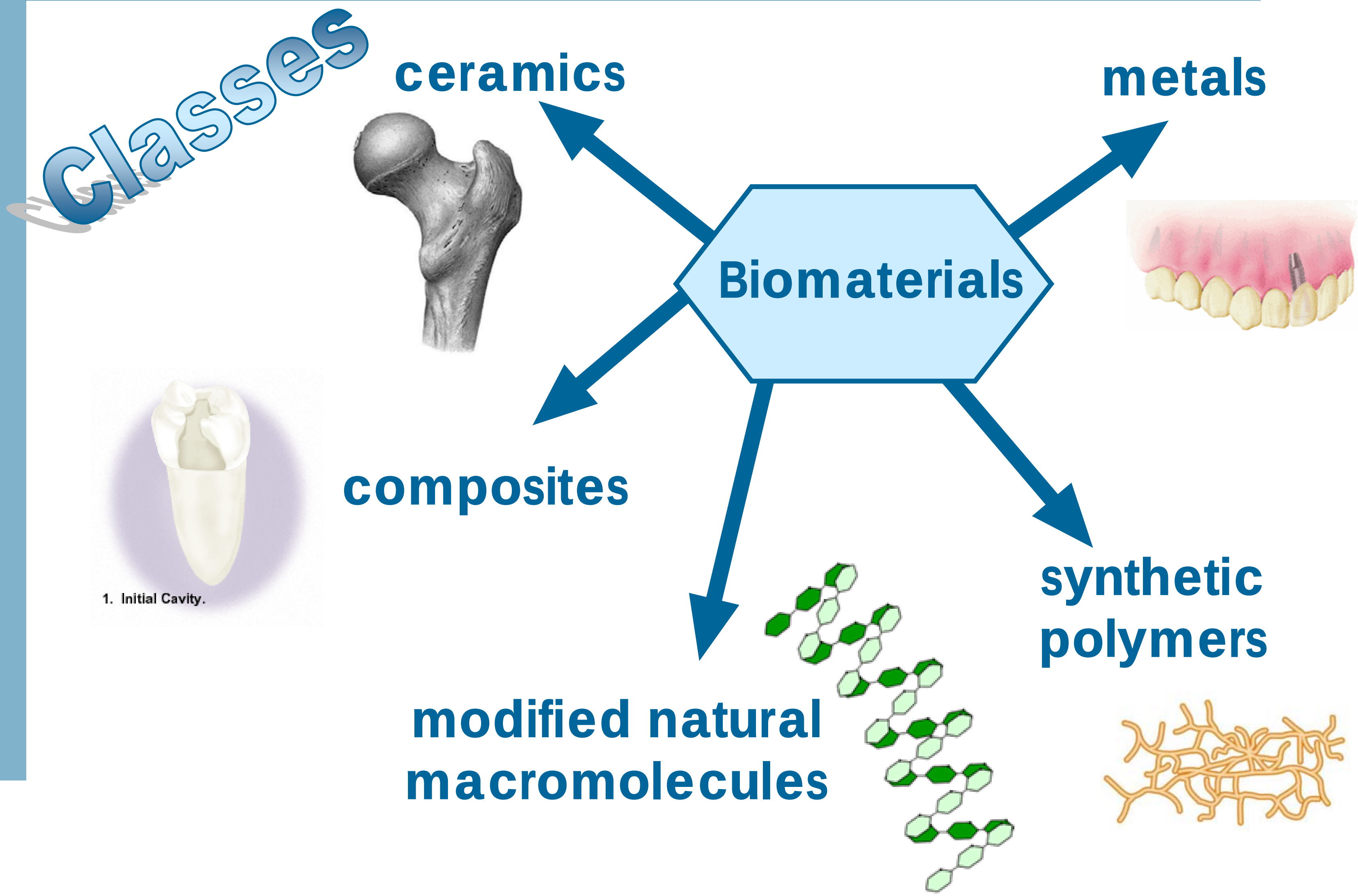
Grupo de Materiais Poliméricos

Prof. Dra Maria Helena Gil

Biomaterials



Biomaterials

Materiais	Vantagens	Desvantagens	Aplicações clínicas
Polímeros	Elasticidade; fácil de preparar; baixa densidade	Baixa força mecânica; degradação	Suturas; veias; dentes; tendões artificiais
Metais	Força de tensão elevada; alta resistência ao uso	Baixa biocompatibilidade corrosão em meios fisiológicos; alta densidade	Ortopedia (parafusos, placas); implantes dentários
Cerâmicos	Boa compatibilidade resistência à corrosão; inerte	Baixa força de impacto; difícil de fabricar; alta densidade	Próteses; dentes
Compósitos Cerâmicos revestidos com metal	Boa compatibilidade resistência à corrosão; inerte	Difícil de fabricar	Válvulas artificiais

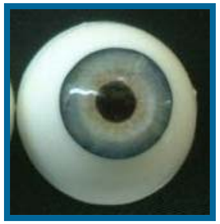
History

> 2000 ⇨ Romans, Chineses, Aztec

⇩

Teeth gold

Glass eye

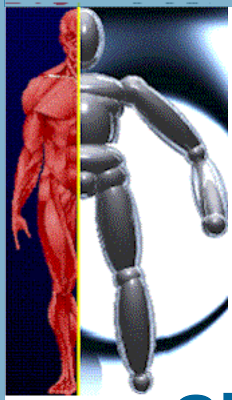


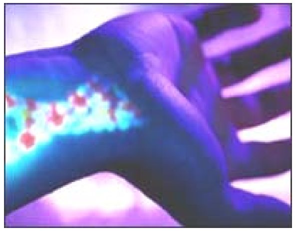
20th century ⇨ Plastics

PMMA ⇨ 1937, Dentistry

PMMA ⇨ 2nd World War ⇨ Lenses

Biomaterials





Biomaterials

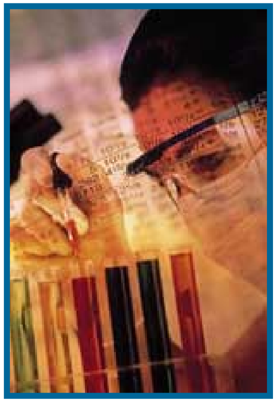
Choice

Preparation

Biocompatibility

Resistance to degradation

Chemical and Physical Characterization



Considerations

(The effect of the organism on the implant and the effect of the implant on the organism)

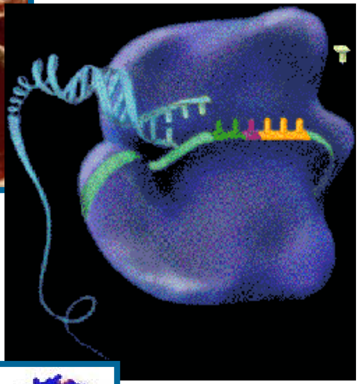
- The material must not leach or release soluble components into the living system
- The living systems must not degrade the implant, unless this degradation is intentional
- Biocompatible
- Non toxic and non carcinogenic
- Chemically inert and stable
- Right mechanical strength
- Right density
- Relatively inexpensive, reproducible and easy to fabricate and process on a large scale

Implants

Success of Biomaterials or implants is highly dependent on three major factors

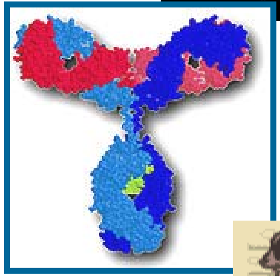
- Properties and biocompatibility of the implant
- Condition of the recipient
- Competency of the surgeon who implants

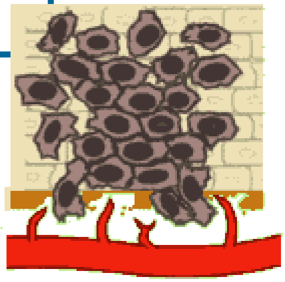
Ideal Biomaterial



Must NOT cause

- Thrombosis
- Alteration of plasma proteins
- Destruction of enzymes
- Adverse immune responses
- Damage to adjacent tissues
- Cancer
- Toxic or allergic reactions

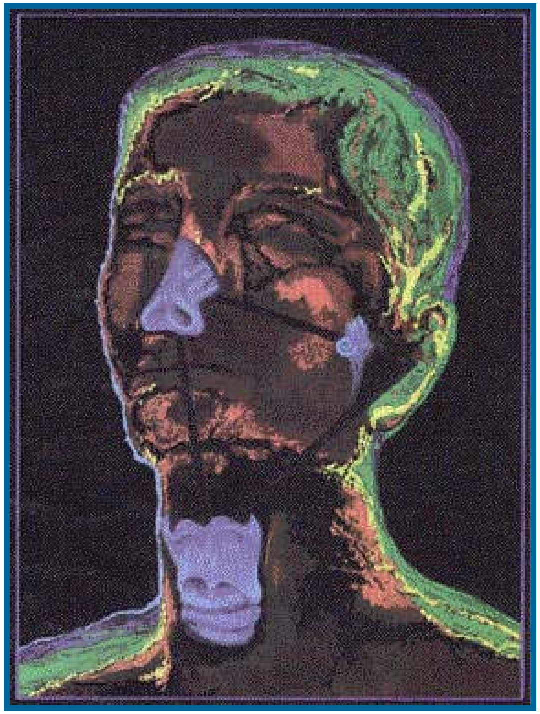




Sterilization

- Steam (15-30 minutes at 121ºC)
- Ethylene oxide (48 hours at 30-50ºC)
- Radiation (UV or Co – 25KGy)
- Electron beam (25KGy)
- Dry heat (> 140ºC)
- New technologies (ClO_2, plasma, ozone, X-ray)

