BIODEGRADABLE MATERIALS FOR MEDICAL APPLICATIONS

Biomedical Engineering

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Overview

- **INTRODUCTION TO BIOMATERIALS**
- **BIODEGRADABLE MATERIALS**
  - SYNTHETIC POLYMERS
  - MAGNESIUM ALLOYS BASED
- **PRELIMINARY MATHEMATIC MODEL FOR DEGRADATION PROCESS**

INTRODUCTION TO BIOMATERIALS

During the last two decades, significant advances have been made in the development of biocompatible and biodegradable materials for medical applications.

In the biomedical field, the goal is to develop and characterize artificial materials or, in other words, “spare parts” for use in the human body to MEASURE, RESTORE and IMPROVE physical functions and enhance survival and quality of life.

What’s a biomaterial?

1980 - *Passive* and *inert* point of view

Any substance or drugs, of synthetic or natural origin, which can be used for any period alone or as part of a system and that increases or replaces any tissue, organ or function of the body

1990 – *Active* point of view

Non-living material used in a medical device and designed to interact with biological systems

Classification of biomaterials

First generation: INERT

Do not trigger any reaction in the host: neither rejected nor recognition

→ “do not bring any good result”

Second generation: BIOACTIVE

Ensure a more stable performance in a long time or for the period you want

Third generation: BIODEGRADABLE

It can be chemically degraded or decomposed by natural effectors (weather, soil bacteria, plants, animals)

Mean features for medical applications

BIOFUNCTIONALITY

Playing a specific function in physical and mechanical terms

BIOCOMPATIBILITY

Concept that refers to a set of properties that a material must have to be used safely in a biological organism

What is a biocompatible material?

1) **Synthetic or natural material used in intimate contact with living tissue (it can be implanted, partially implanted or totally external).**
2) **Biocompatible materials are intended to interface with biological system to EVALUATE, TREAT, AUGMENT or REPLACE any tissue, organ or function of the body.**

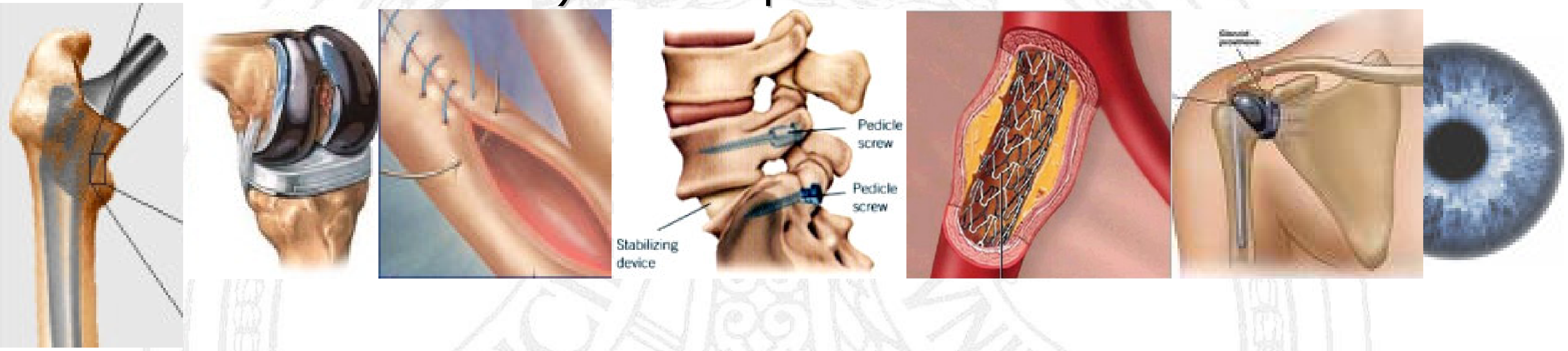
A biocompatible device must be fabricated from materials that will not elicit an adverse biological response

Biocompatible material features

1) Absence of carcinogenicity (the ability or tendency to produce cancer)
2) Absence of immunogenicity (absence of a recognition of an external factor which could create rejection)
3) Absence of teratogenicity (ability to cause birth defects)
4) Absence of toxicity

