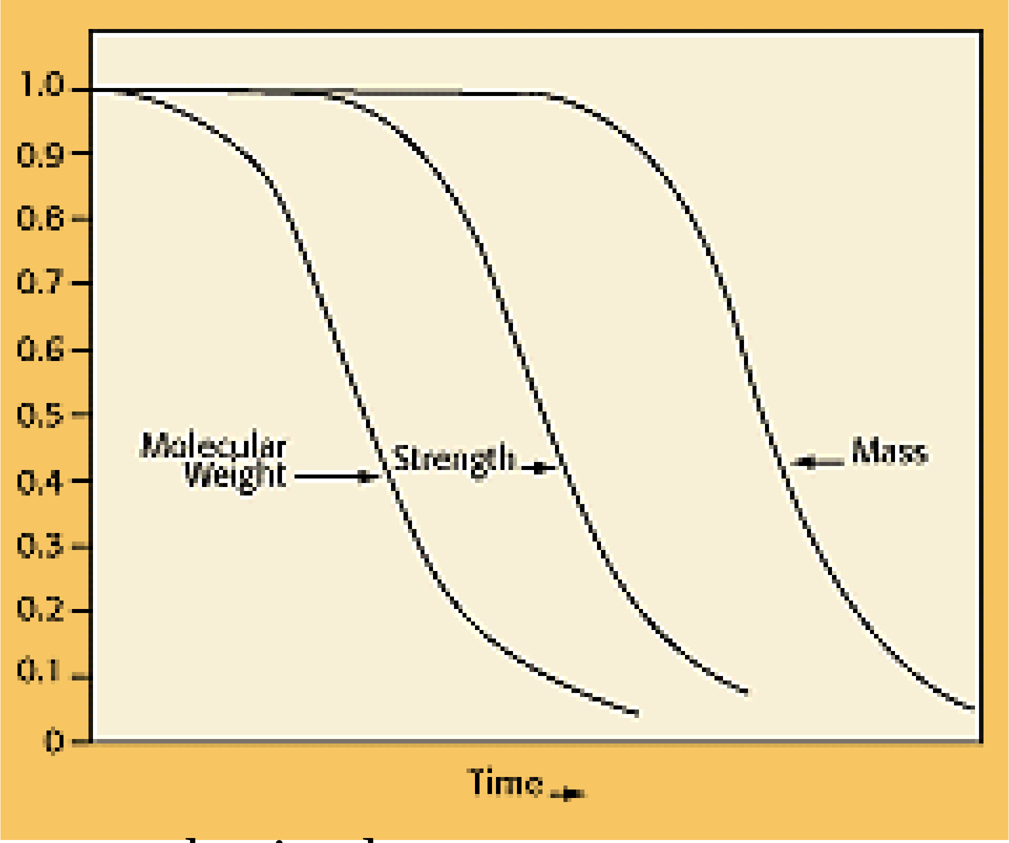
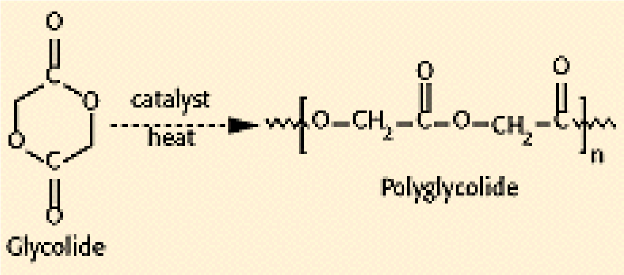
Biodegradable Polymers:
Chemistry, Degradation and Applications

Lecture 7 : Prof.Dr.Jenan S.Kashan

What is Polymer Degradation?



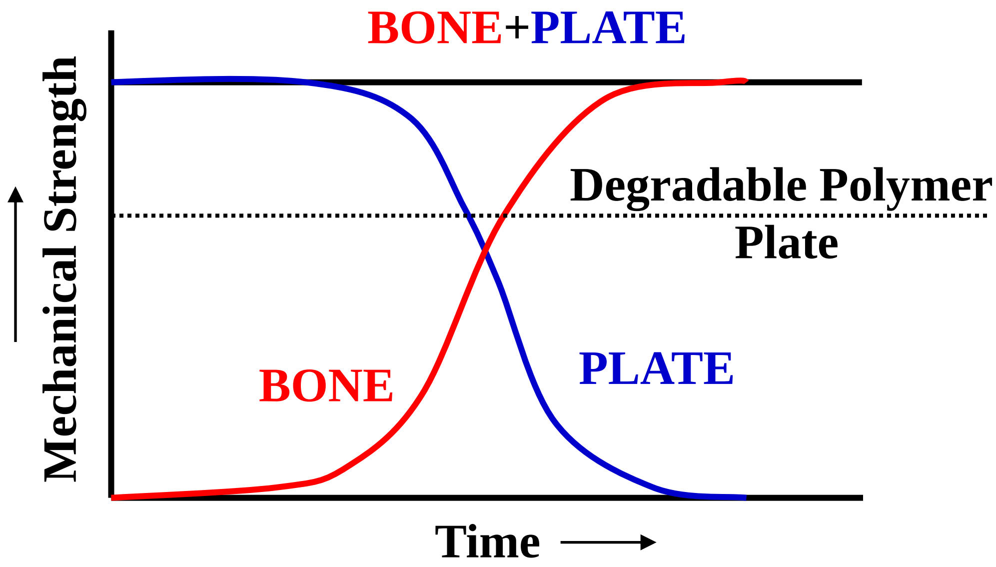
polymers were synthesized from glycolic acid in 1920s



