PRINCIPLES AND SYSTEMS OF DRUG DELIVERY · SEMINARS 6–8

Materials for drug delivery systems and their surfaces

Educational program “Pharmacy” · 4th year · Al-Farabi Kazakh National University

After these seminars you will be able to

1. List the requirements for a material used in a DDS
2. Classify polymers by origin and biodegradability, with examples
3. Explain how PLGA composition controls degradation and release
4. Describe uses of metals, ceramics and carbon nanomaterials
5. Explain how charge, wettability and the protein corona decide the fate of a carrier

What a DDS material must do

Biocompatible

No toxic, inflammatory or immune reaction at the dose used

Safe degradation

Breaks down to products the body clears, or is removable

Compatible with drug

Does not react with or denature the active substance

Right mechanics

Strength, flexibility, swelling suited to the site

Sterilisable

Survives gamma, ethylene oxide or aseptic processing

Reproducible

Same molecular weight and purity from batch to batch

Polymers by origin and fate in the body

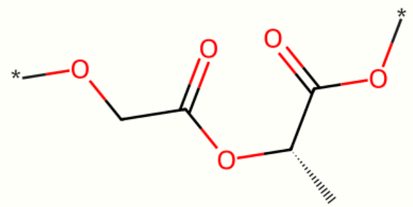
	Biodegradable	Non-biodegradable
Natural	Chitosan, alginate, gelatin, albumin, hyaluronic acid, collagen	Cellulose (in the body), silk fibroin (slow)
Semi-synthetic	Hydroxyethyl starch	HPMC, ethylcellulose, CMC
Synthetic	PLA, PGA, PLGA, PCL, polyanhydrides, poly(ortho esters)	Silicone, EVA, polyurethane, PEG*, acrylates (Eudragit)

Natural: biocompatible, mucoadhesive, cheap; but variable and may be immunogenic.

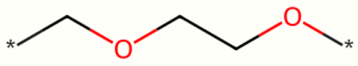
Synthetic: pure and tunable; degradation products must be safe.

Seminar 6 · *PEG is not degraded but is excreted by the kidney below about 30–40 kDa · Ratner et al. (2020)

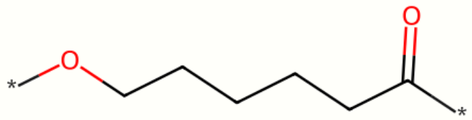
Repeat units of key DDS polymers



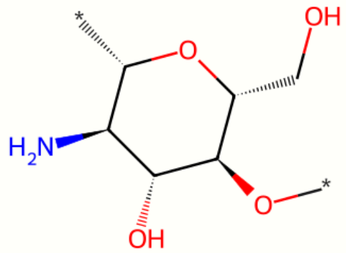
PLGA (lactide glycolide unit)



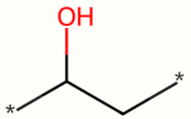
PEG (ethylene oxide unit)



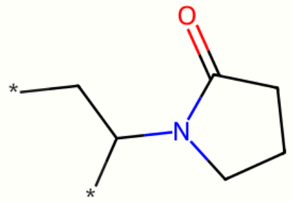
PCL (caprolactone unit)



Chitosan (glucosamine unit)



PVA (vinyl alcohol unit)



PVP (vinylpyrrolidone unit)

Ester bonds (PLGA, PCL) → hydrolysis → biodegradable

Ether bonds (PEG) → stable, hydrophilic, “stealth”

