Local drug delivery from bone implants

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Ceramic materials and powder metallurgy
OUTLINE

• orthopaedic implant related infections
• systemic versus local drug delivery
• optimal antibiotic release profile
• porous Ti (alloy) bone implants
• calcium phosphate coatings
• biomimetic precipitation
• hydroxyapatite fibres
• polymer coatings
• conclusion
ORTHOPAEDIC IMPLANT RELATED INFECTIONS

• enormous number of orthopaedic implants
• low incidence of infection (0.5-5%)
• serious consequences:
  ▪ simple debridement and antibiotic treatment
  ▪ implant removal and replacement
  ▪ patient trauma
  ▪ prolonged hospitalization
  ▪ high medical costs

osteomyelitis
SYSTEMIC VERSUS LOCAL DRUG DELIVERY

- **Systemic antibiotic administration:**
  - limited blood circulation
  - biofilm
  - high doses
  - systemic adverse effects

- **Local drug delivery systems:**
  - high local concentrations
  - no systemic adverse effects

![Pie chart showing frequency of main pathogenic species (Campoccia et al., 2006)]

Frequency of main pathogenic species

(Campoccia et al., 2006)
OPTIMAL ANTIBIOTIC RELEASE PROFILE

• initial burst release
• therapeutic concentrations during 4-6 weeks
POROUS Ti (ALLOY) BONE IMPLANTS

• porosity: new bone ingrowth $\Rightarrow$ implant fixation

• Ti (alloy):
  • excellent biocompatibility
  • mechanical properties for load bearing applications
CALCIUM PHOSPHATE COATINGS

- bioactive: bone bonding
- drug delivery matrix

HA coated hip stem
BIOMIMETIC PRECIPITATION

- Ti substrate
- Na$_2$Ti$_5$O$_{11}$ layer
- OCP crystals
- HA globules

- Oxidation
- Crystal growth
- Nucleation
BIOMIMETIC PRECIPITATION

SEM

XRD

hydroxyapatite

gravimetric analysis

mg HA/cm² Ti

time (days)

0 2 4 6 8 10 12
BIOMIMETIC PRECIPITATION

EPMA mapping
BIOMIMETIC PRECIPITATION

carbonated apatite

octacalcium phosphate
HYDROXYAPATITE FIBRES

as a model for the calcium phosphate drug delivery matrix

porosity: 51 v%
pore size: 1 µm
HYDROXYAPATITE FIBRES

suspension of ceramic powder (HA) in solution of polymer (PSF) in solvent (NMP)

phase inversion, calcination, sintering

ceramic HA fibre

drug

loading

drug delivery system

biodegradable polymer

spray coating

drug delivery system with controlled release

HA: hydroxyapatite; NMP: N-methylpyrrolidone; PSF: polysulfone
BIODEGRADABLE POLYMER COATING

spray coating

- 3% poly(D,L-lactide)
- 2% poly(D,L-lactide)
- 1% poly(D,L-lactide)

coating thickness (µm) vs. spray time (min)
BIODEGRADABLE POLYMER COATING

![Graph showing riboflavin phosphate release over time for different polymer coatings.]

- **Y-axis**: Riboflavin phosphate release (wt%)
- **X-axis**: Time (days)

- **Legend**:
  - Red: PLGA 3.2μm
  - Green: PLGA 7.9μm
  - Blue: PLGA 14.5μm
  - Pink: PDLLA 13.6μm
CONCLUSION

porous Ti (alloy) bone scaffolds,
coated with a calcium phosphate matrix,
loaded with an antibiotic and
coated with a biodegradable polymer

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• new bone ingrowth into the implant
• load bearing applications
• bone bonding
• high local antibiotic concentrations
• no systemic adverse effects
• optimal drug release profile