Biomaterials Characterization



Chemical

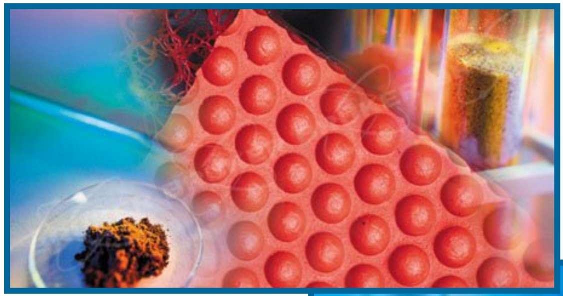
Physical

Biocompatibility

"in vivo"

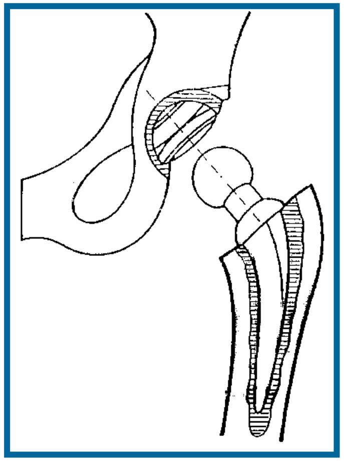
"in vitro"

Surface characterization



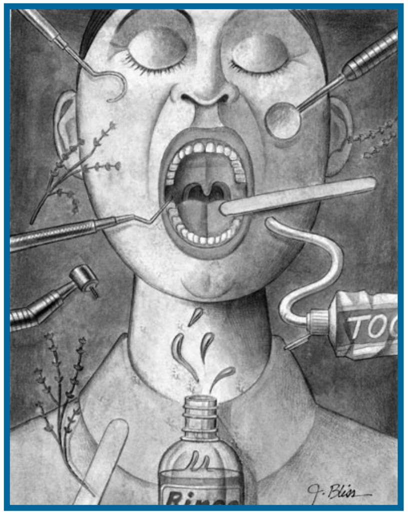
Applications

Orthopedy



Ophtalmology

Dentistry

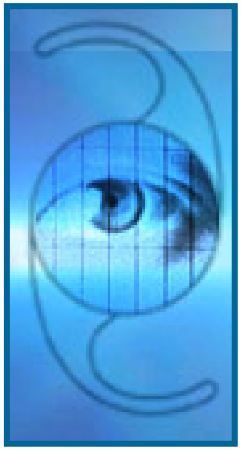


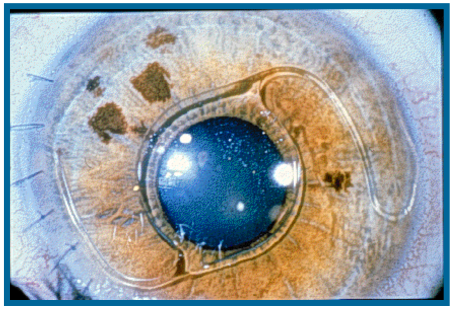
Cosmetic

Cardiology

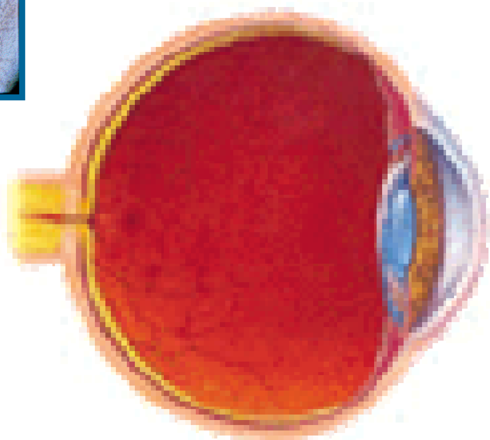
Ophtalmology

Intraocular Lenses



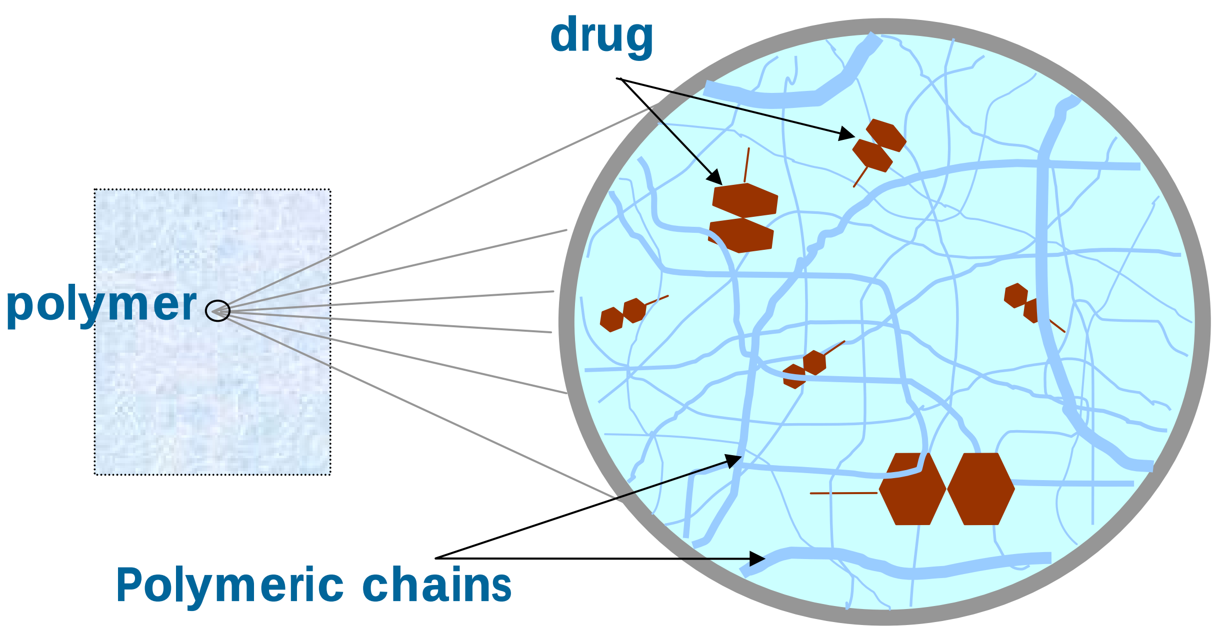


cataract



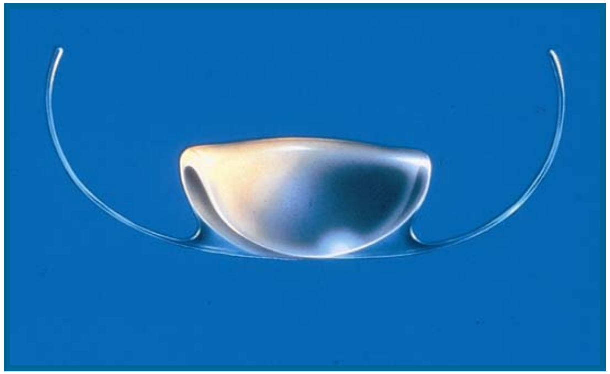