At that time, polymer degradation was viewed negatively as a process where properties and performance deteriorated with time.

Why Would a Medical Practitioner Like a Material to Degrade in the Body?

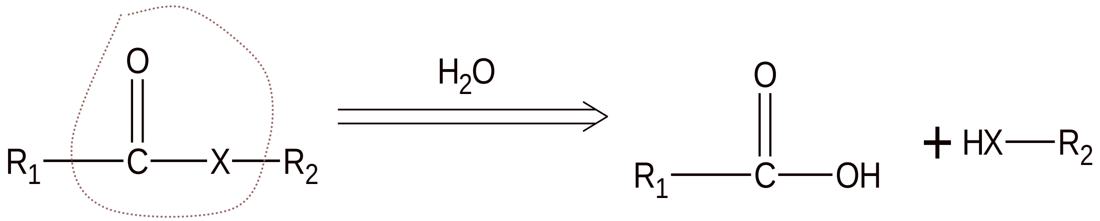
- Do not require a second surgery for removal
- Avoid stress shielding
- Offer tremendous potential as the basis for controlled drug delivery



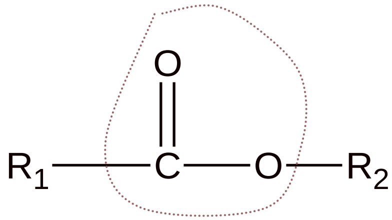
Biodegradable Polymers

- ✓ **Carbonyl bond to** { O, N, S }

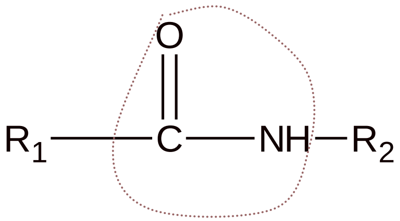
A.



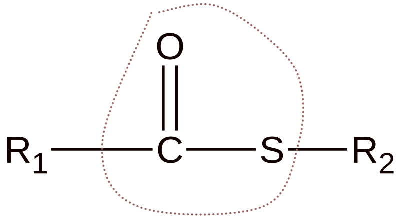
Where X= O, N, S



Ester



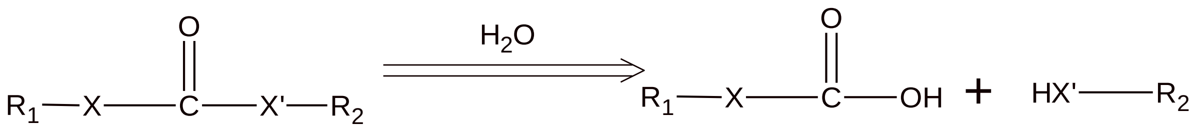
Amide



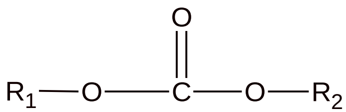
Thioester

Biodegradable Polymers

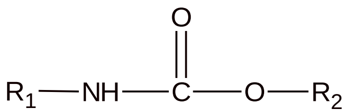
B.



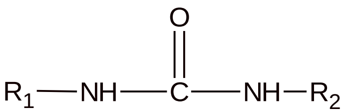
Where X and X'= O, N, S



Carbonate

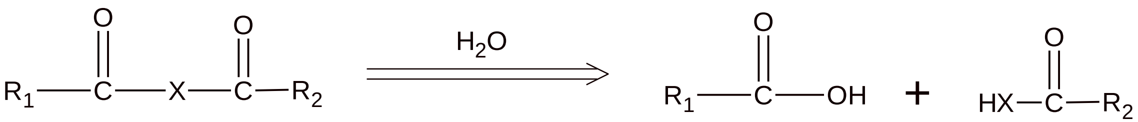


Urethane

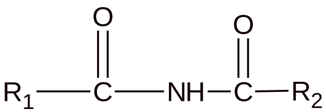


Urea

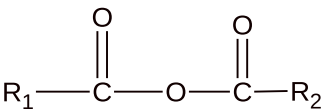
C.



