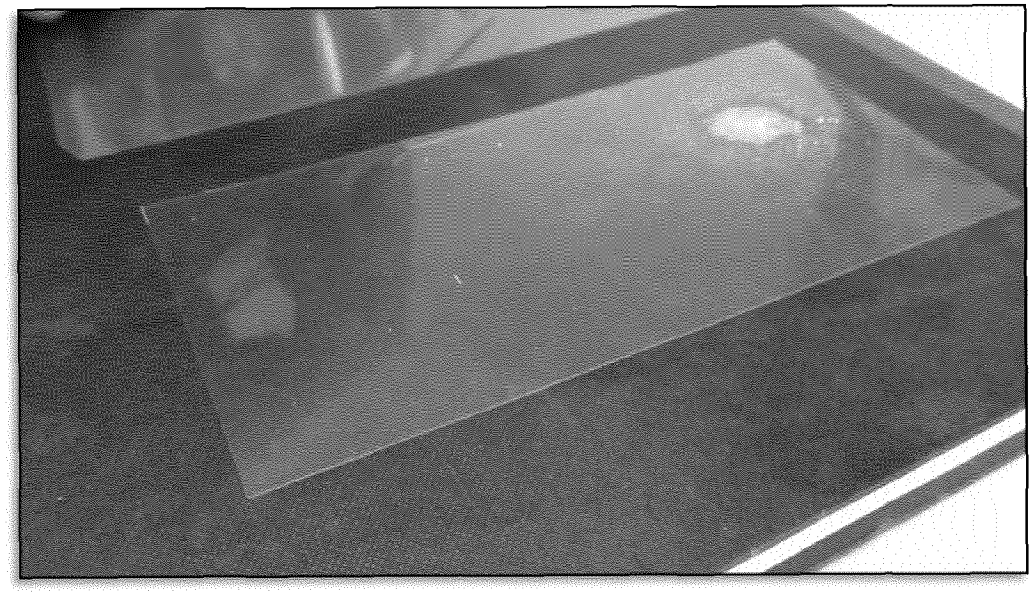
Figure 8

# Fabrication of drug-delivery layer

## Solubility of electrospun materials

- Fast dissolution of PVP in water
  - ✓ < 1 second
- Gel with bioadhesive properties
- Rapid drug release

**Solubility test on artifical saliva**



**Bioadhesiveness test of PVP/PCL on pig mucosa**

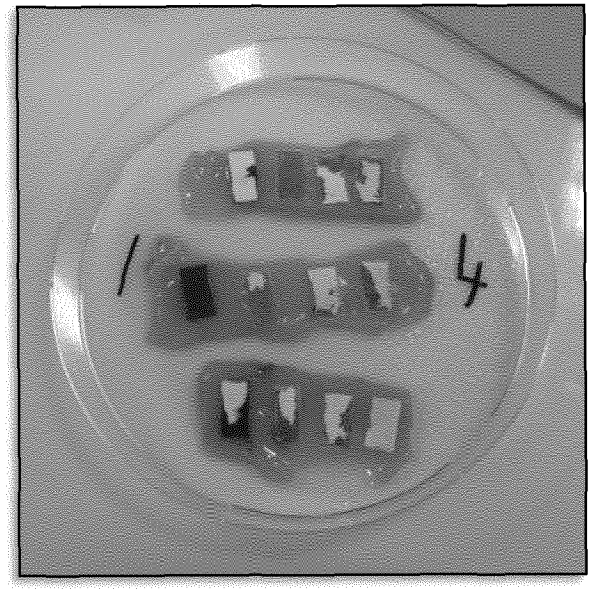


Figure 9

# Fabrication of dual layer system

## Electrospinning of backing layer

- Attachment through thermal treatment
  - ✓PCL melts at lower temperature than PVP (i.e. 60°C vs >180°C)