Ophtalmology

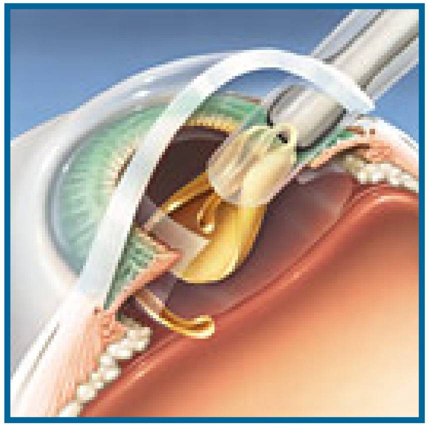
Intraocular Lenses



Ideal copolymers

- release kinetics
- transparence
- flexibility
- hydrophilicity

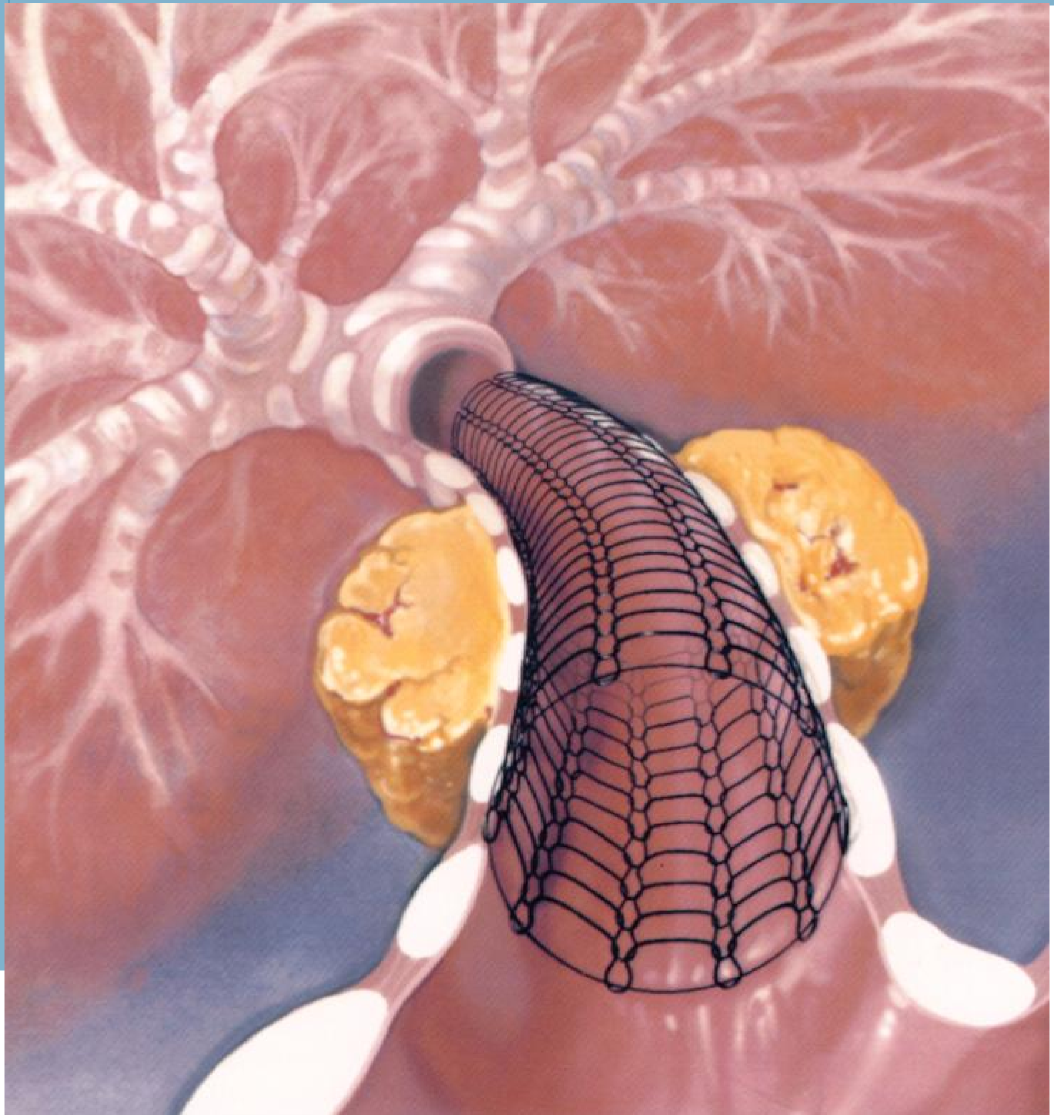




Copolymers

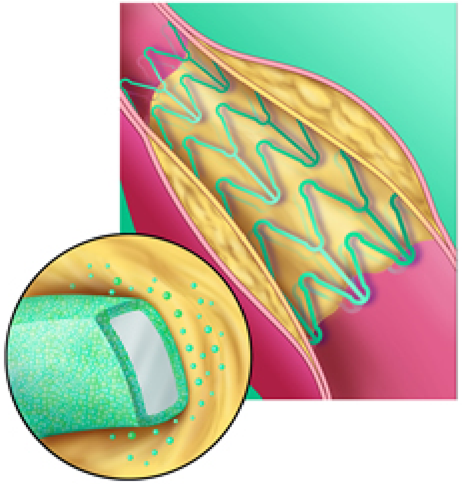
60% MMA / 40% ODMA

80% MMA / 20% EHA

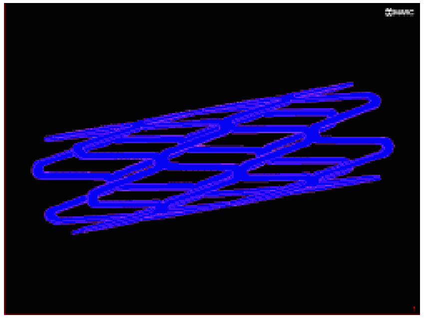


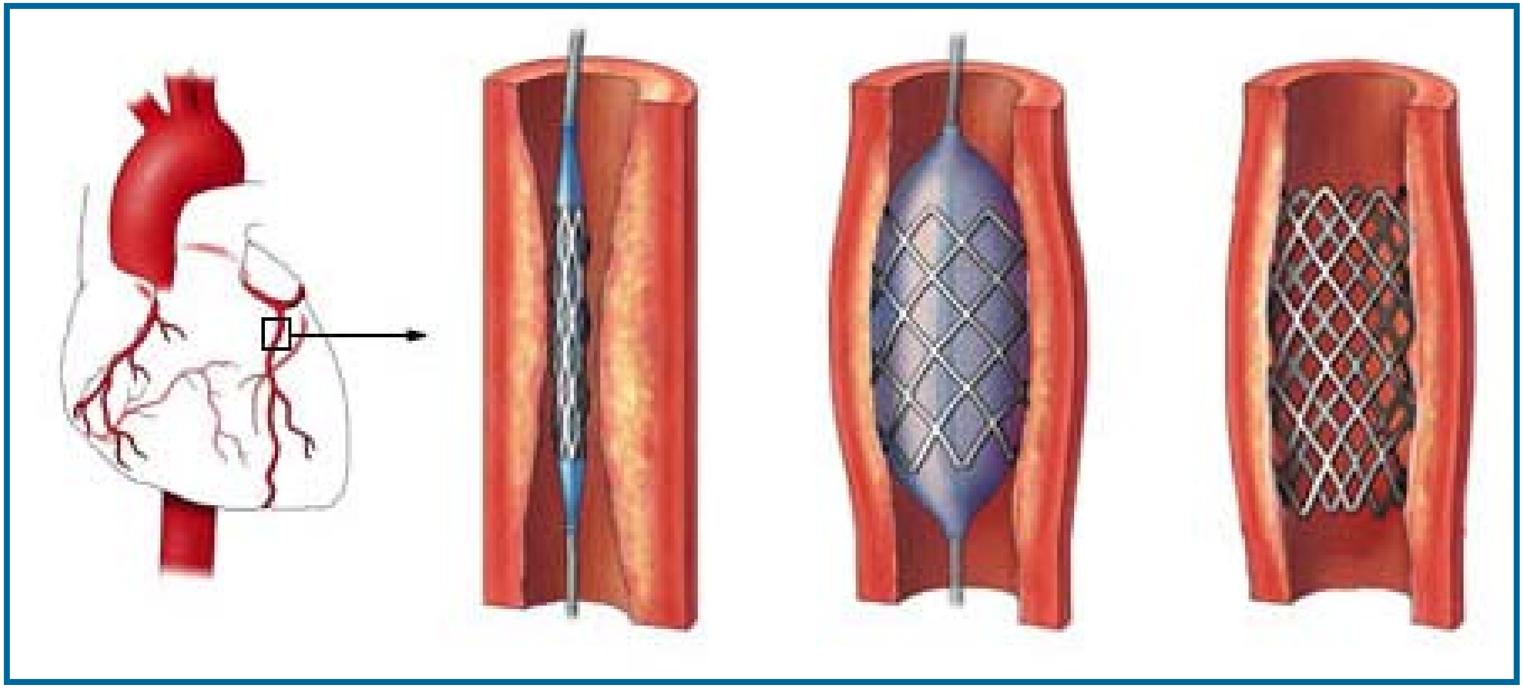
Cardiology

Stent

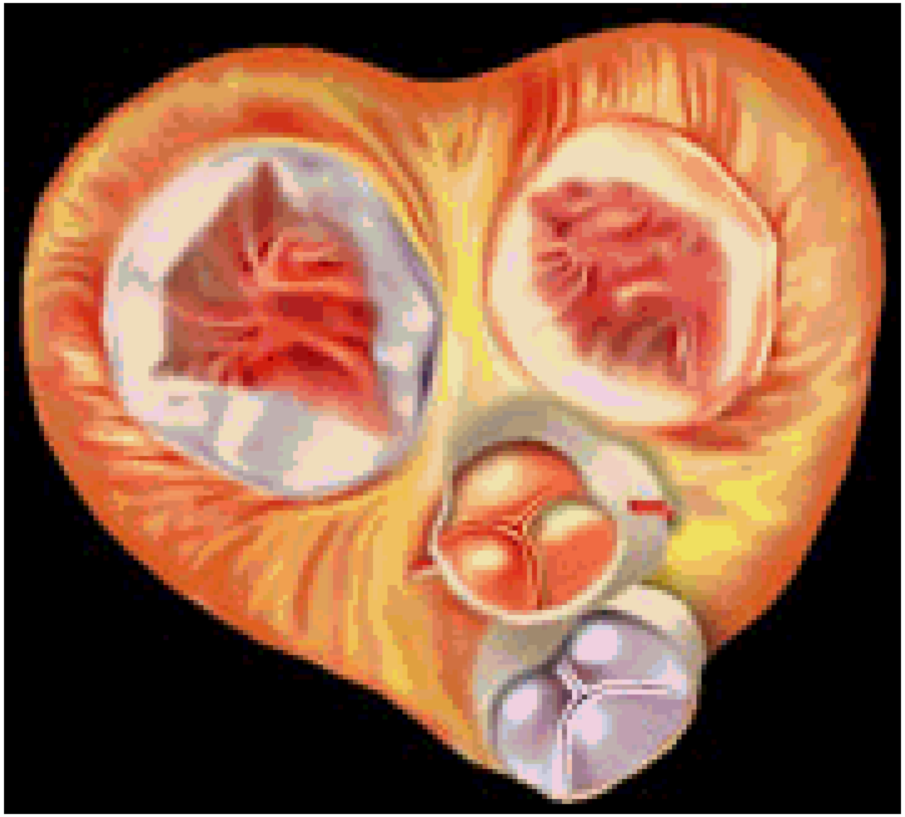


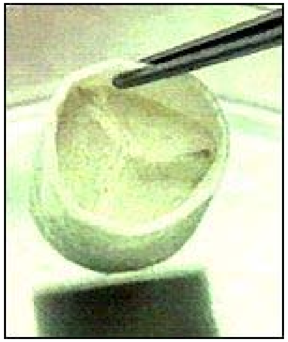
Stent application

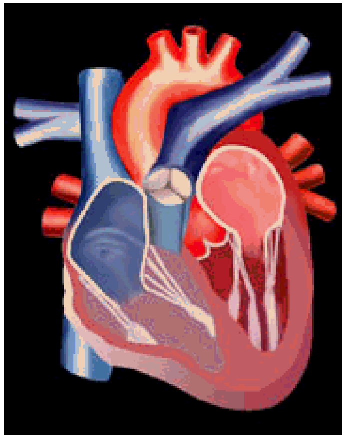