Where X and X'= O, N, S



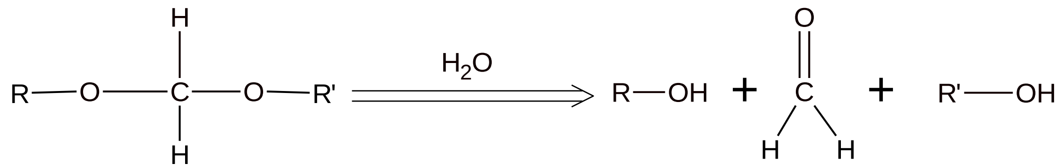
Imide



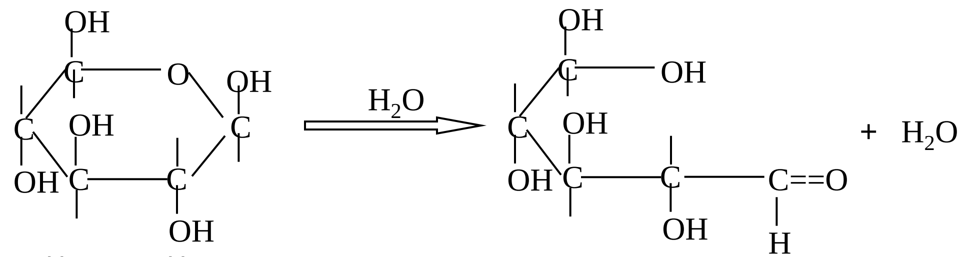
Anhydride

Biodegradable Polymers

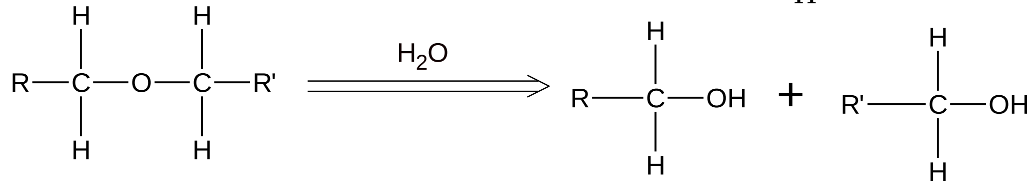
- ✓ Acetal:



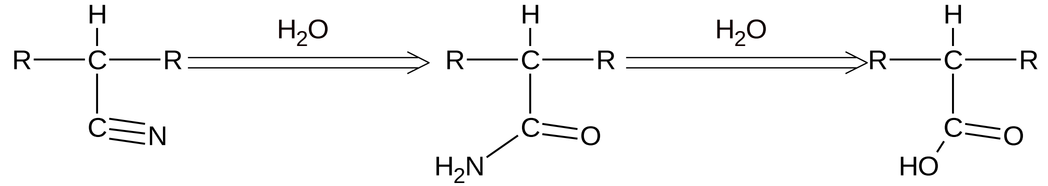
- Hemiacetal:



