CHAPTER 6. FUNDAMENTALS OF CONTROLLED DRUG DELIVERY

CONTROLLED RELEASE DOSAGE FORMS

DRUG + DELIVERY MODULE

DELIVERING A DRUG
MAILING A LETTER
LETTER + DELIVERY VEHICLE
(1ST CLASS US POSTAL SERVICE: SLOW, UNPREDICTABLE
FEDERAL EXPRESS: SELECTION ON THE DELIVER SPEED, PREDICTABLE)

CONVENTIONAL DOSAGE FORMS: 1ST CLASS DELIVERY
CONTROLLED RELEASE DOSAGE FORMS: FEDEX

WHY DO WE DEVELOP CONTROLLED RELEASE DOSAGE FORMS?

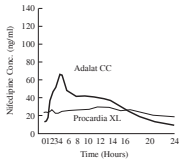
A. ALTERNATIVE TO DEVELOPMENT OF NEW DRUGS

1. HIGH COST OF DEVELOPING NEW DRUGS

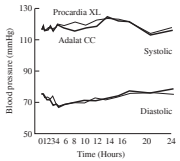
2. NEW TRICKS FOR OLD DRUGS

WHY DO WE DEVELOP CONTROLLED RELEASE DOSAGE FORMS?

B. EXTENSION OF PRODUCT LIFE (I.E., PATENT LIFE)
PROCARDIA (BID) TO PROCARDIA XL (ONCE A DAY)



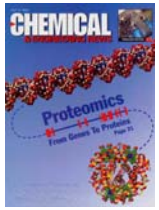
PHARMACOKINETICS



PHARMACODYNAMICS

WHY DO WE DEVELOP CONTROLLED RELEASE DOSAGE FORMS?

C. DELIVERY OF MACROMOLECULAR DRUGS
(PROTEIN DRUGS, DNA, RNA)



❖Synergistic partnership with drug discovery

Participation in the early stage of drug development

Drugs with unfavorable properties

Poor water solubility
Poor permeability
Poor stability

Polaroid to Digital Camera

CONTROLLED RELEASE DOSAGE FORMS ADVANTAGES

1. MAINTENANCE OF OPTIMUM CONCENTRATION
2. IMPROVED EFFICACY WITH LESS DRUG
3. MINIMAL SIDE EFFECT

THERAPEUTIC INDEX, DOSE INDEX

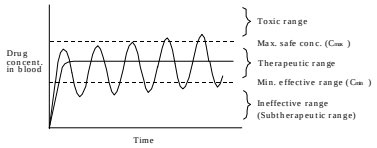


Table 6-1. TI values of selected drugs

Drug	TI
Theophylline	∞
Triphenylamine	19,000
Diphenhydramine	2,300
Chlorpheniramine	1,400
Penicillin	>100
Acetaminophen	20-40
Barbiturates	2-7
Quinidine	2-3
Digitoxin	1.5

ADVANTAGES

4. LESS FREQUENT ADMINISTRATION

ADVANTAGES

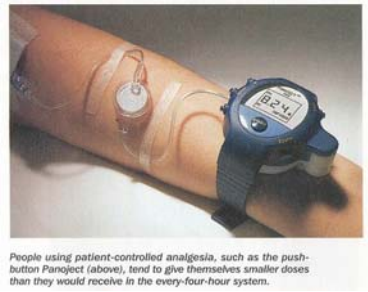
5. IMPROVED PATIENT CONVENIENCE & COMPLIANCE

FOUR TIMES A DAY
THREE TIMES A DAY
TWICE A DAY
ONCE A DAY
ONCE A WEEK
ONCE A MONTH

FOUR TIMES A YEAR
TWICE A YEAR
ONCE A YEAR

While the arsenal of painkillers has not changed in recent years, the methods for administering drugs have expanded. Below, a patient is taught how to use the drug-releasing pump in patient-controlled analgesia.

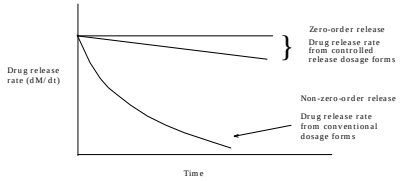
Increasingly doctors are recognizing that timely and proper pain management can lead to faster, more complete recovery from surgery, and could even save lives.



People using patient-controlled analgesia, such as the push-button Panoject (above), tend to give themselves smaller doses than they would receive in the every-four-hour system.

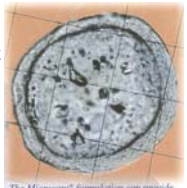
CONTROLLED RELEASE DOSAGE FORMS ADVANTAGES

6. APPLICATION TO PK AND PD STUDIES



CONTROLLED RELEASE DOSAGE FORMS DISADVANTAGES

1. RELATIVELY HIGH PRODUCTION COST
2. DOSE DUMPING
3. SURGICAL OPERATION
4. DIFFICULTY IN STOPPING DRUG RELEASE
5. BIOCOMPATIBILITY ISSUE



The Microcaps® formulation can provide taste-masking as well as gastro-protection.

