Compounding Altered-Release Pharmaceuticals

Part IV

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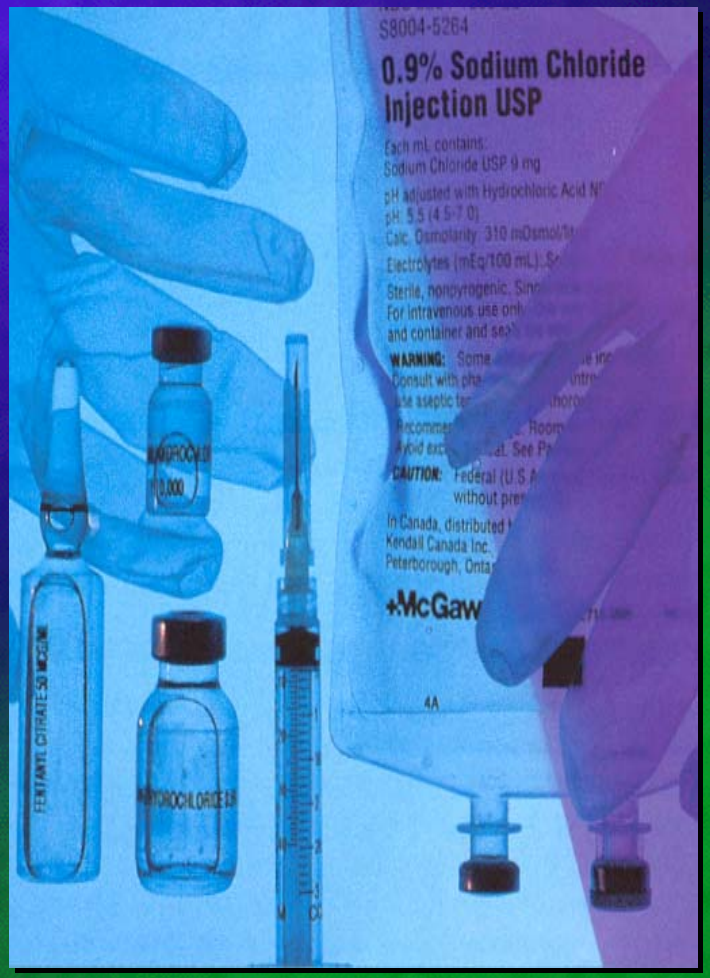
Compounding Altered-Release Pharmaceuticals-Part IV

- Parenteral
- Miscellaneous
- Drug Examples that are Good Candidates
- Excipients Used For Altered-Release Pharmaceuticals
- Summary/Conclusions

Compounding Altered-Release Pharmaceuticals-Part IV

- Parenteral
  - Internal
  - External
  - IV Drip
  - IM Injection

Compounding Parenterals



Internal

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Internal

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

Hydromorphone 2% and Bupivacaine HCl 0.75% Intrathecal Injection, PF

- Hydromorphone HCl USP 2 g
- Bupivacaine HCl Usp 750 mg
- 0.9% Sodium chloride inj 42 mL
- Sterile water for injection qs 100 mL

Morphine sulfate 20 mg/mL and Clonidine HCl 10 ug/mL Epidural Injection

Morphine sulfate		2 g
Clonidine HCl		1 mg
0.9% Sodium chloride injection		69 mL
Sterile water for injection	qs	100 mL

IV Drip/Infusion

- Factors Affecting
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

IV Drip/Infusion

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

IM Injection

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

IM Injection

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

Progesterone 100 mg/mL in Oil Injection

Progesterone		10 g
Benzyl benzoate		10 mL
Benzyl alcohol		10 mL
Sesame oil	qs	100 mL

