

## CHAPTER 6. FUNDAMENTALS OF CONTROLLED DRUG DELIVERY

### CONTROLLED RELEASE DOSAGE FORMS

#### DRUG + DELIVERY MODULE

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

CONVENTIONAL DOSAGE FORMS: 1<sup>ST</sup> CLASS DELIVERY  
 CONTROLLED RELEASE DOSAGE FORMS: FEDEX

#### WHY DO WE DEVELOP CONTROLLED RELEASE DOSAGE FORMS?

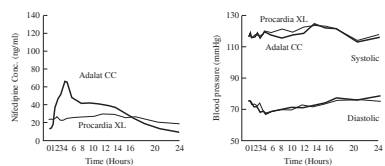
A. ALTERNATIVE TO DEVELOPMENT OF NEW DRUGS

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

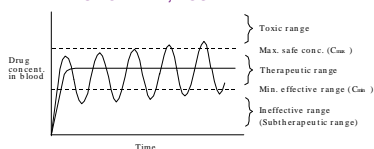


Table 6-1. TI values of selected drugs

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

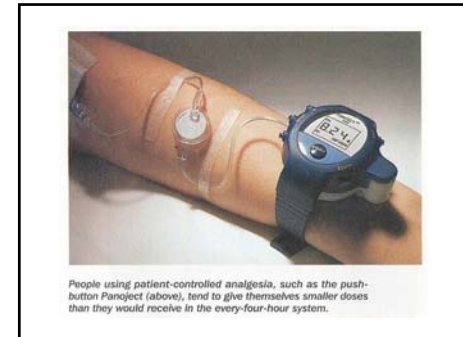
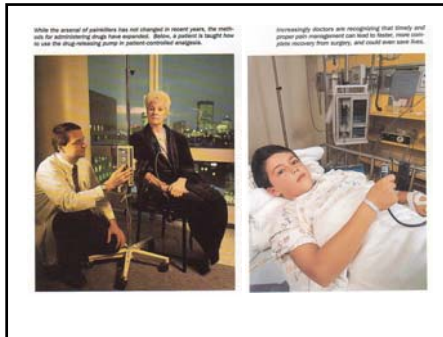


## ADVANTAGES

### 5. IMPROVED PATIENT CONVENIENCE & COMPLIANCE

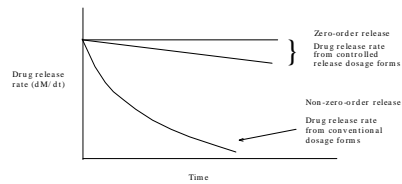
FOUR TIMES A DAY  
THREE TIMES A DAY  
TWICE A DAY  
ONCE A DAY  
ONCE A WEEK  
ONCE A MONTH

FOUR TIMES A YEAR  
TWICE A YEAR  
ONCE A YEAR



## 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



## BIOCOMPATIBILITY OF CONTROLLED RELEASE DOSAGE FORMS

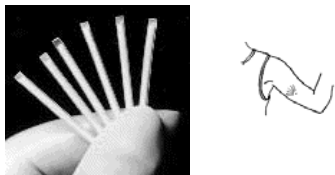
### BIOMATERIALS AND BIOCOMPATIBILITY

#### EXAMPLES

1. SILICONE GEL BREAST IMPLANT

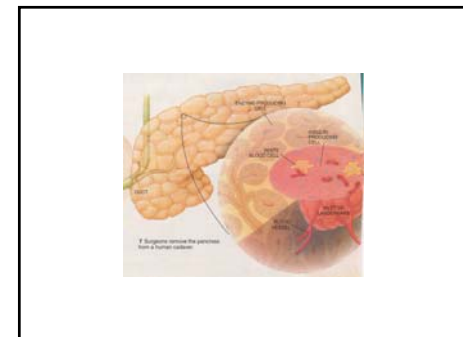
## EXAMPLES

1. SILICONE GEL BREAST IMPLANT
2. NORPLANT

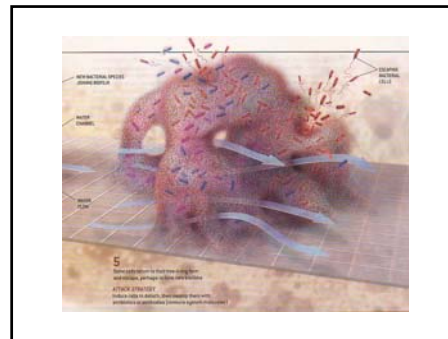
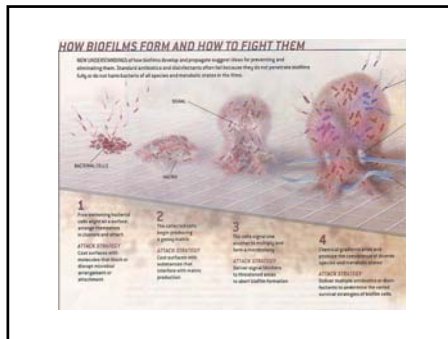


## EXAMPLES

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







**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**