BIOCOMPATIBILITY OF CONTROLLED RELEASE DOSAGE FORMS

BIOMATERIALS AND BIOCOMPATIBILITY

EXAMPLES

1. SILICONE GEL BREAST IMPLANT

EXAMPLES

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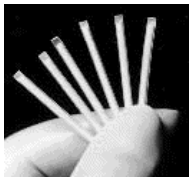
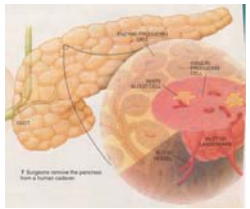
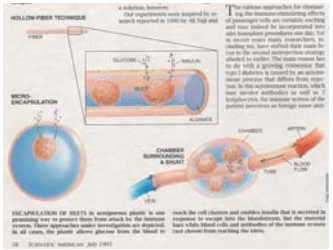
2. NORPLANT



EXAMPLES

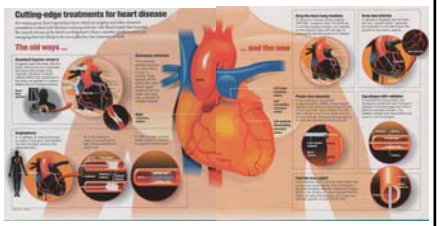
1. SILICONE GEL BREAST IMPLANT
2. NORPLANT
3. SELF-REGULATING INSULIN DELIVERY DEVICES

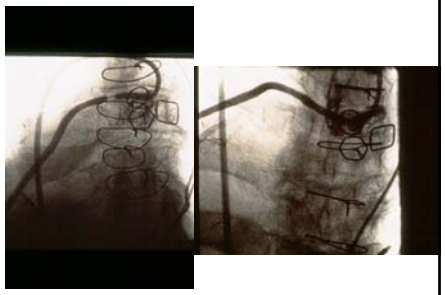


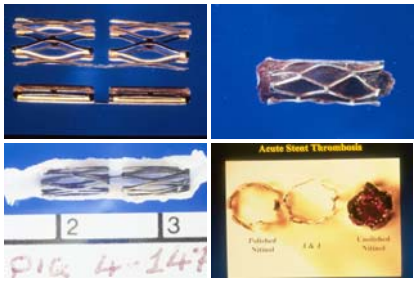


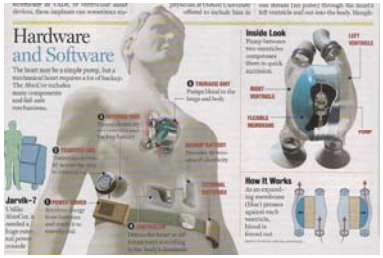
EXAMPLES

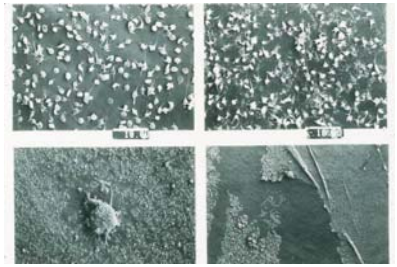
1. SILICONE GEL BREAST IMPLANT
2. NORPLANT
3. SELF-REGULATING INSULIN DELIVERY DEVICES
4. ARTIFICIAL HEART, VASCULAR GRAFT. ASSIST DEVICES





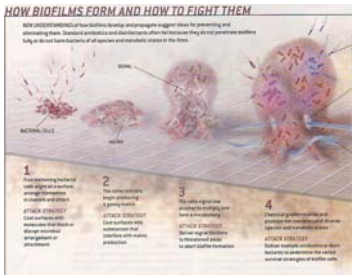


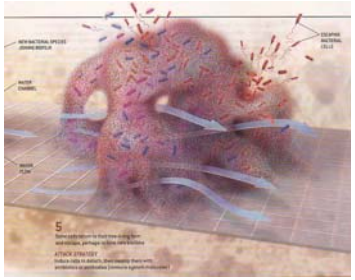




EXAMPLES

1. SILICONE GEL BREAST IMPLANT
2. NORPLANT
3. SELF-REGULATING INSULIN DELIVERY DEVICES
4. ARTIFICIAL HEART, VASCULAR GRAFT. ASSIST DEVICES
5. CATHETERS





THE BIOMATERIALS ACCESS INSURANCE ACT OF 1998

PROTECTION OF SUPPLIERS OF RAW MATERIALS AND PARTS OF BIOMATERIALS

e.g., Teflon in biomaterials

DEVELOPMENT OF CONTROLLED RELEASE DOSAGE FORMS

1. MEDICAL RATIONALE
   DRUG EFFICACY, DRUG SAFETY, PATIENT COMPLIANCE
2. DRUG INPUT RATE
   MATCHING WITH DRUG ELIMINATION RATE
3. BIOLOGICAL INTERFACE
4. COST EFFECTIVENESS