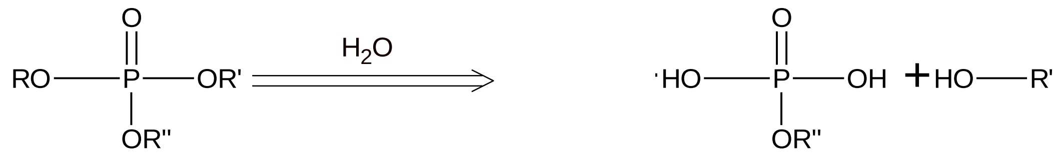
- ✓ Ether



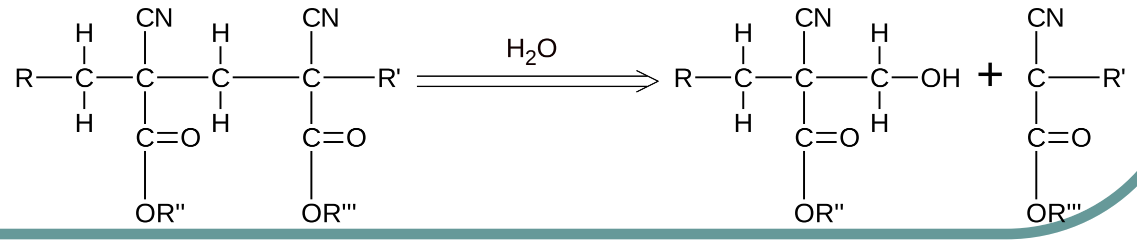
- ✓ Nitrile



- ✓ Phosphonate



- ✓ Polycyanocrylate



Biodegradable Polymers Used for Medical Applications

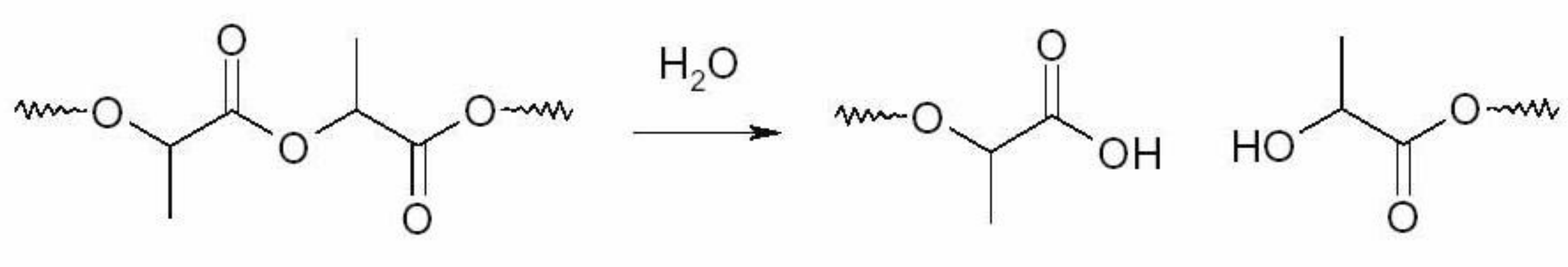
- **Natural polymers**
  - Fibrin
  - Collagen
  - Chitosan
  - Gelatin
  - Hyaluronan ...
- **Synthetic polymers**
  - PLA, PGA, PLGA, PCL, Polyorthoesters …
  - Poly(dioxanone)
  - Poly(anhydrides)
  - Poly(trimethylene carbonate)
  - Polyphosphazenes ...

Synthetic or Natural Biodegradable Polymers
Why Do We Prefer Synthetic Ones?

- Tailor-able properties
- Predictable lot-to-lot uniformity
- Free from concerns of immunogenicity
- Reliable source of raw materials

Degradation Mechanisms

- Enzymatic degradation
- Hydrolysis
  (depend on main chain structure: anhydride > ester >



  - Homogenous degradation
  - Heterogenous degradation

Degradation can be divided into 4 steps:

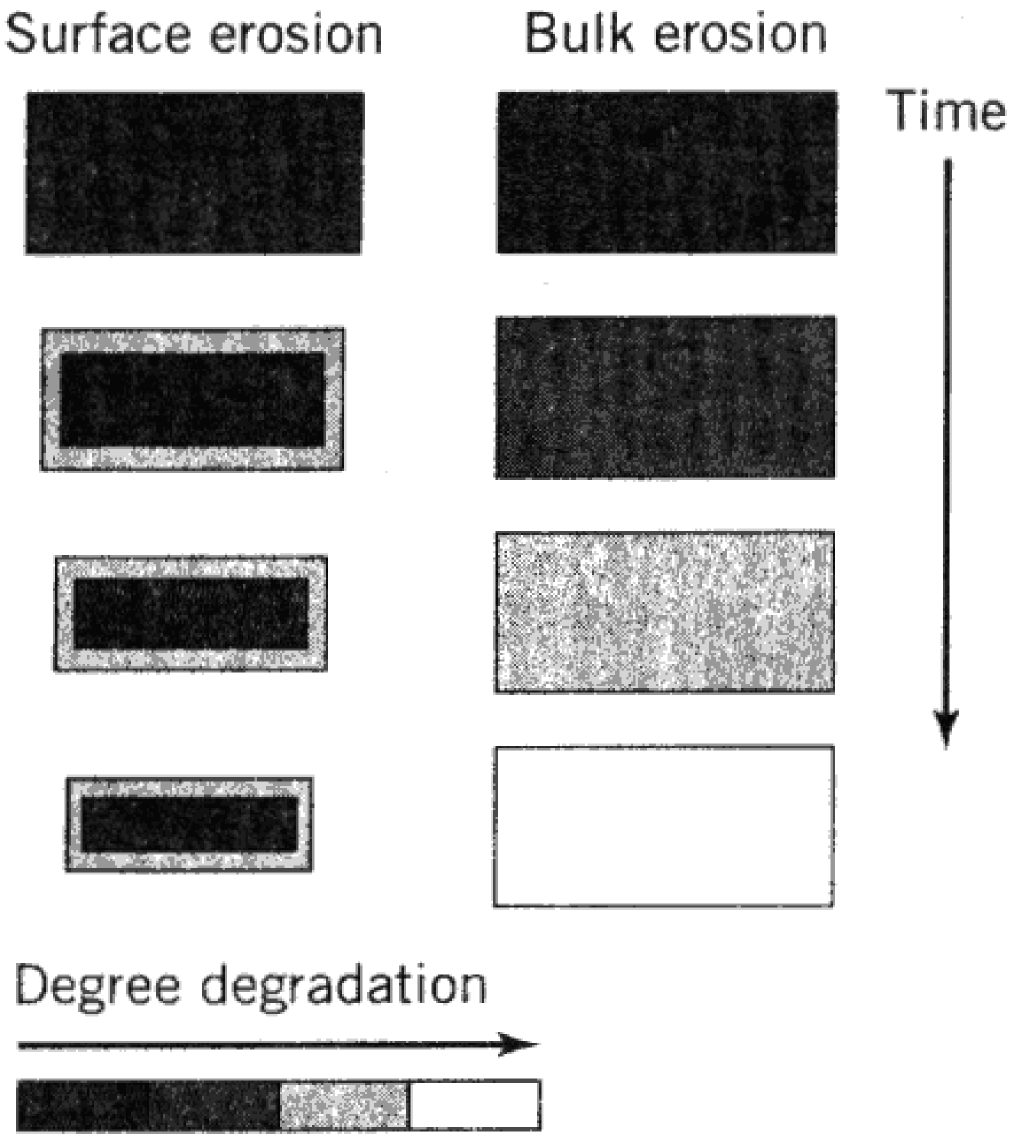
- water sorption
- reduction of mechanical properties (modulus & strength)
- reduction of molar mass
- weight loss