Heart valves

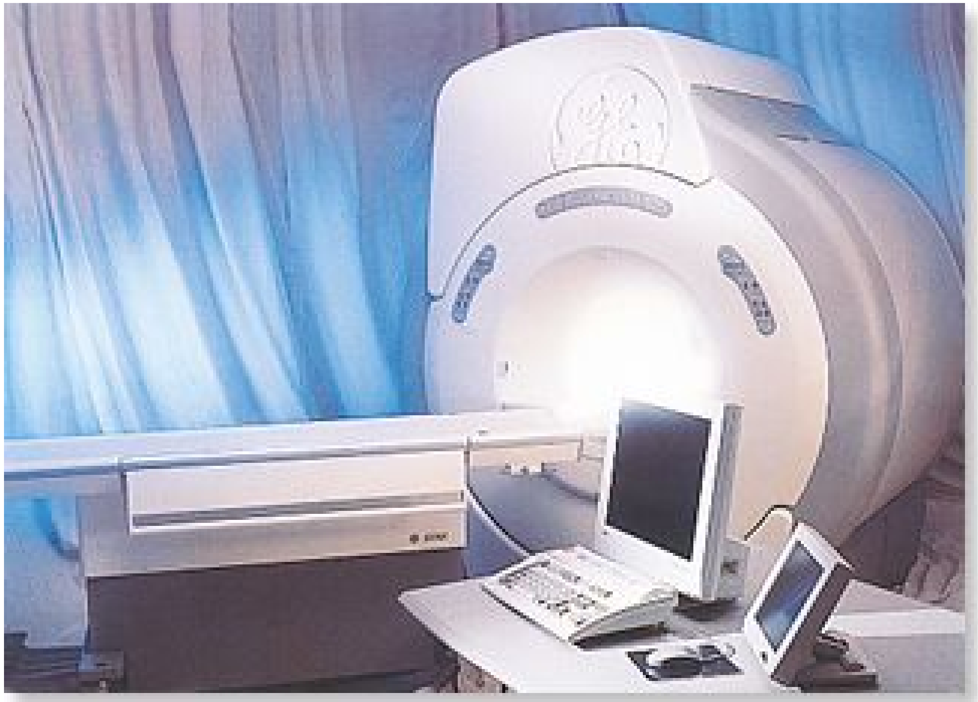






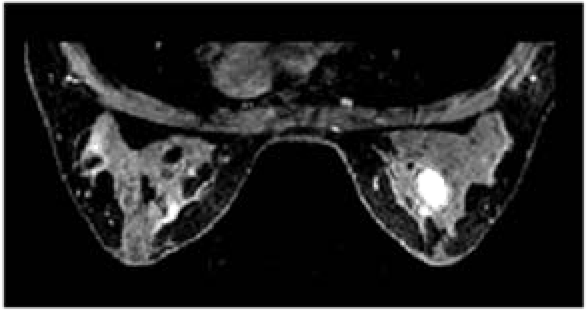
Magnetic Resonance Imaging

MRI

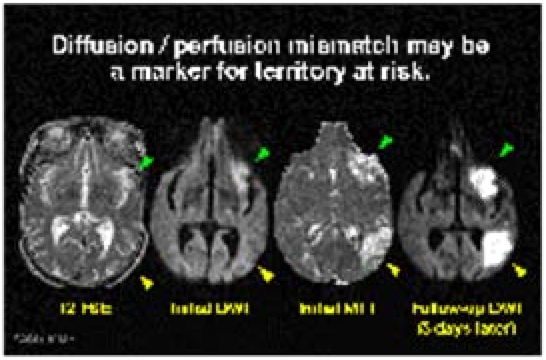


Applications of MRI

heart

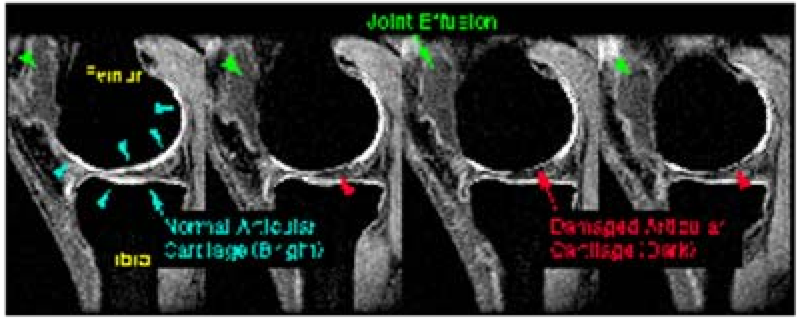


cancer



Brain stroke

nerves

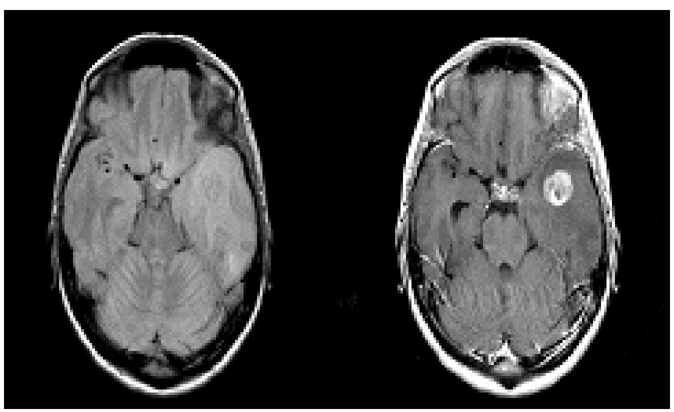


joins

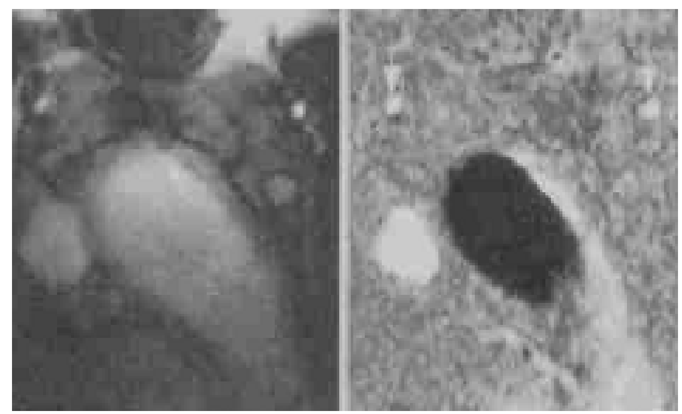
lungs

MRI with Constrast Agents

Gadolinium chelates

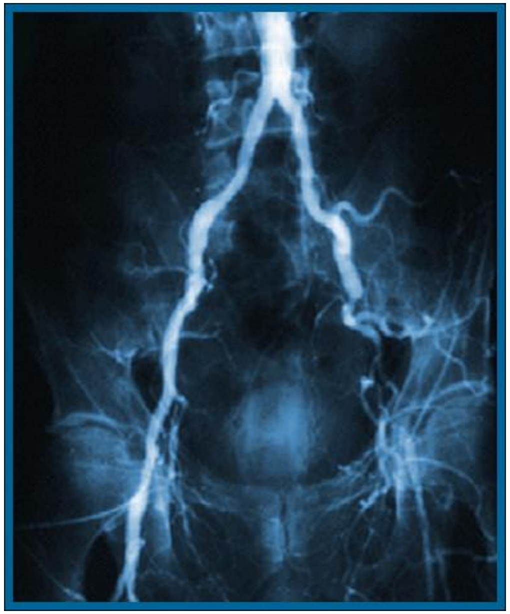


without AC with AC



without AC with AC

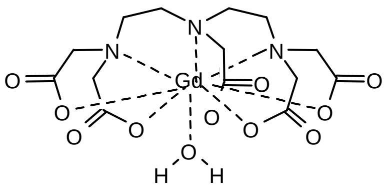