Amino groups (chitosan) → positive charge, mucoadhesion

C–C backbone (PVA, PVP) → not degraded

PLGA: the workhorse of injectable depots

What controls degradation

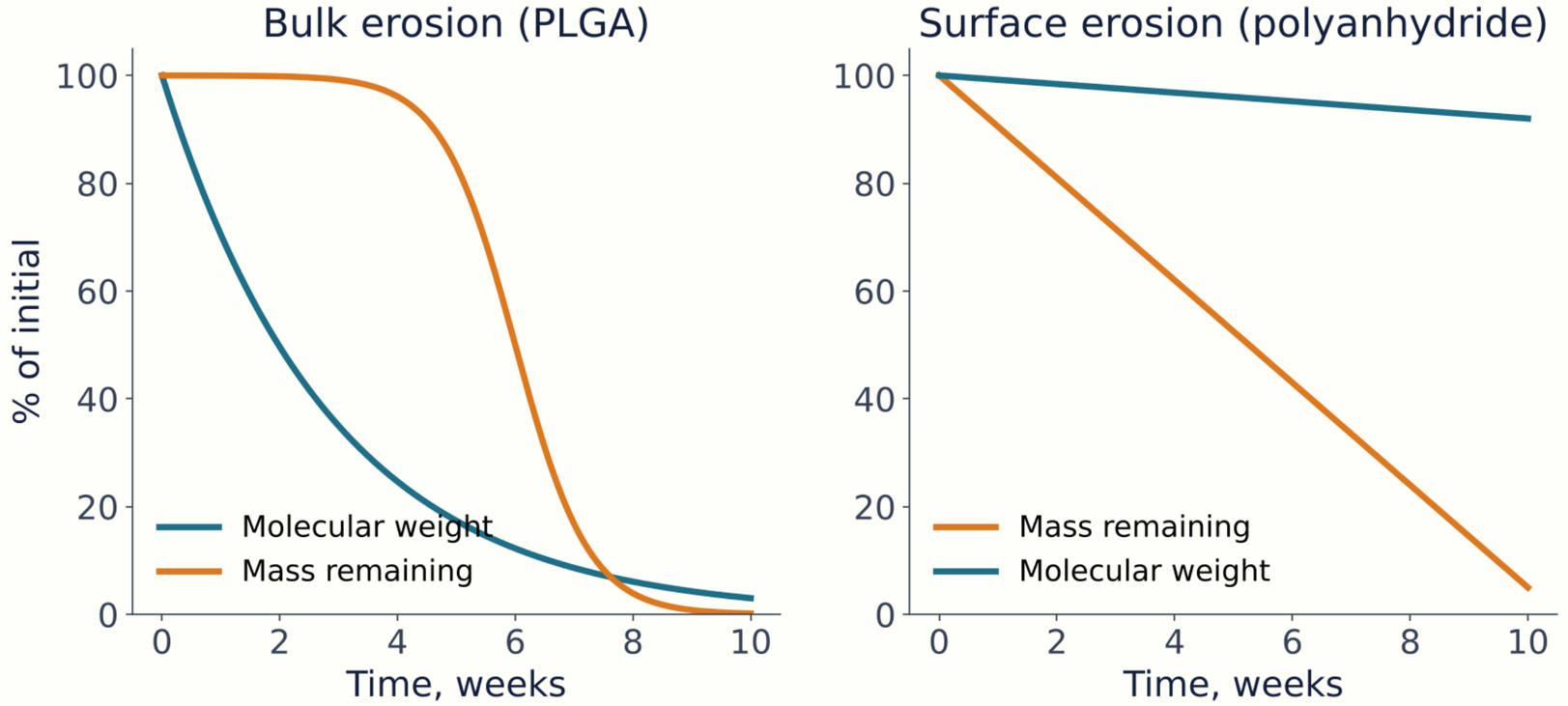
- LA:GA ratio — 50:50 degrades fastest
- More lactide → more hydrophobic → slower
- Molecular weight and end group (acid end is faster)
- Particle size and porosity

Marketed products

- Lupron Depot (leuprolide), 1–6 months
- Sandostatin LAR (octreotide), 4 weeks
- Risperdal Consta (risperidone), 2 weeks
- Bydureon (exenatide), weekly
- Zoladex implant (goserelin)

Degrades by hydrolysis to lactic and glycolic acid → Krebs cycle → CO_2 and water.

Bulk erosion versus surface erosion



Water enters **faster** than bonds break → whole device degrades (PLGA). Bonds break **faster** than water enters → device shrinks layer by layer, near zero-order release (polyanhydride, Gliadel wafer).

Metals and alloys in drug delivery

Material	Key property	DDS use
Titanium and alloys	Inert, strong, light	Implantable pumps, Susvimo port, iDose implant
Cobalt–chromium	Very strong in thin struts	Drug-eluting coronary stents
Nitinol (Ni–Ti)	Shape memory, superelastic	Self-expanding stents
Magnesium alloys	Corrode safely in the body	Bioresorbable scaffolds
Gold, iron oxide (nano)	Optical, magnetic	Theranostics, magnetic targeting (seminars 24, 27)

In a drug-eluting stent the metal gives strength; a thin polymer coating holds and releases the drug (sirolimus, everolimus, paclitaxel).