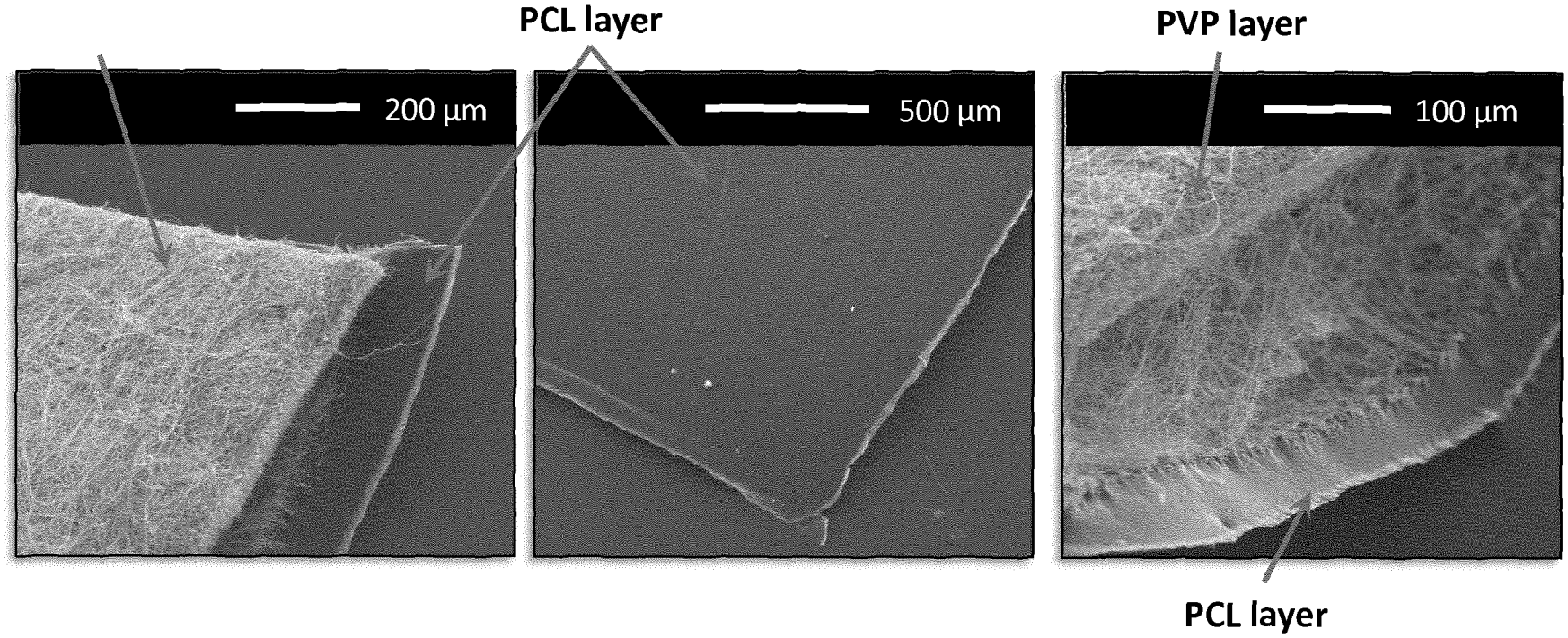


Figure 10

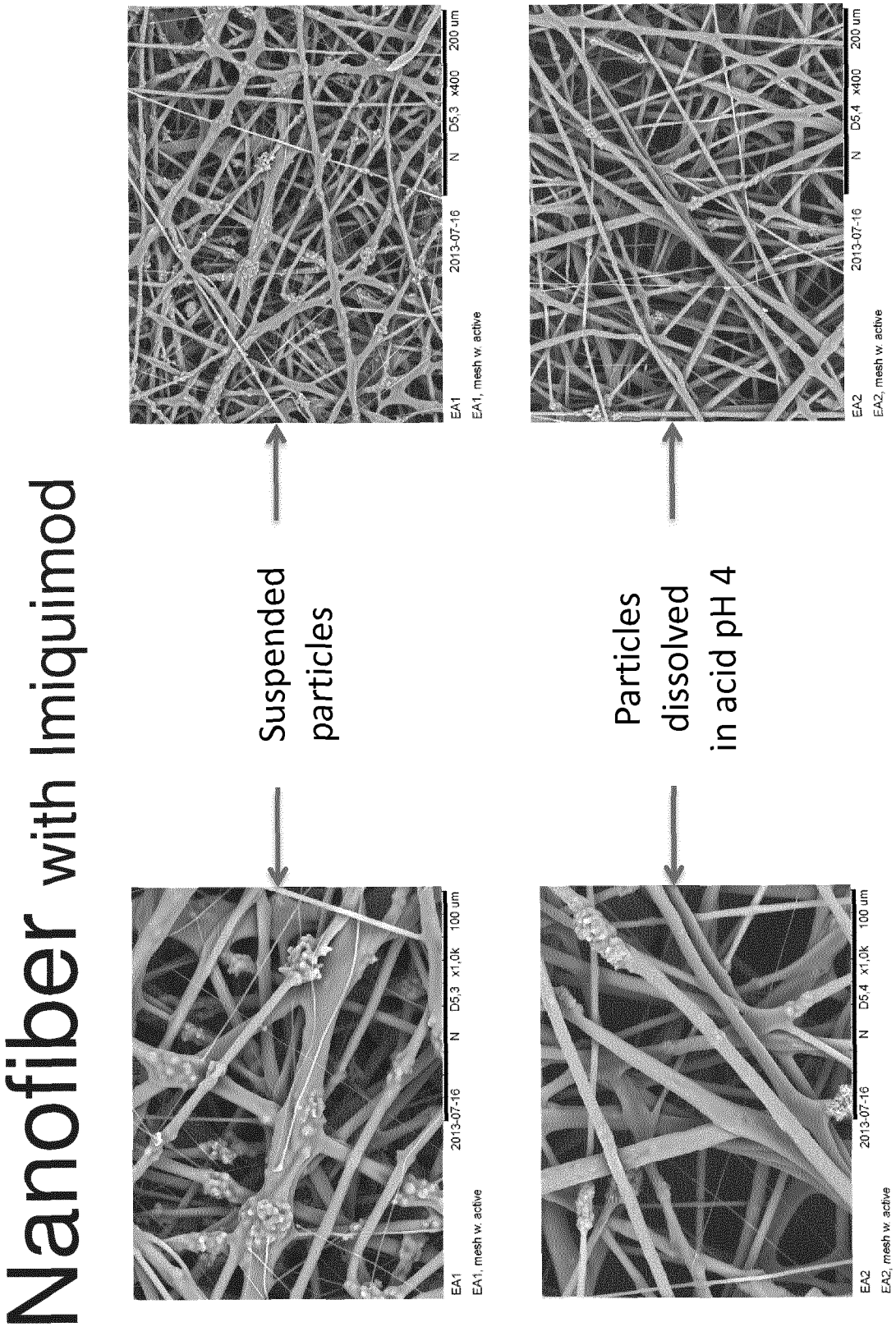