Degradation Schemes

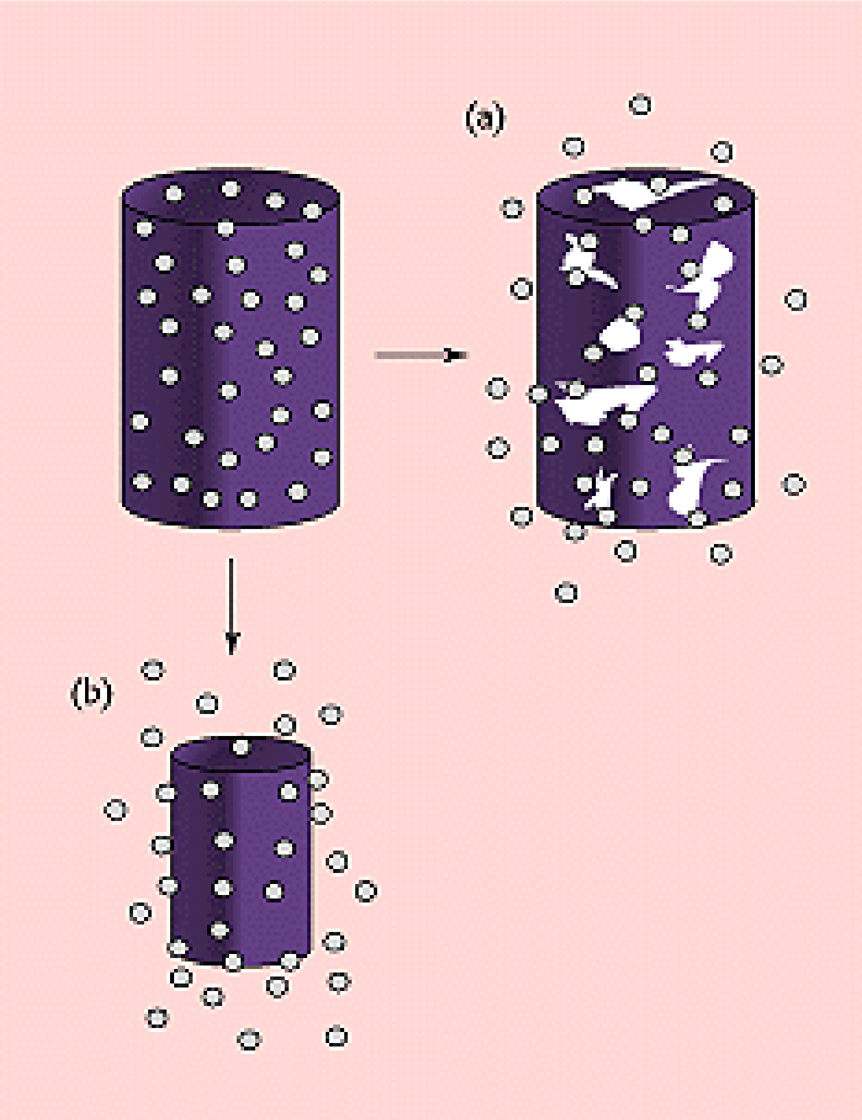
- Surface erosion (poly(ortho)esters and polyanhydrides)
  - Sample is eroded from the surface
  - Mass loss is faster than the ingress of water into the bulk