Polymeric Ln(III) Agents in MRA



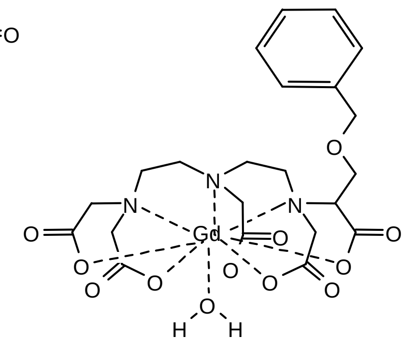
Conventional X-ray

MRI + Contrast Agent

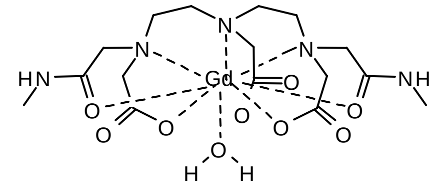
Constrast agents of Gd(III) in medicine



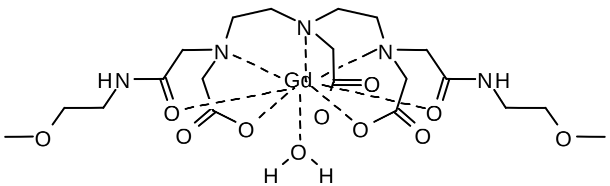
[Gd(DTPA)(H_2O)]$^{-2}$
Magnevist™



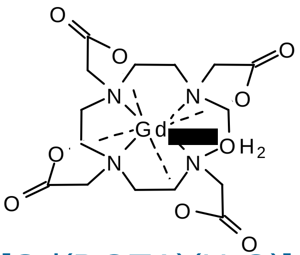
[Gd(BOTPA)(H_2O)]$^{-2}$
Multihance™



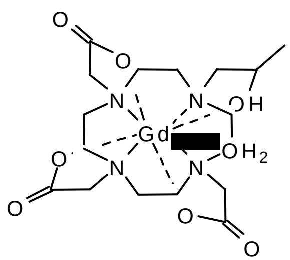
[Gd(DTPA-BMA)(H_2O)]
Omniscan™



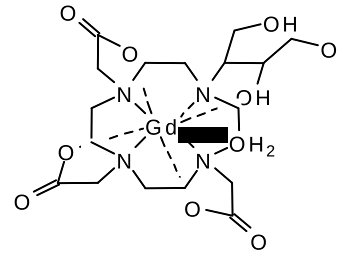
[Gd(DTPA-BMEA)(H_2O)]
OptiMARK™



[Gd(DOTA)(H_2O)]
Dotarem™



[Gd(HP-DO3A)(H_2O)]
ProHance™