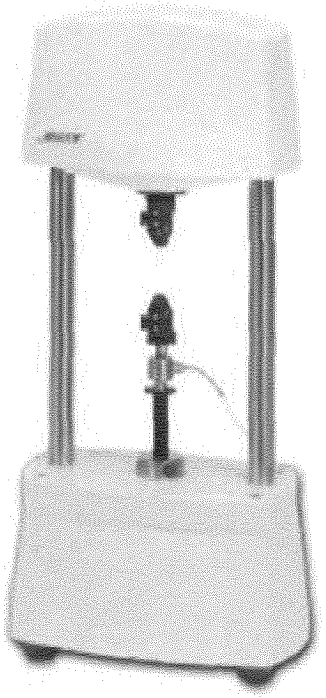
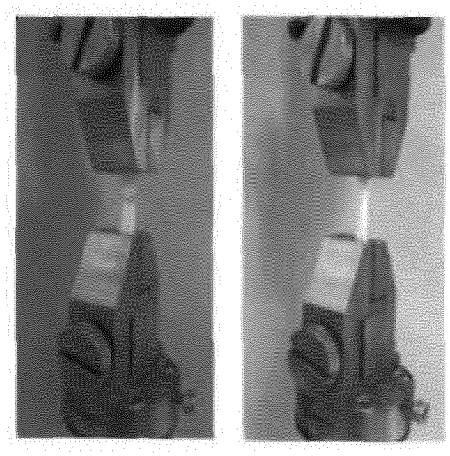