- Bulk degradation (PLA,PGA,PLGA, PCL)
  - Degradation takes place throughout the whole of the sample
  - Ingress of water is faster than the rate of degradation

Polymer Degradation by Erosion (1)



Erodible Matrices or Micro/Nanospheres



- (a)
  - ✓ Bulk-eroding system
- (b)
  - ✓ Surface-eroding system

General Fabrication Techniques

Molding (formation of drug matrix)

- compression molding
- melt molding
- solvent casting

Molding (compression molding) (1)

- Polymer and drug particles are milled to a particle size range of 90 to 150 µm
- Drug / Polymer mix is compressed at ~30,000 psi
- Formation of some types of tablet / matrix

Molding (melt molding / casting) (1)

- Polymer is heated to ~10°C above it melting point (T_m) to form a viscous liquid
- Mix drug into the polymer melt
- Shaped by injection molding

Molding (melt molding / casting) (2)

Advantages

- More uniform distribution of drug in polymer
- Wide range of shapes possible

Disadvantages

- Thermal instability of drugs (heat inactivation)
- Drug / polymer interaction at high temperature
- Cost

Molding (Solvent casting) (1)

- Co-dissolve drug and polymer in an organic solvent
- Pour the drug / polymer solution into a mold chilled under dry ice
- Allow solvent to evaporate
- Formation of a drug-polymer matrix

Molding (Solvent casting) (2)

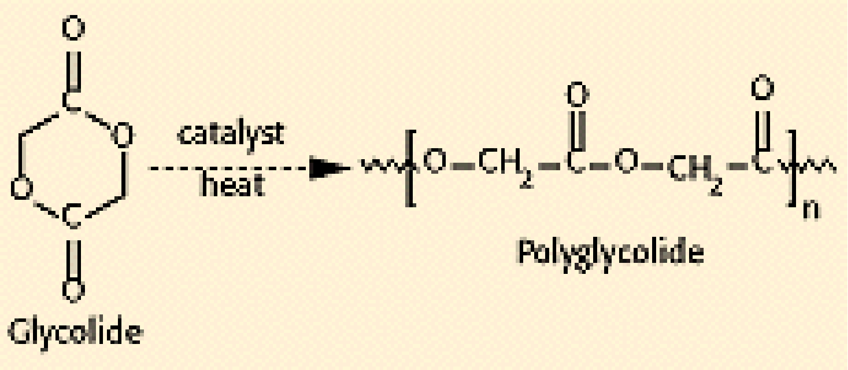
Advantages

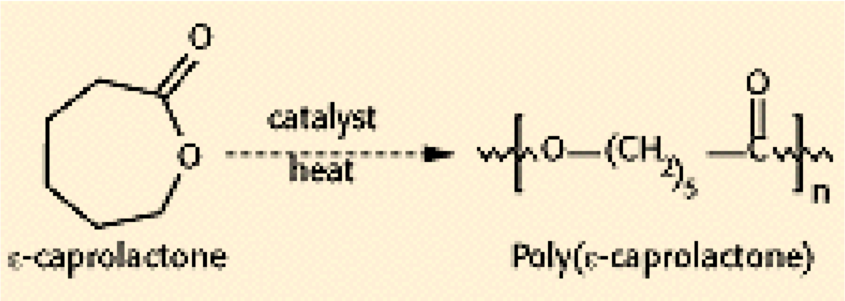
- Simplicity
- Room temperature operation
- Suitable for heat sensitive drugs