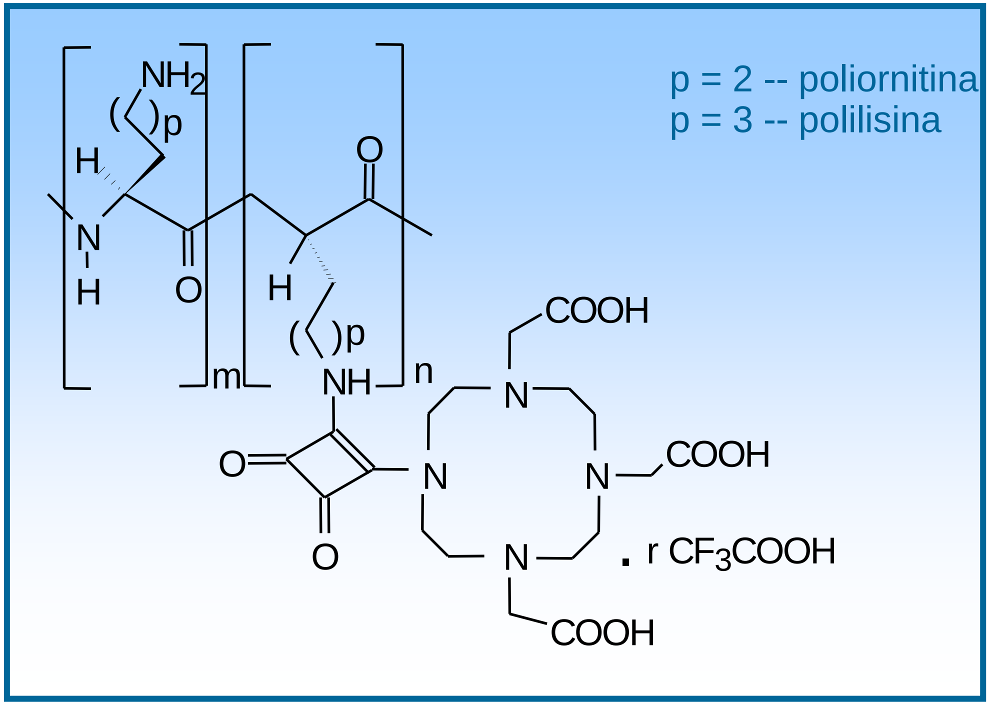


[Gd(DO3a-butrol)(H_2O)]
Gadovist™

MRI

Magnetic Resonance Imaging

Quelate → Polymers

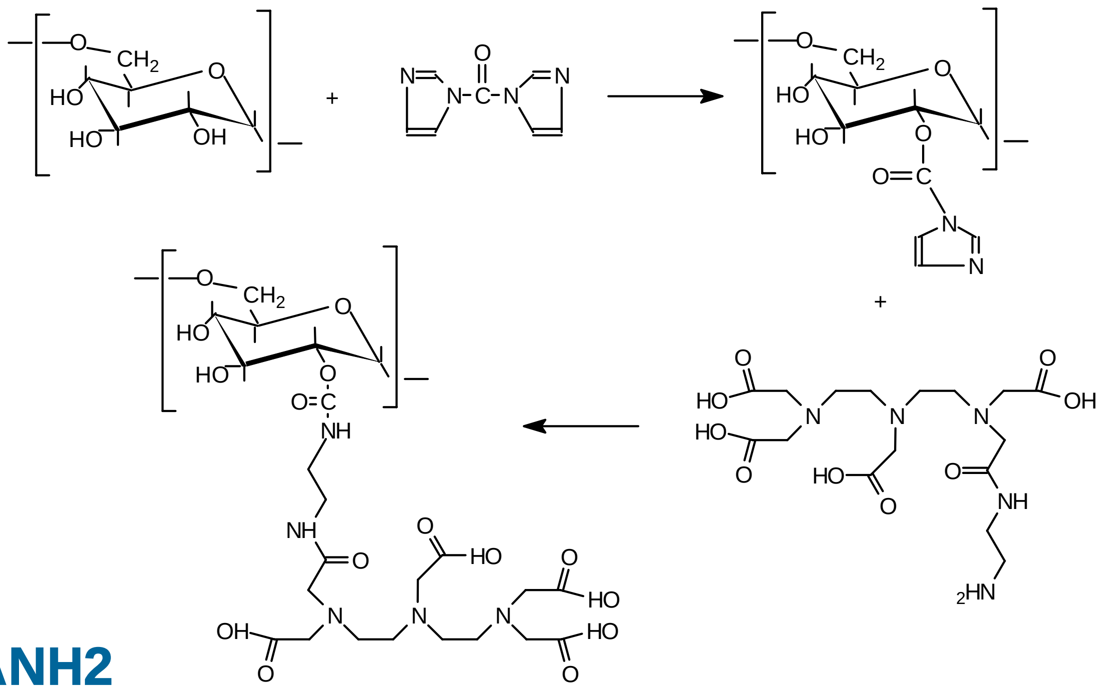


Conjugation of quelates to polymers ex. polylisine, polyornitine

New contrast agents for MRI

Linkage of the chelates to polymers

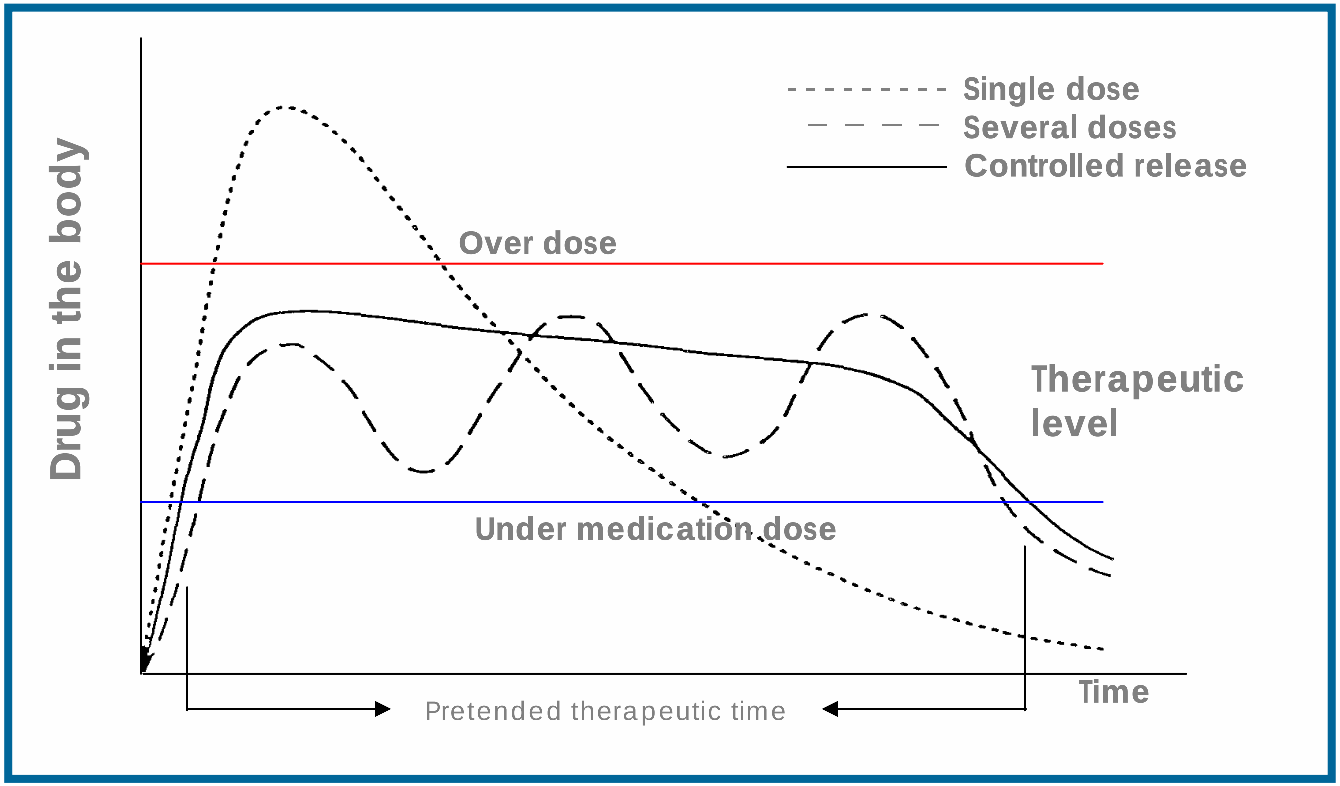
Linkage to Dextran



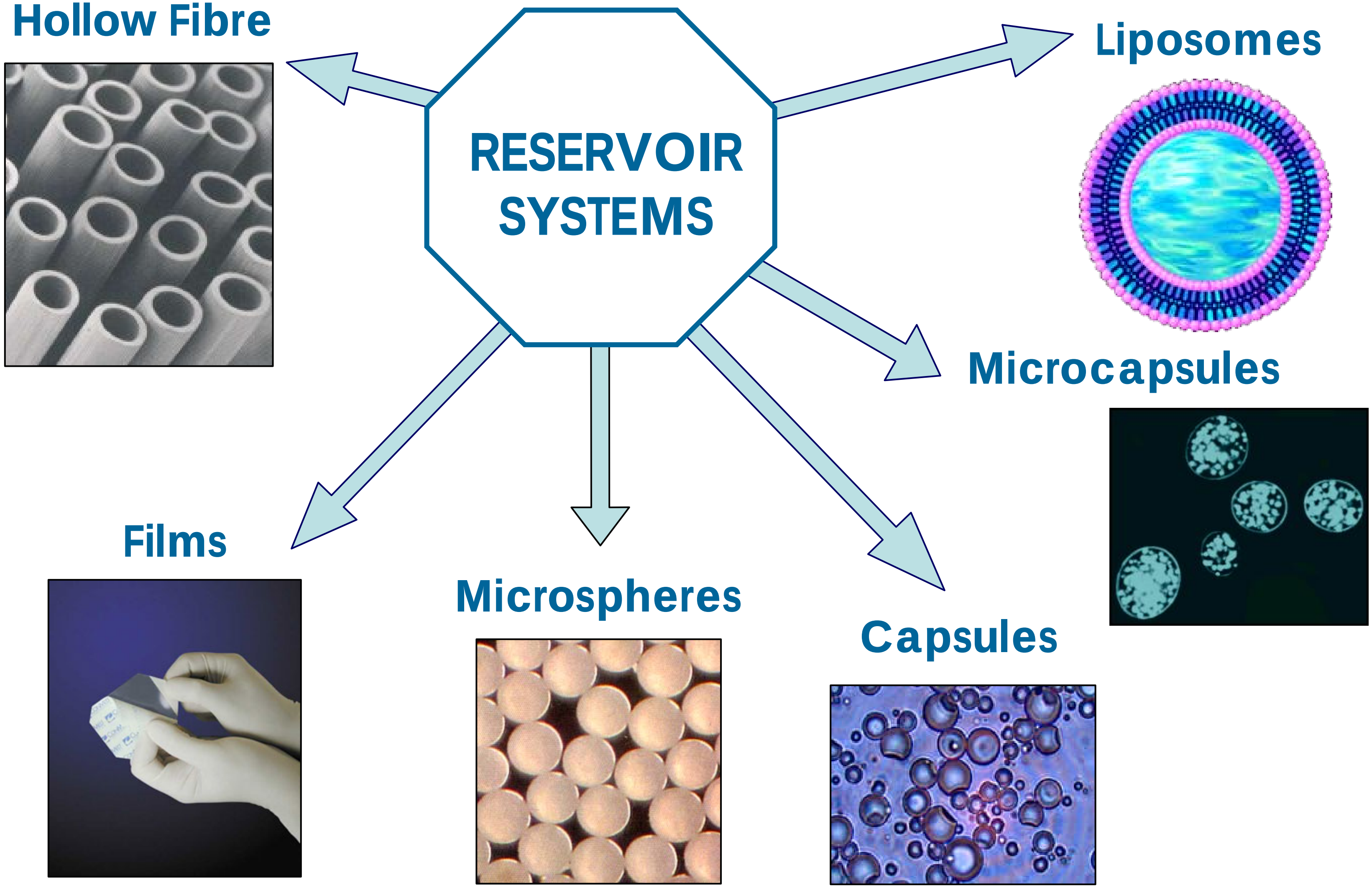
Dextran - DTPANH2

Drug delivery

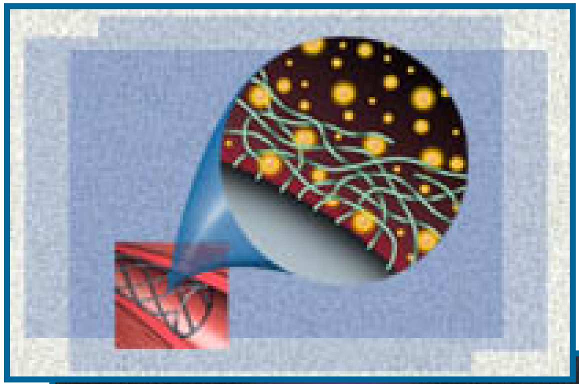
Effect in drug concentration by using different administration methods