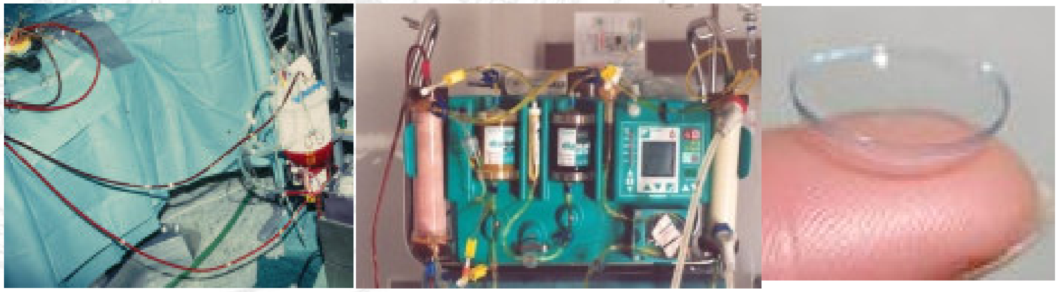
Applications for Medical Devices

1)Total implanted device



2)Partially implanted device

3)Totally externals device



Some examples

Categories of implantable materials	Composition	Use
Polymers carbon	Gore-Tex(PTFE expanded)	Thoracic and abdomen rebuilding Filling Defect of the soft tissue Cranio-facial reconstruction
	Poly-propylene (Marlex, Prolene)	Thoracic and abdominal wall reconstruction Surgical Suture
	Poly-ethylene (Medpore)	Filling Defect of the soft tissue
	Poly-ethylene tereftalato (Dacron,Mersilene)	Surgical Suture Vascular prosthesis
	Poliuretano	Coating of breast implants
	Polyesters aliphatic (ac. Poly-latic, poly-glycolic ecc.)	Surgical Suture Absorbable mini plates and screws
	Metilmetacrilato (MMA)	Thoracic and abdomen rebuilding Cranio-facial reconstruction

Categories of implantable materials	Composition	Use
Not carbon Polymers	Silicon	Breast implants Prosthetics for increased facial characteristics
Ceramics	Hydroxyapatite	Small cellular defects reconstruction
	Phosphate tricalcium	Small bone defect reconstruction
Metals	Titanium, stainless steels and cobalt and magnesium alloys	Mini plates and screws Orthopedic prosthesis Surgical tools

What’s a biodegradable implant?

Once implanted, should maintain its mechanical properties until it is no longer needed and then be absorbed and excreted by the body, leaving no trace

Biodegradable implants are designed to overcome the disadvantages of permanent metal-based devices

Problems caused by permanent implants

- **Physical irritations**
- **Chronic inflammatory local reactions**
- **Thrombogenicity and long term endothelial dysfunction (for cardiovascular applications)**
- **Inability to adapt to growth**
- **Not allowed or disadvantageous after surgery**
- **Stress shielding, corrosion, accumulation of metal in tissues (for internal fixation applications)**
- **Repeat surgery necessary**

Advantages of biodegradable implants

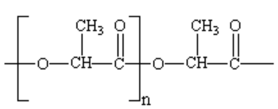
- **More physiological repair**
- **Possibility of tissue growth**
- **Less invasive repair**
- **Temporary support during tissue recovery**
- **Gradual dissolution or absorption by the body afterwards.**

Note: these implants may act a new biomedical tool satisfying requirement of compatibility and integration.

More used materials

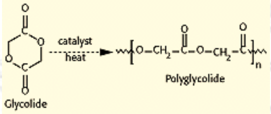
❑ Synthetic polymers:

- Poly-lactic acid (PLA) and its isomers and copolymers

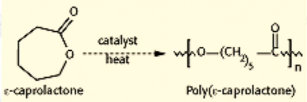


$$-\!\left[O-\underset{}{CH(CH_3)}-\overset{O}{\overset{\|}{C}}\right]_n\!-O-CH(CH_3)-\overset{O}{\overset{\|}{C}}-$$

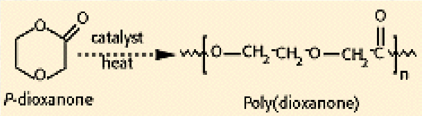
- Poly-glycolic acid (PGA)



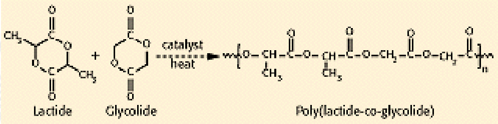
- Poly-caprolactone (PCL)



- Poly(dioxanone)



- Poly-lactide-co-glycolide.



■ Magnesium alloys based:

- Mg, Zn, Li, Al, Ca and rare earths are the main elements used.