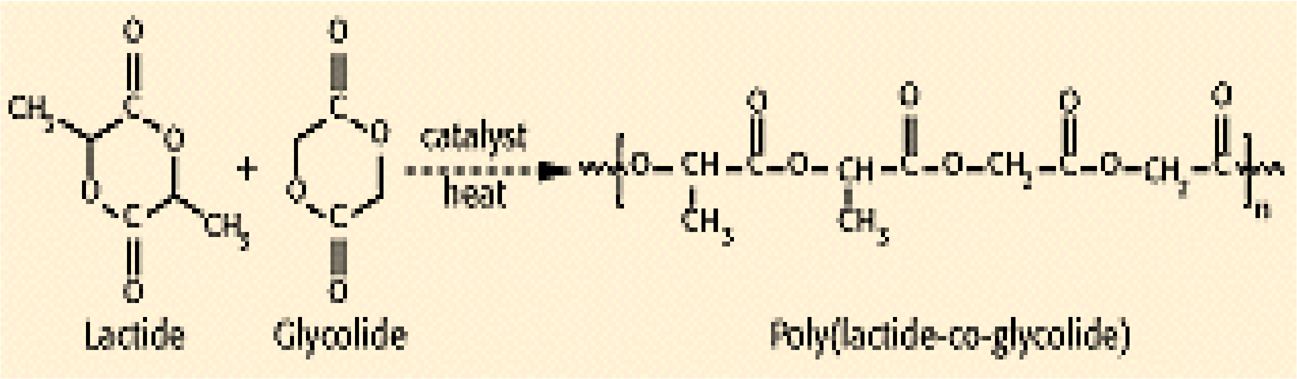
Disadvantages

- Possible non-uniform drug distribution
- Proper solvents for drugs and polymers
- Fragility of the system
- Unwanted matrix porosity
- Use of organic solvents / Solvent residues

Polyesters


catalyst
heat
Glycolide
Polyglycolide


catalyst
heat
ε-caprolactone
Poly(ε-caprolactone)


catalyst
heat
Lactide
Glycolide
Poly(lactide-co-glycolide)

Comparison

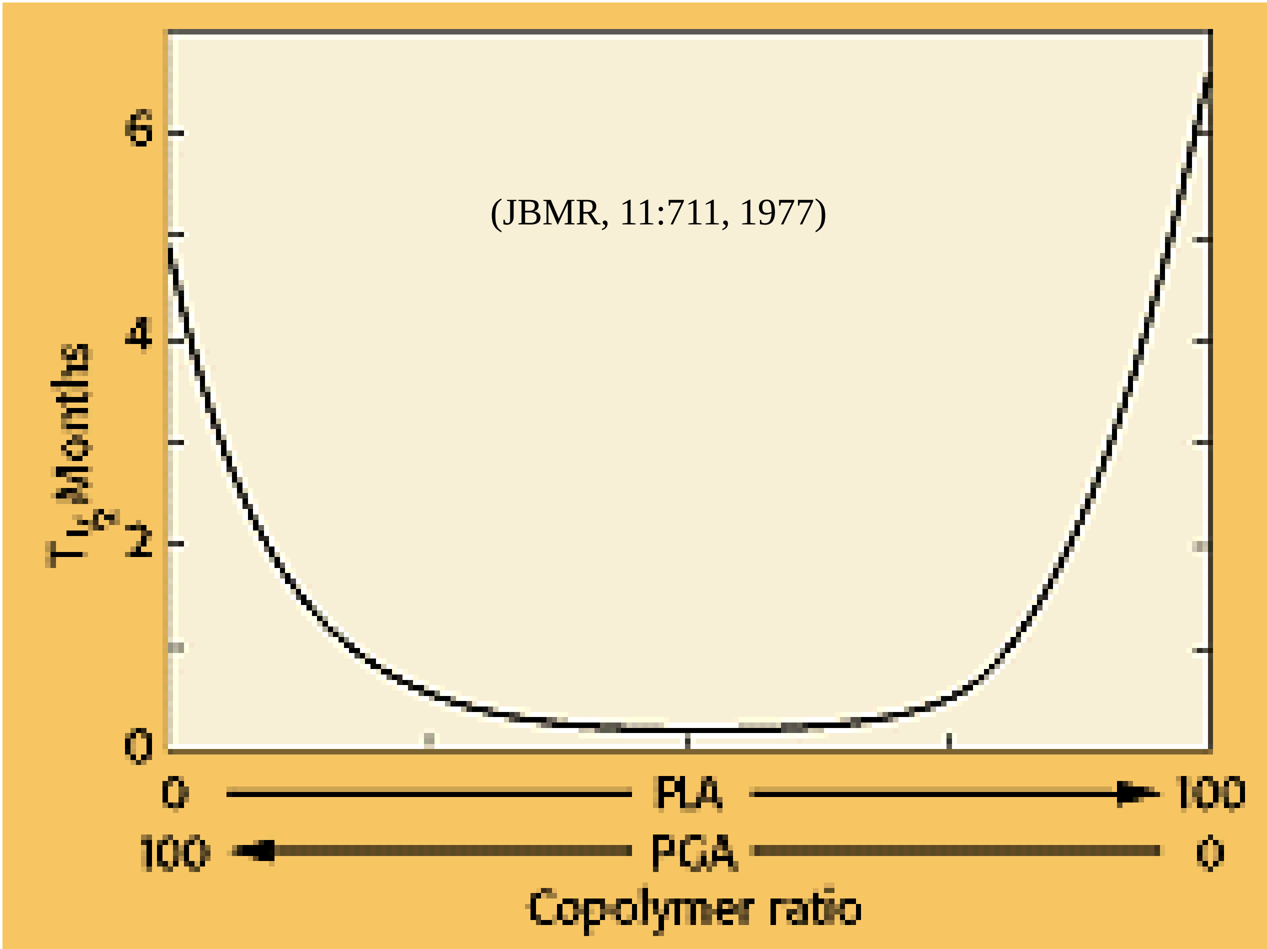
Properties	PLA	PS	PVC	PP
Yield Strength, MPa	49	49	35	35
Elongation, %	2.5	2.5	3.0	10
Tensile Modulus, GPa	3.2	3.4	2.6	1.4
Flexural Strength, MPa	70	80	90	49