Nanofiber with Imiquimod
Suspended particles
Particles dissolved in acid pH 4
EA1
EA1, mesh w. active
2013-07-16
D5,3 x1,0k 100 um
EA2
EA2, mesh w. active
D5,4 x1,0k 100 um
D5,3 x400 200 um
D5,4 x400 200 um

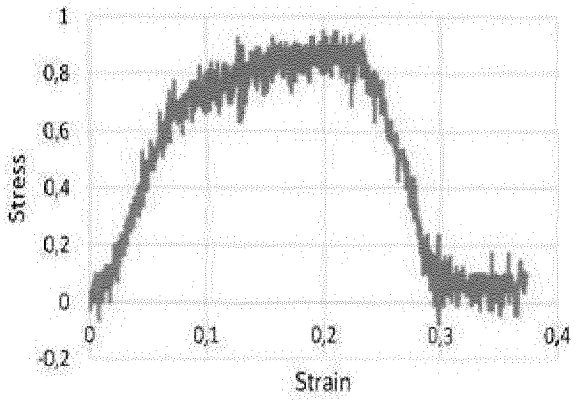
Figure 11

# Tensile Testing of Rivelin Patch

- Bose Electroforce 3100
- 9mm original length between clamps
- Displacement of 0.02mm/s to 6mm
- Young's modulus – measure of stiffness
- % elongation
- Ultimate tensile strength

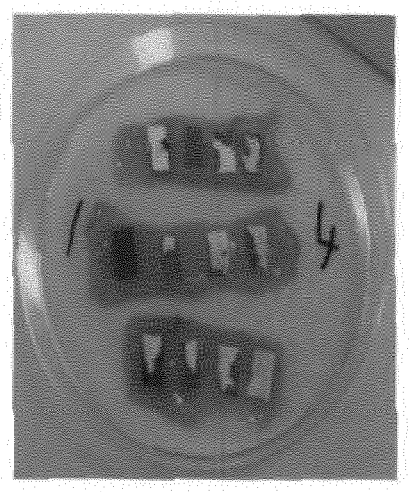






# Residence Time of Rivelin Patch on Porcine Oral Mucosa

- Porcine mucosa adherence to petri dish using cyanoacrylate glue
- Saliva aerosol onto surface of porcine mucosa
- 5 second applied force
- Mucosa sub-merged in PBS (simulated saliva)
- 30-50rpm mechanical stirring
- Residence time = time taken for patch detachment