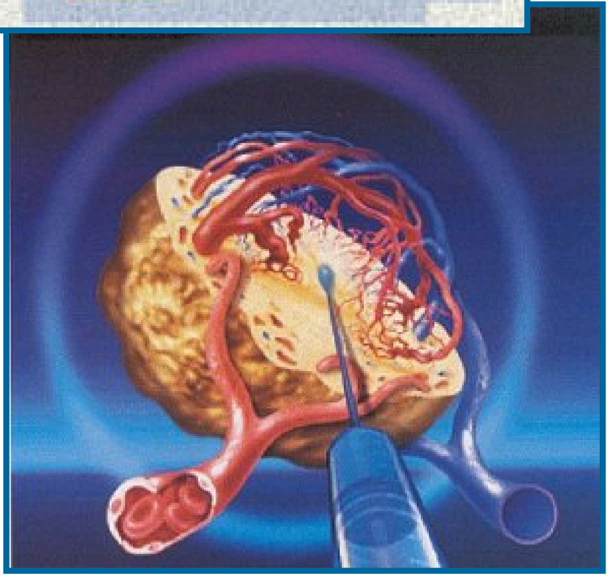


Biomaterials



Biomaterials





Biocompatible

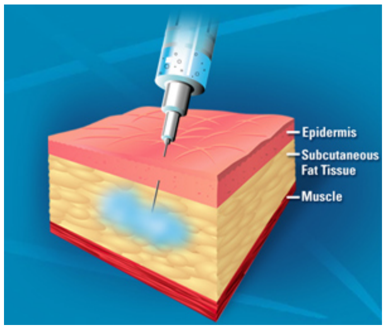
Biodegradable

Carriers for Drug Delivery Systems

Not Induce Inflamation

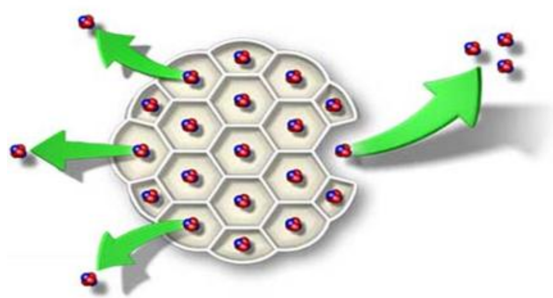
Sterizable

Biomaterials

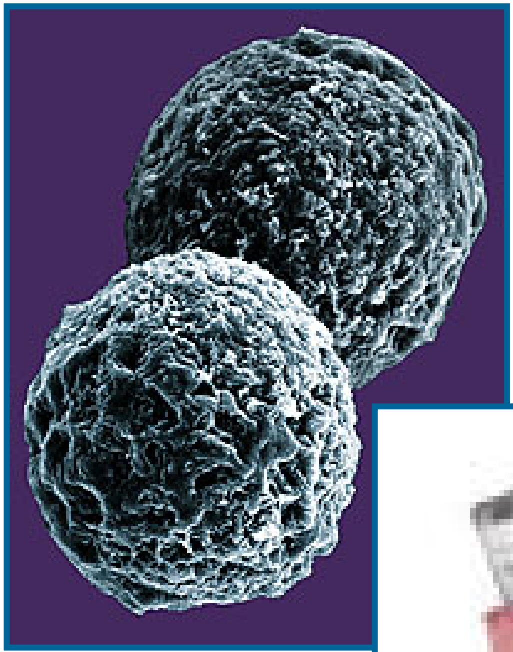


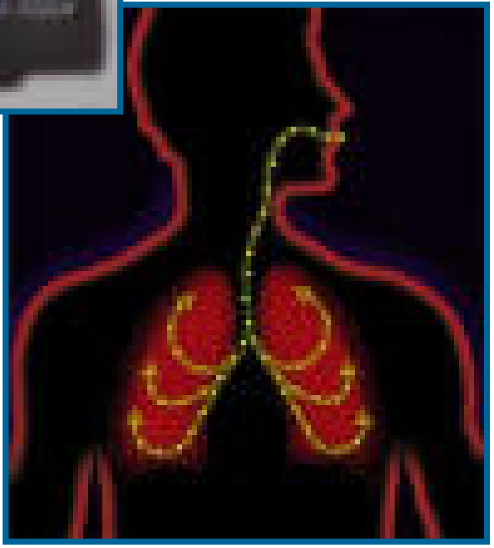
Important

- Chemical composition
- Difusion process
  - Degree of Swelling
  - Crystalline Phase
  - Crosslinking
  - Hydrophilicity
- Problems related to the structure and morphology



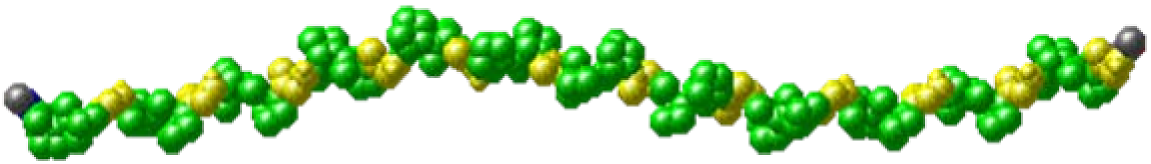
Drug delivery systems
Inhalation



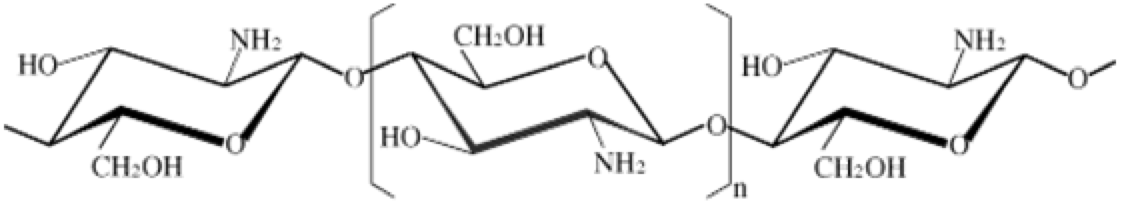



Drug delivery

Glaucoma treatment
TIMOLOL MALEATE



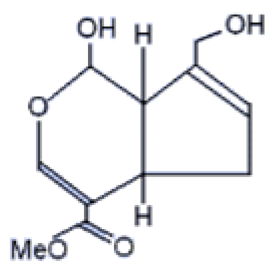
Gelatine



Chitosan

Crosslinkers

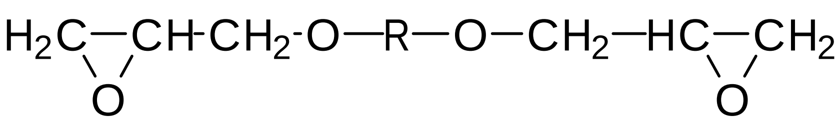
Genipin



1-(3-(Dimethylamino)propyl)-3-
-Ethylcarbodiimide hydrocholide (CDI)

C_2H_5-N=C=N-$(CH_2)_3N^{(+)}(CH_2)_3HCl^-$

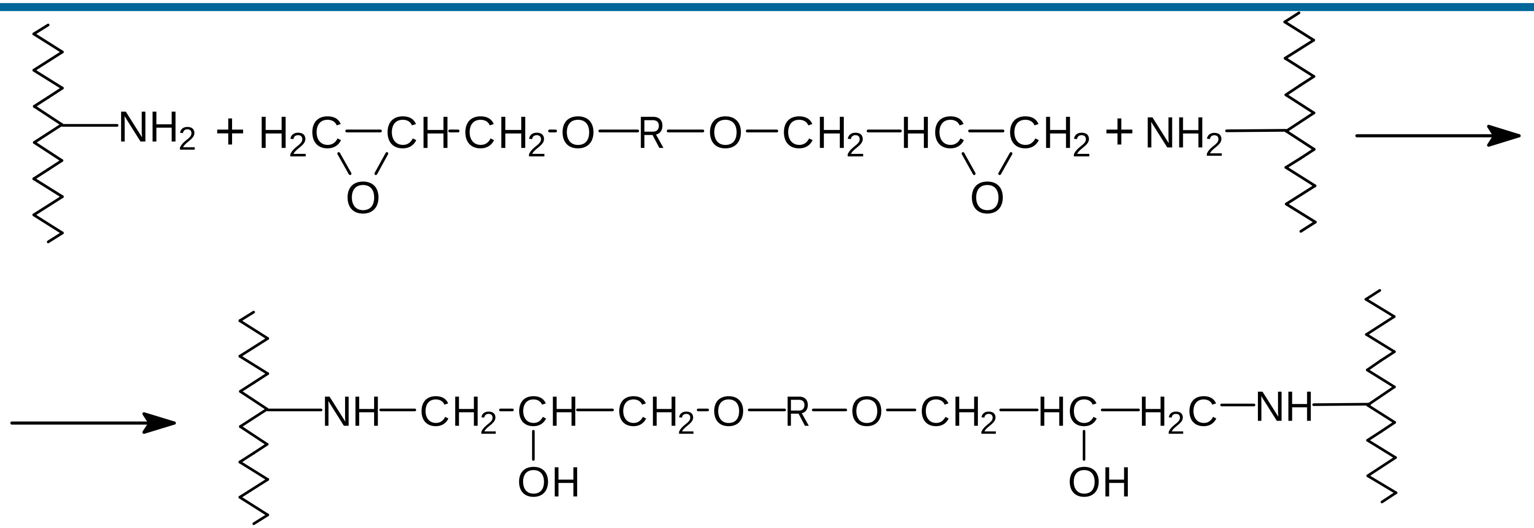
Diepoxydes



1,4-Butanodiol diglycidyl ether R = $CH_2CH_2CH_2CH_2$

Ethylene glycol diglycidyl ether R= CH_2CH_2

Crosslinking

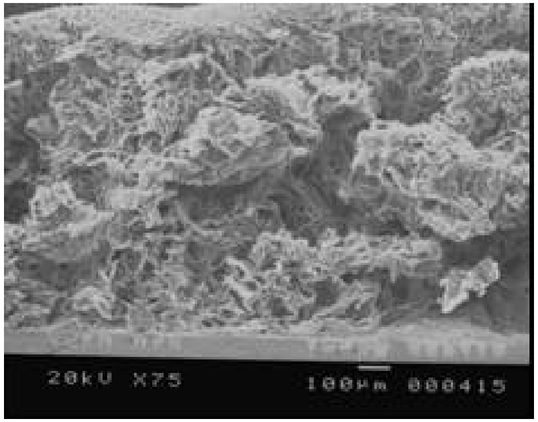


R = $CH_2CH_2CH_2CH_2$ 1,4-Butanodiol diglycidyl ether

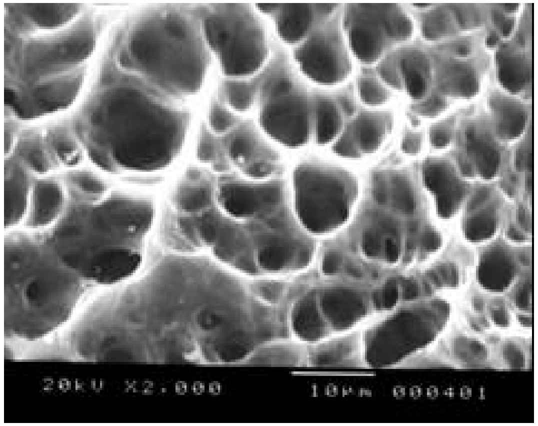
R= CH_2CH_2 Ethylene glycol diglycidyl ether