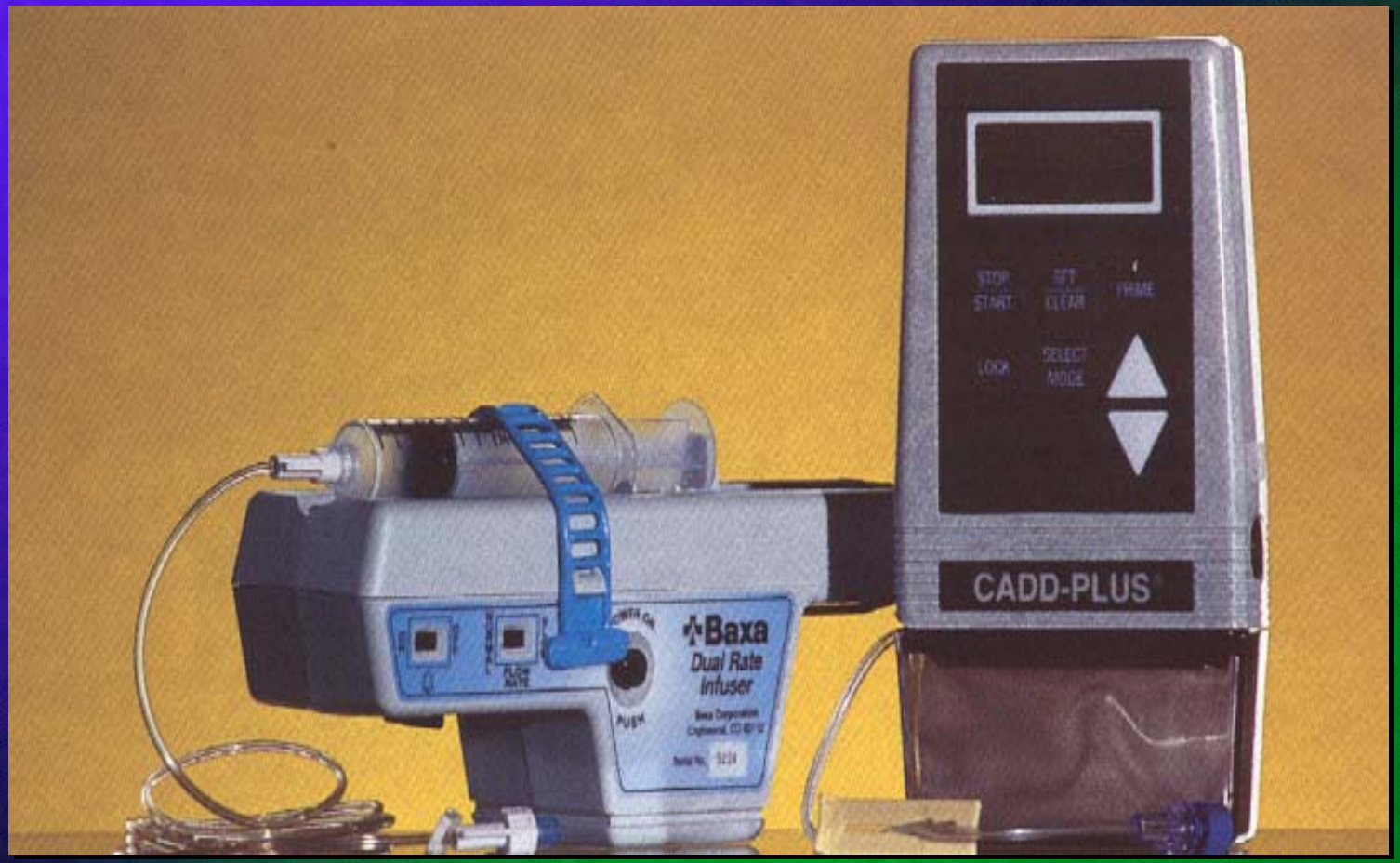
External

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

External

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

Ambulatory Pumps



Ceftazidime 20 mg/mL for Ambulatory Infusion Pump

Ceftazidime		2.5 g
Sterile water for injection		qs
0.9% Sodium chloride inj	qs	125 mL

Compounding Altered-Release Pharmaceuticals

- Miscellaneous
  - Soaking a membrane or gelatin in solution (casting)
  - Cyclodextrins
  - Implants
  - Nanoparticles
  - Resealed Erythrocytes
  - Antibiotic Bone Cement
  - Antibiotic Beads Implanted
  - Self-Regulated Chelating Agents

Soaking A Membrane or Gelatin in Solution (Casting)

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Soaking A Membrane or Gelatin in Solution (Casting)