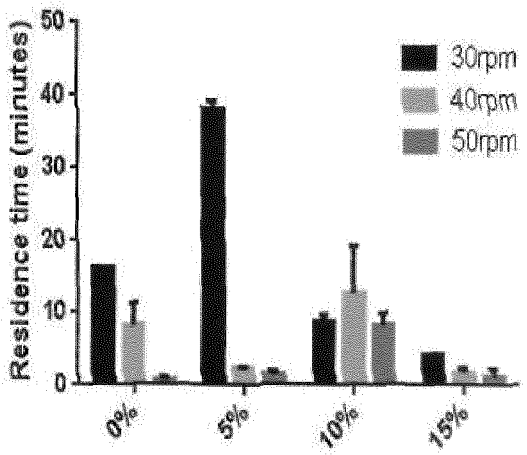


Figure 13

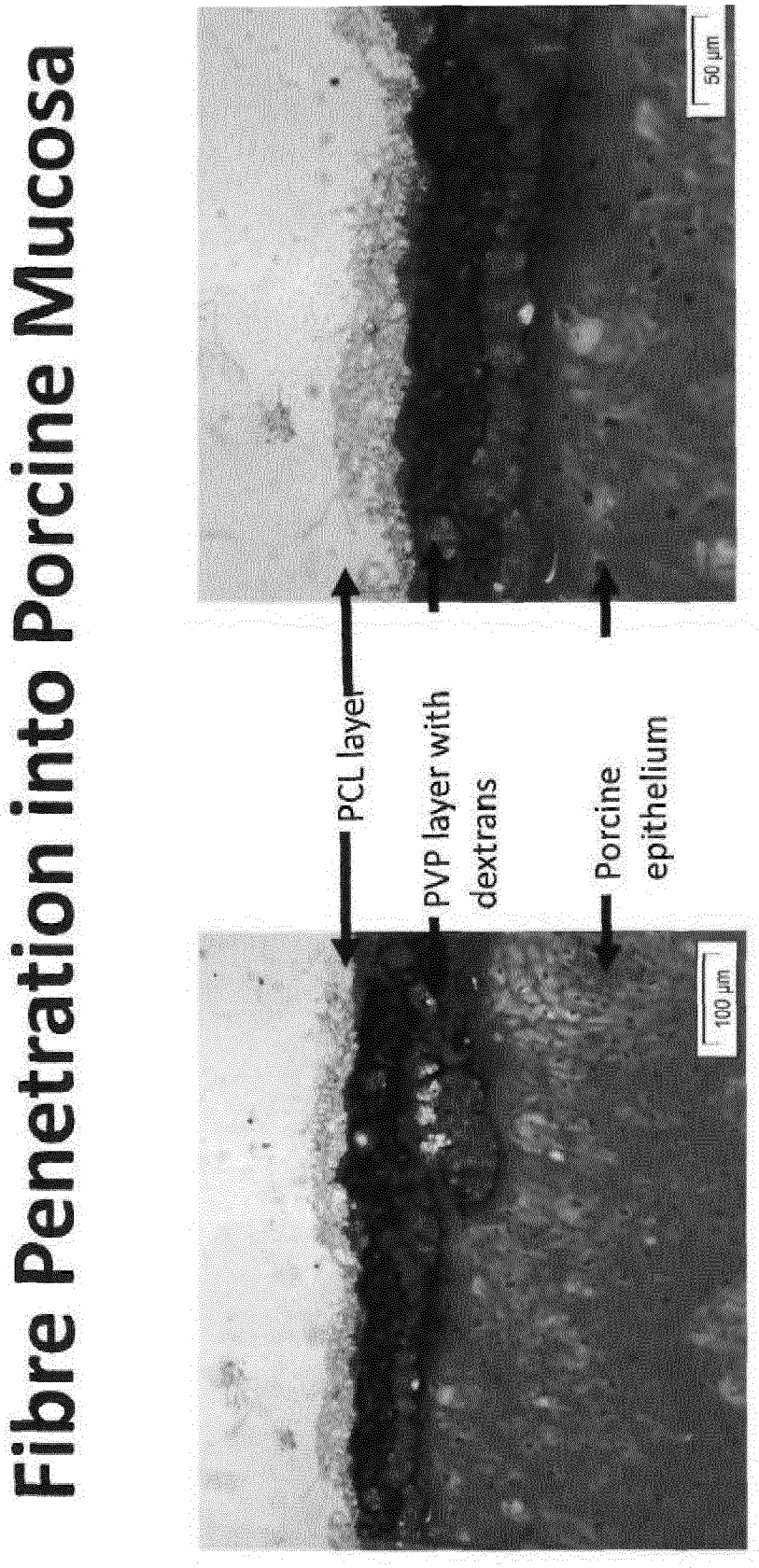
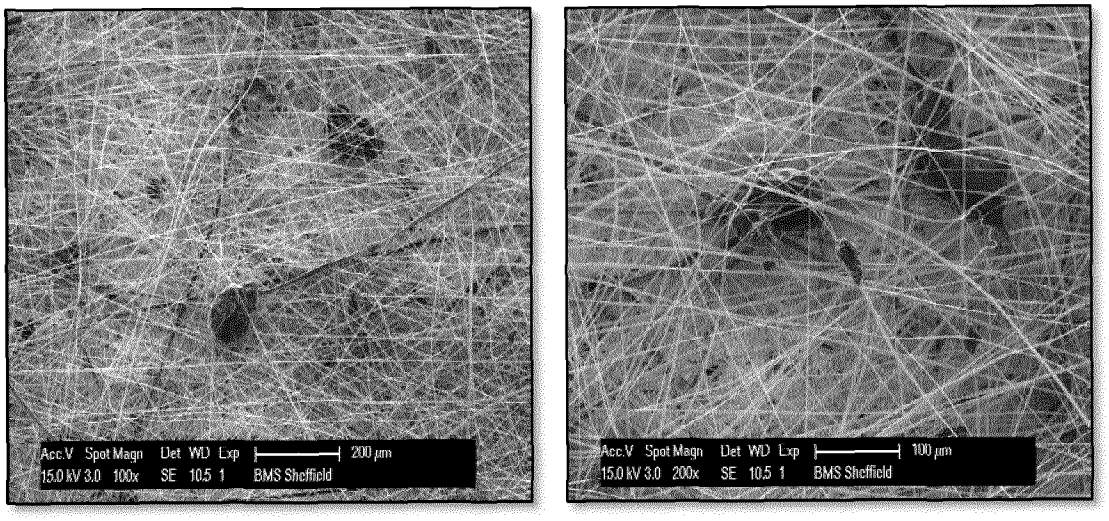