Synthetic Polymers

General criteria of selection for medical applications

- **Mechanical properties and time of degradation must match application needs**

Ideal polymer:

- **must be sufficiently strong until surrounding tissue has healed**
- **does not invoke inflammatory or toxic response**
- **to be metabolized in the body after fulfilling its purpose, leaving no trace**
- **to be easily processable into the final product form**
- **must demonstrates acceptable shelf life**
- **to be easily sterilized**

Synthetic Polymers

- Wound management
  - Sutures
  - Clips
  - Adhesives
  - Surgical meshes
- Orthopedic devices
  - Pins (spilli)
  - Rods (barre)
  - Screws (viti)
  - Tacks (chiodini)
  - Ligaments
- Tissue engineering
- Dental applications
  - Guided tissue regeneration
  - Membrane
  - Void filler following tooth extraction
- Cardiovascular applications
  - Stents
- Intestinal applications
  - Anastomosis rings
- Drug delivery system
  - Covering of permanent implants

Mean applications

Synthetic Polymers

Main advantages

- Good biocompatibility
- Possibility of changing in composition and in physical-mechanical properties
- Low coefficients of friction
- Easy processing and workability
- Ability to change surface chemically and physically
- Ability to immobilize cells or biomolecules within them or on the surface (Drug Eluting Stent)

Synthetic Polymers

Main disadvantages

- **Presence of substances that may be issued in the body [monomers (*toxic*), catalysts, additives] after degradation**
- **Ease of water and biomolecules absorption from surrounding**
- **Low mechanical properties**
- **In some cases, difficult sterilization**

Note: the final properties of a device depends both intrinsic molecular structure of the polymer and chemical and mechanical processes which it is undergone.

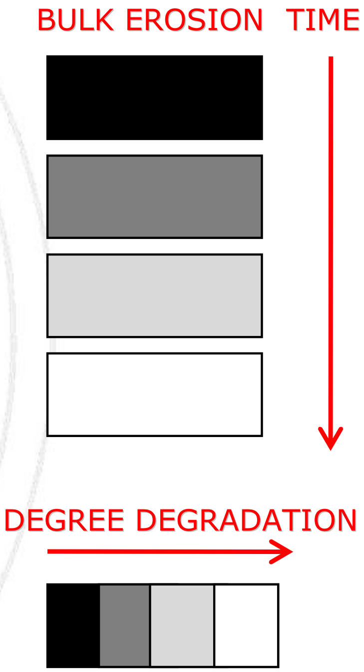
Synthetic Polymers

Polymers degradation (bulk erosion)

Implanted materials subject to degradation processes

Saline solution in human body as an excellent electrolyte that facilitates **hydrolysis** mechanisms

Most polymers used in medical devices allows the spread of water within molecular structure and can therefore result in processes hydrolysis



Magnesium Alloys Based

- Orthopedic devices
    - Pins
    - Rods
    - Screws
    - Tacks (chiodini)

- Cardiovascular applications
    - Stents

Mean applications

Magnesium Alloys Based

Main advantages

- **High biocompatibility (Mg is present into the body and then recognized as a not foreign element)**
- **Alloy's elements are dissolved into human body during the degradation process → Not toxic risk**
- **Not visible by X-ray and not seen by CT or MRI → Do not cause any artifacts.**

Magnesium Alloys Based

Main disadvantages

- Too high corrosion rate *(Es: Mg stents corrode quickly both in vivo than in vitro after ~ 1 month)*.
- Degradation occurs before the end of healing process

How to adjust this ??

By alloy and surface treatment

or

By mechanical pre-processing to affect biocorrosion resistance

Magnesium Alloys Based

Metal degradation

- Biodegradability expressed in terms of corrosion.
- Very slow process, "ideally" should not influence device mechanical properties until tissue healings not over
- Biocompatibility is reduced from ion accumulation released from metal
- Rate of corrosion and mechanisms vary with applied "shear-stress"

Polymers VS Metals

Considerations in the selection

- Strength
- Overall time and rate of degradation/corrosion (a very high degradation rate can be associated with inflammations)
- Biocompatibility
- Lack of toxicity

Polymers VS Metals

Orthopedic applications (screws, tacks…)

- Metal alloys present greatest load bearing, with similar results to non biodegradable metals (stainless steel)
- Polymers present lower load bearing. Appropriate pre-processing may improve their mechanical characteristics

Polymers VS Metals

Vascular applications (stents…)

- Magnesium alloys degrade too fast in biological environment and they dissolve in the body, not permitting the correct vascular remodeling. Mg is an element that exists naturally into the body, then it is good tolerated

- Polymers degrade slower than magnesium alloys. Fundamental to care about degradation product concentration, which may be toxic

Non-linear viscoelastic model

As the material degrades and softens, the applied stresses lead to greater deformations that lead to greater increases in degradation.