Ceramics and composites

Calcium phosphates

Hydroxyapatite and tricalcium phosphate: bone-like; carry antibiotics in bone cement and grafts.

Mesoporous silica

Pores of 2–10 nm, huge surface: keep poorly soluble drugs amorphous; gated release.

Bioactive glass

Bonds to bone and releases ions (Ca, Si); can carry drugs.

Composites combine strengths

Gentamicin in PMMA bone cement; polymer-coated metal stents; hydroxyapatite in PLGA scaffolds. Each phase brings one property: strength, degradation or drug loading.

Carbon nanomaterials

Carbon nanotubes

Rolled graphene; enter cells; concern: fibre-like toxicity like asbestos

Graphene oxide

Flat sheets with large area for π-stacking of aromatic drugs (doxorubicin)

Nanodiamonds

4–5 nm, surface easy to functionalise, low toxicity in studies

Fullerenes, carbon dots

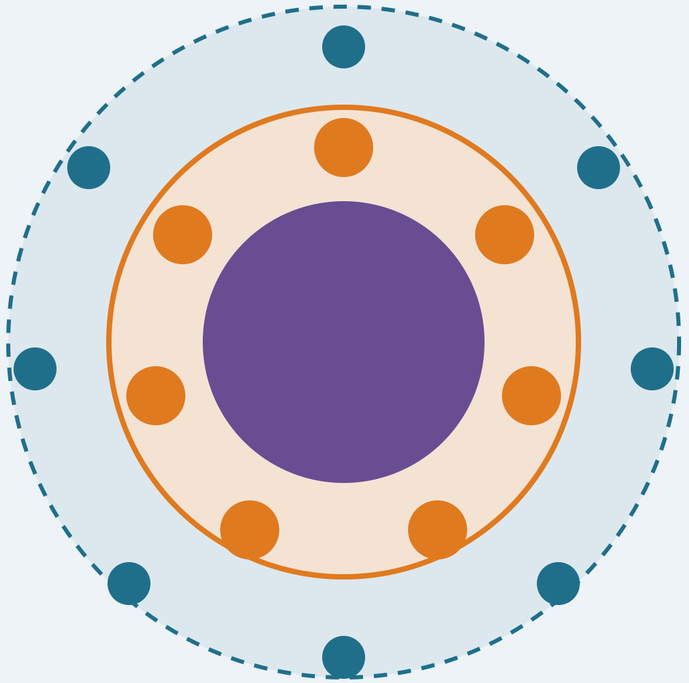
Antioxidant cages; fluorescent dots for imaging

Status: research stage; no carbon nanomaterial is yet an approved drug carrier, mainly because of persistence and toxicity questions.

Surface properties decide the biological response

Property	Measured by	Effect
Charge	Zeta potential	Positive: binds cells and mucus, more toxic; negative or neutral: longer circulation
Wettability	Water contact angle	Hydrophobic surfaces adsorb more protein and are cleared faster
Roughness, topography	AFM, SEM	Changes cell adhesion, platelet activation, bacterial colonisation
Size and shape	DLS, TEM	Uptake route, filtration in kidney, liver or spleen
Surface chemistry	XPS, FTIR	Ligands for targeting; PEG for stealth

The protein corona: what the cell actually sees



Particle enters the blood

Hard corona: tightly bound proteins (apolipoproteins, complement, immunoglobulins)

Soft corona: loosely bound, exchanging proteins

Opsonins → uptake by liver and spleen macrophages. **PEG** reduces adsorption → longer circulation.

HOW BIOCOMPATIBILITY IS PROVEN

ISO 10993 sets the tests: cytotoxicity, sensitisation, irritation, haemocompatibility, implantation, genotoxicity

The test list depends on contact type (surface, blood, implant) and duration (< 24 h, up to 30 days, longer).

Questions for discussion

1. Why does PLGA 50:50 degrade faster than PLGA 75:25?
2. Which erosion type gives release closer to zero order, and why?
3. Why is chitosan mucoadhesive?
4. What is the role of the metal and of the polymer in a drug-eluting stent?
5. Why are positively charged nanoparticles cleared faster and more toxic?
6. How does PEG change the protein corona?

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