Fibre Penetration into Porcine Mucosa
PCL layer
PVP layer with dextrans
Porcine epithelium
50 µm
100 µm

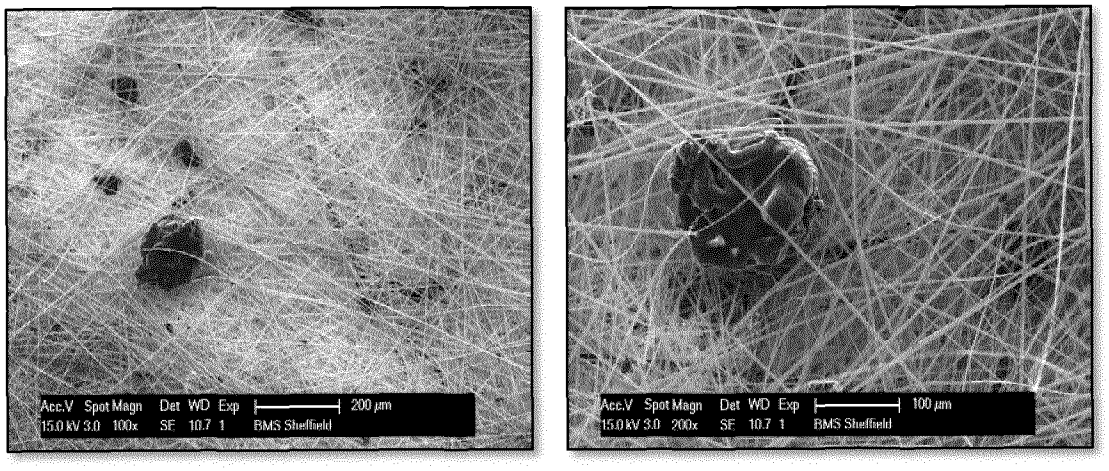
Figure 14

Eudragit L100-55 + Sodium alginate




A B

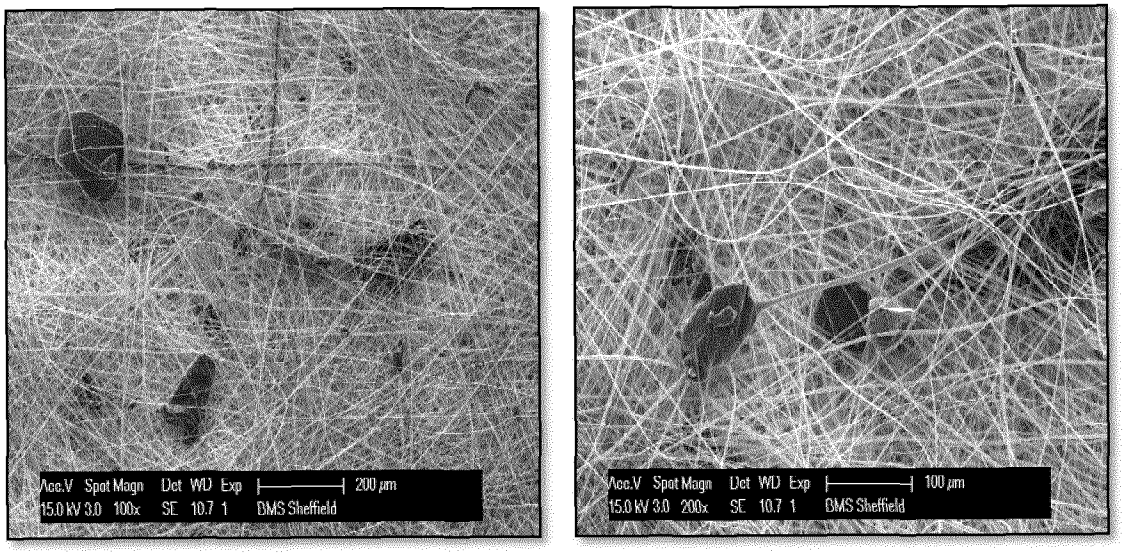
Eudragit L100-55 + Sodium carboxymethyl cellulose




C D

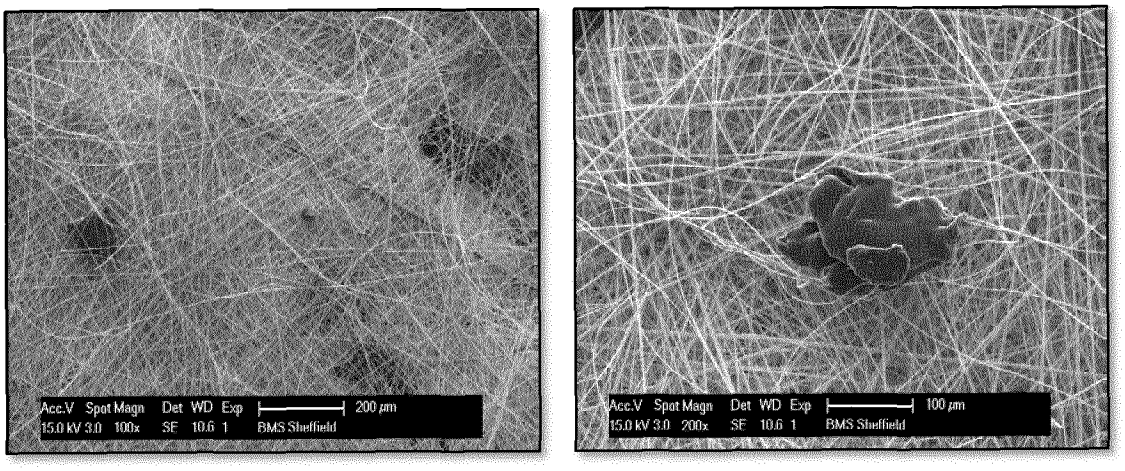
Figure 15

Eudragit L100-55 + Chitosan




A B

Eudragit L100-55 + Poly(vinyl alcohol)




C D

Figure 16




1) L100-55
2) L100-55 + Dextran
3) L100-55 + Polyethylene oxide
4) L100-55 + Carboxymethyl cellulose
5) L100-55 + Poly(vinyl alcohol)
6) L100-55 + Chitosan
7) L100-55 + Alginate