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

- Topical Application

Cyclodextrins

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Cyclodextrins

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

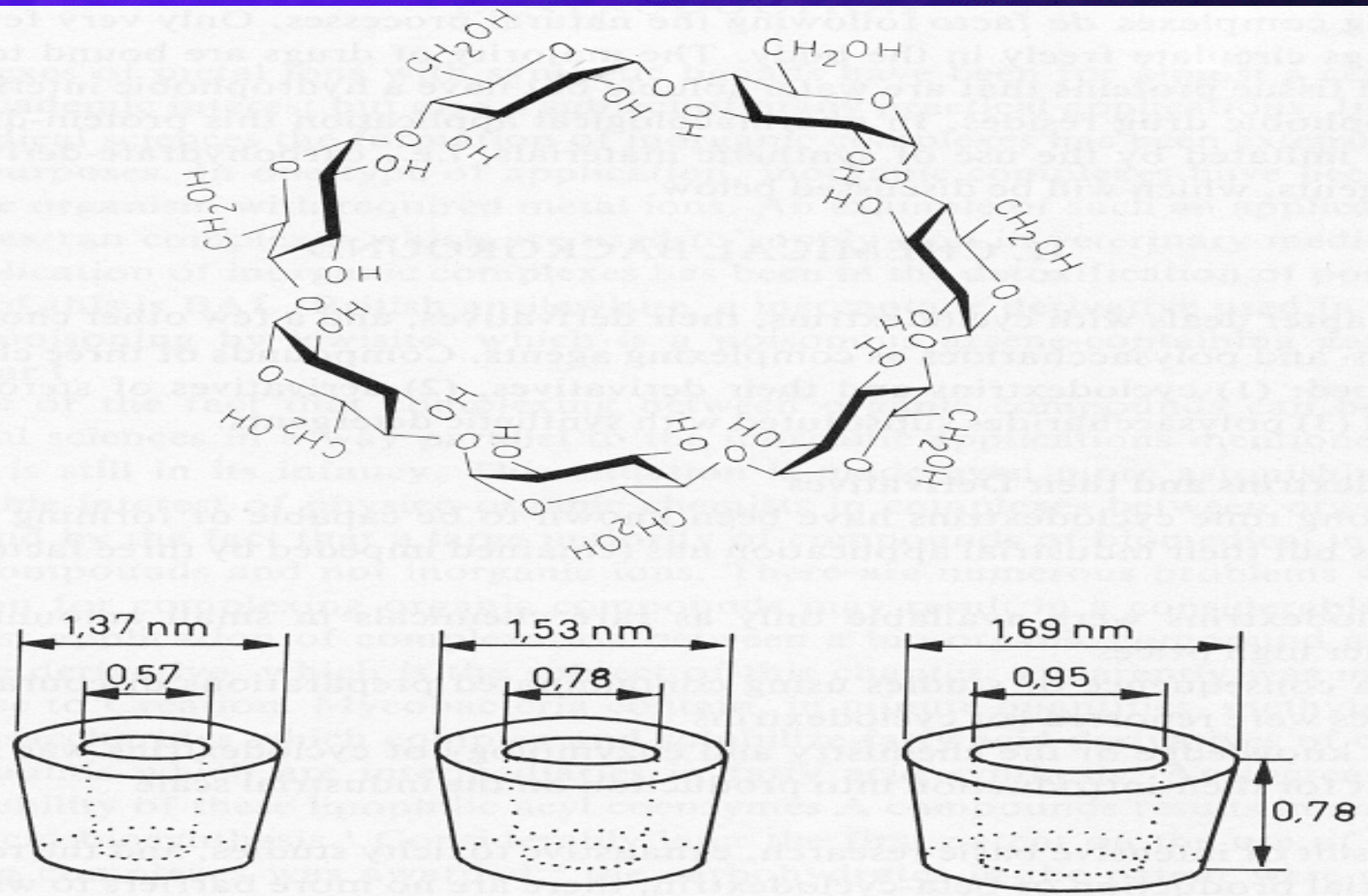
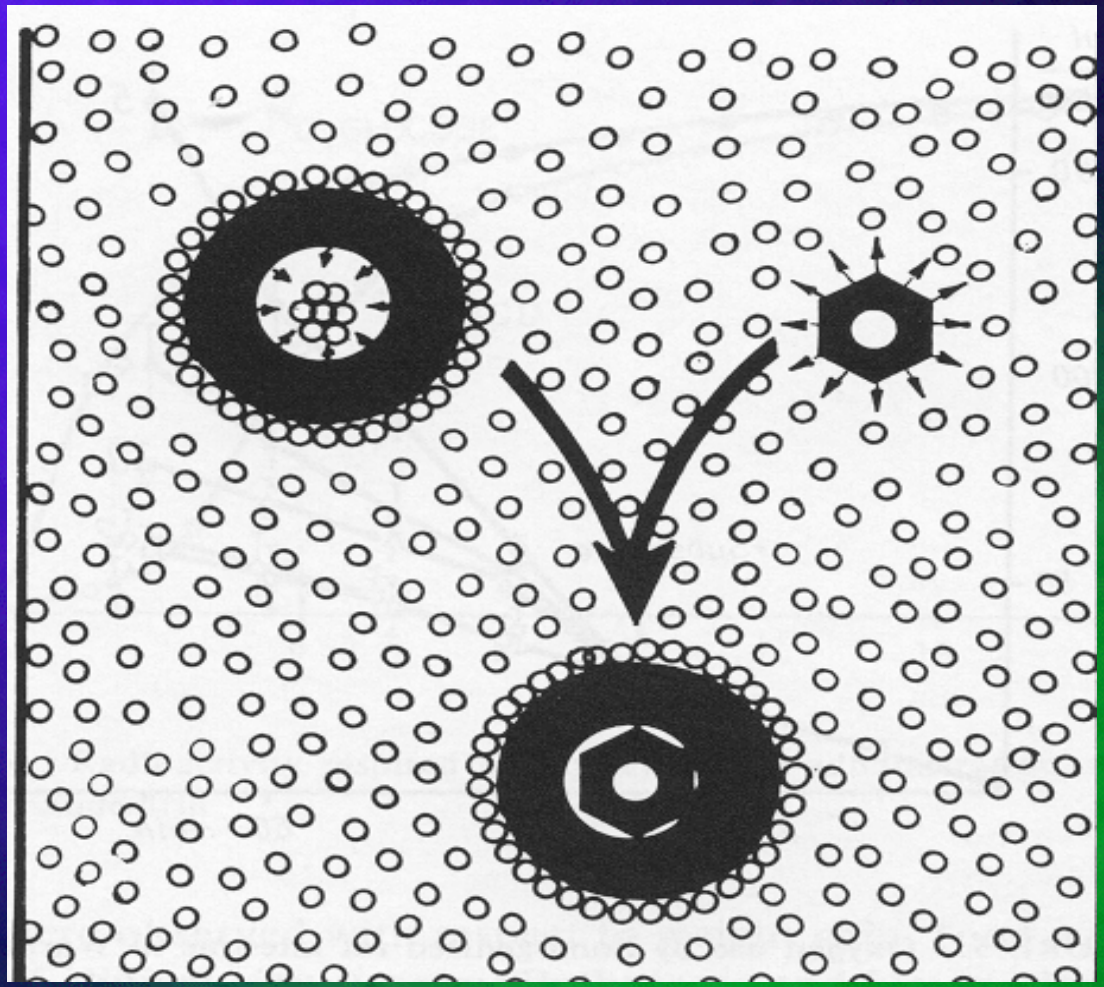