Mobley, D. P. Plastics from Microbes. 1994

Factors Influence the Degradation Behavior

- Chemical Structure and Chemical Composition
- Distribution of Repeat Units in Multimers
- Molecular Weight
- Polydispersity
- Presence of Low Mw Compounds (monomer, oligomers, solvents, plasticizers, etc)
- Presence of Ionic Groups
- Presence of Chain Defects
- Presence of Unexpected Units
- Configurational Structure
- Morphology (crystallinity, presence of microstructure, orientation and residue stress)
- Processing methods & Conditions
- Method of Sterilization
- Annealing
- Storage History
- Site of Implantation
- Absorbed Compounds
- Physiochemical Factors (shape, size)
- Mechanism of Hydrolysis (enzymes vs water)

Poly(lactide-co-glycolide) (PLGA)



Factors That Accelerate Polymer Degradation

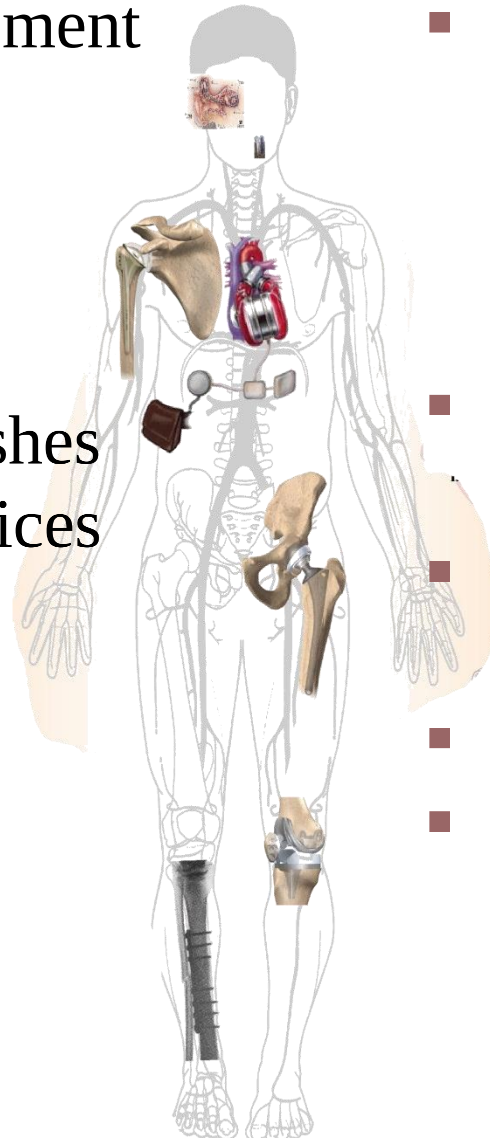
- More hydrophilic backbone.
- More hydrophilic endgroups.
- More reactive hydrolytic groups in the backbone.
- Less crystallinity.
- More porosity.
- Smaller device size.

Methods of Studying Polymer Degradation

- Morphological changes (swelling, deformation, bubbling, disappearance…)
- Weight lose
- Thermal behavior changes
  - Differential Scanning Calorimetry (DSC)
- Molecular weight changes
  - Dilute solution viscosity
  - Size exclusion chromatograpgy(SEC)
  - Gel permeation chromatography(GPC)
  - MALDI mass spectroscopy
- Change in chemistry
  - Infared spectroscopy (IR)
  - Nuclear Magnetic Resonance Spectroscopy (NMR)
  - TOF-SIMS

Medical Applications of Biodegradable Polymers

- Wound management
  - Sutures
  - Staples
  - Clips
  - Adhesives
  - Surgical meshes
- Orthopedic devices
  - Pins
  - Rods
  - Screws
  - Tacks
  - Ligaments



- Dental applications
  - Guided tissue regeneration Membrane
  - Void filler following tooth extraction
- Cardiovascular applications
  - Stents
- Intestinal applications
  - Anastomosis rings
- Drug delivery system
- Tissue engineering