FIGURE 1. Structure of β-cyclodextrin and the molecular dimensions of α-, β-, and γ-cyclodextrins.



Implants

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Implants

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices (Mg Stearate, PLA, PGA, Silicone Polymers)
- Preparation Methods

Fibrin Glue

- Aprotinin 70,000 KIU
- Thrombin 10,000 IU
- Calcium chloride 0.5 M sol 2 mL

Nanoparticles

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Nanoparticles

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

Resealed Erythrocytes

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility

Resealed Erythrocytes

- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices
- Preparation Methods

Resealed Erythrocytes

- Whole Blood
- Spin it down and remove the red blood cells
- Place in sterile hypotonic saline or water
- Add concentrated sterile solution of drug
- Readjust tonicity to isotonic
- Erythrocytes will “reseal”
- Administer to patient…….last up to 3 weeks

Antibiotic Bone Cement

- Factors Affecting
  - Particle size
  - Concentration
  - Diffusion coefficients
  - Partition coefficients
  - Solubility
- Mechanism of Release
- Stability
- Equipment Required
- Materials/Matrices (Palacos Bone Cement + Drug)
- Preparation Methods

Tobramycin-Impregnated Polymethylmethacrylate Beads

- Tobramycin sulfate 1.2 g
- Palacos Bone Cement 40 g

- 0.25 inch beads contain approx 3.26 mg of tobramycin (as the sulfate)

Vancomycin 5 mg Sponge Disks

- Vancomycin HCl 5 mg
- Sponge (collagen or gelatin) qs

Compounding Altered-Release Pharmaceuticals

- Drug Examples That Are Good Candidates
- The lower the dose the better
- Lower solubility is better
- Short half-life vs long half-life
- Large therapeutic index

Drug Examples That Are Good Candidates

- Solubility
- Dose
- ADME--Duration of action
- Pharmacokinetics

Compounding Altered-Release Pharmaceuticals

- Summary/Conclusions
- YES, some are feasible
- No, some are not
- Quality Control is important
- Always monitor clinical response

A LOOK INTO THE NEAR FUTURE

- New Compounded Drug Delivery Systems (DDS)
- Next 5-10 years

Future Trends

- Adhesive Site-Specific DDS
- Antibody-Based DDS
- Biocompatible Microsphere DDS
- Biodegradable Polymers DDS
- Biologic-Based DDS
- Electromagnetic/Radiation-Activated DDS

Future Trends

- Immunomodulator DDS
- Implant-Enhanced DDS
- Microorganism-Containing Microcapsules
- Lipid Microcylinders
- Liposome Enhancements
- Living-Cell Therapies

Future Trends

- Magnetic System DDS
- Maze-Escape DDS
- Monoclonal Antibody DDS
- Novel Nasal DDS
- New Osmotic DDS
- Transmucosal DDS
- Polymer Drug Complex DDS

Future Trends

- Pulsatile DDS
- Respiratory DDS
- Self-Assembling Controlled Release DDS
- Programmed Skin Surface DDS