Biomaterials

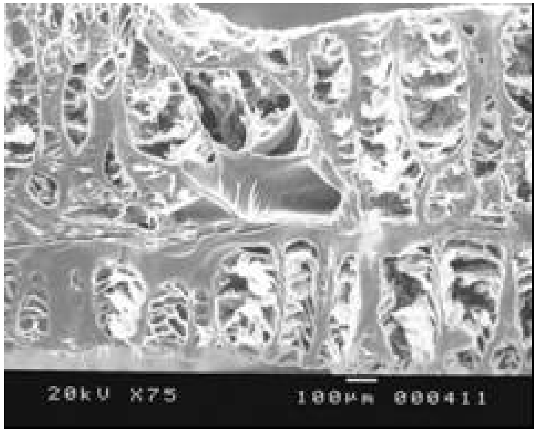
SEM



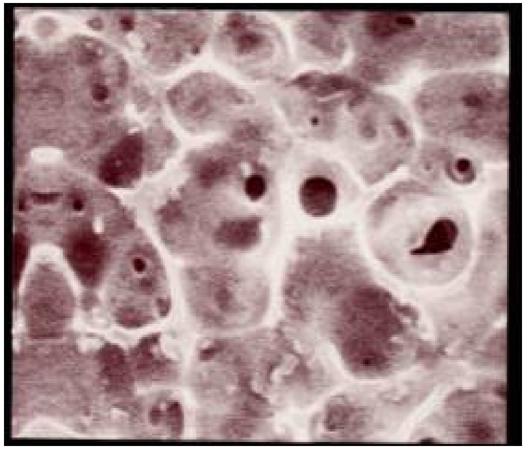
Gelatine



Gelatine + Diepoxyde 0,5%



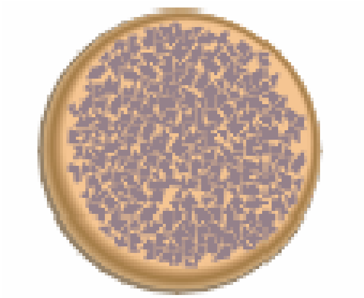
Gelatine + CDI 1%

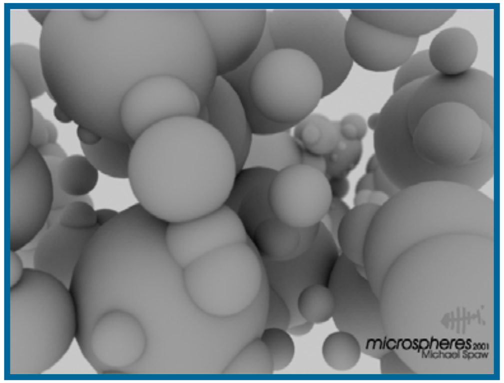


Chitosan + Diepoxyde 0,5%

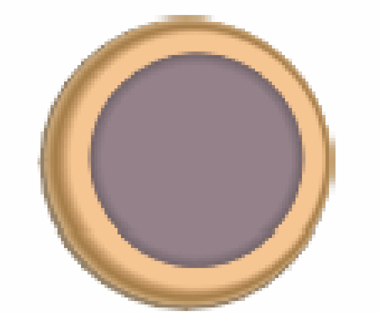
Microparticles

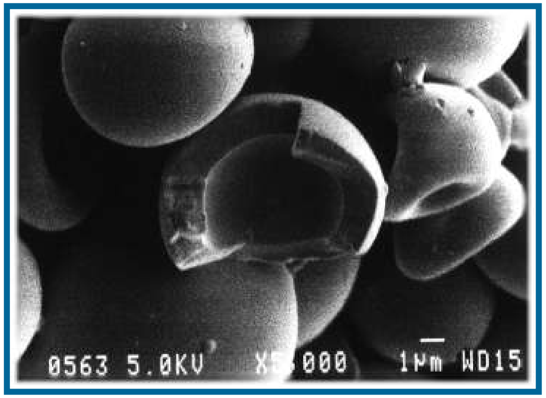
Microspheres





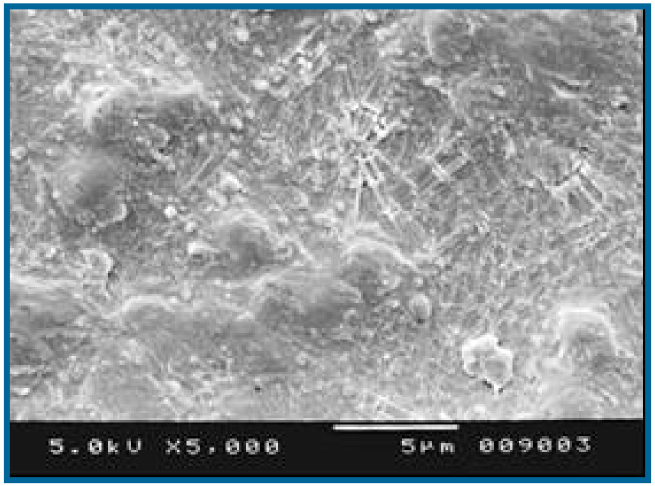
Microcapsules



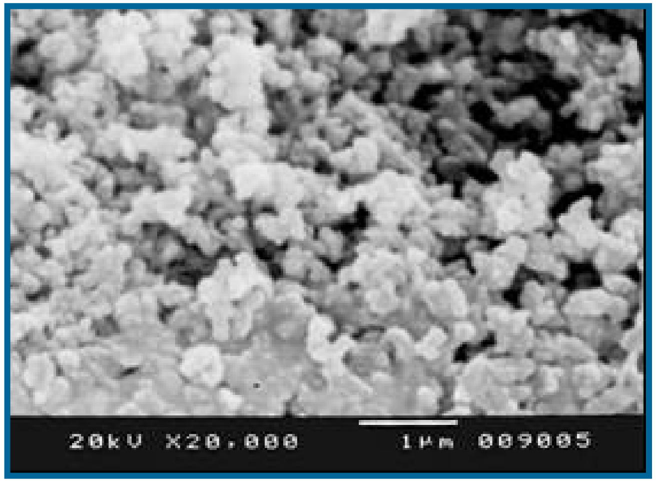


Drug delivery

Glaucoma treatment
TIMOLOL MALEATE



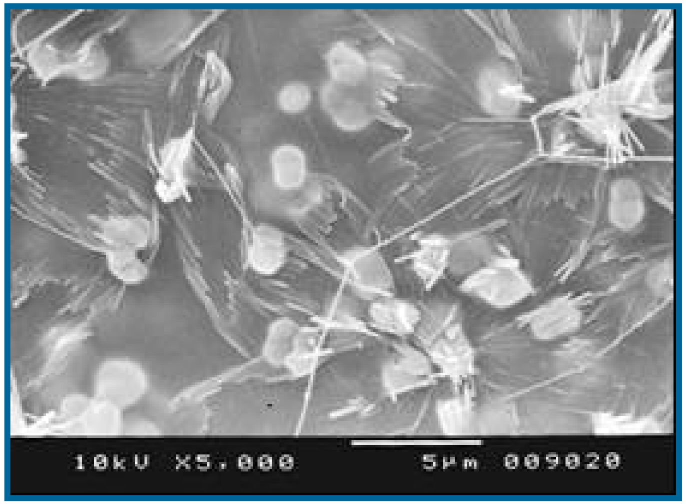
Surface of PVA membrane



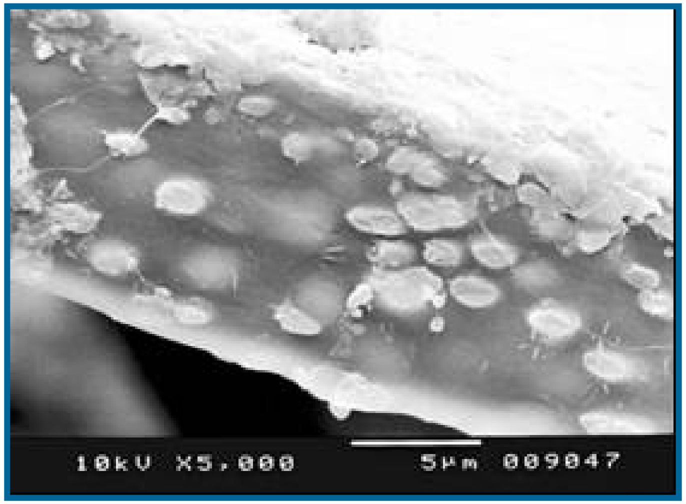
Liophilizated microspheres of dextran

Drug delivery

Glaucoma treatment



Surface of PVA membrane with microspheres of dextran



Transversal cut of PVA membrane with microspheres of dextran

In this work

Drug delivery system

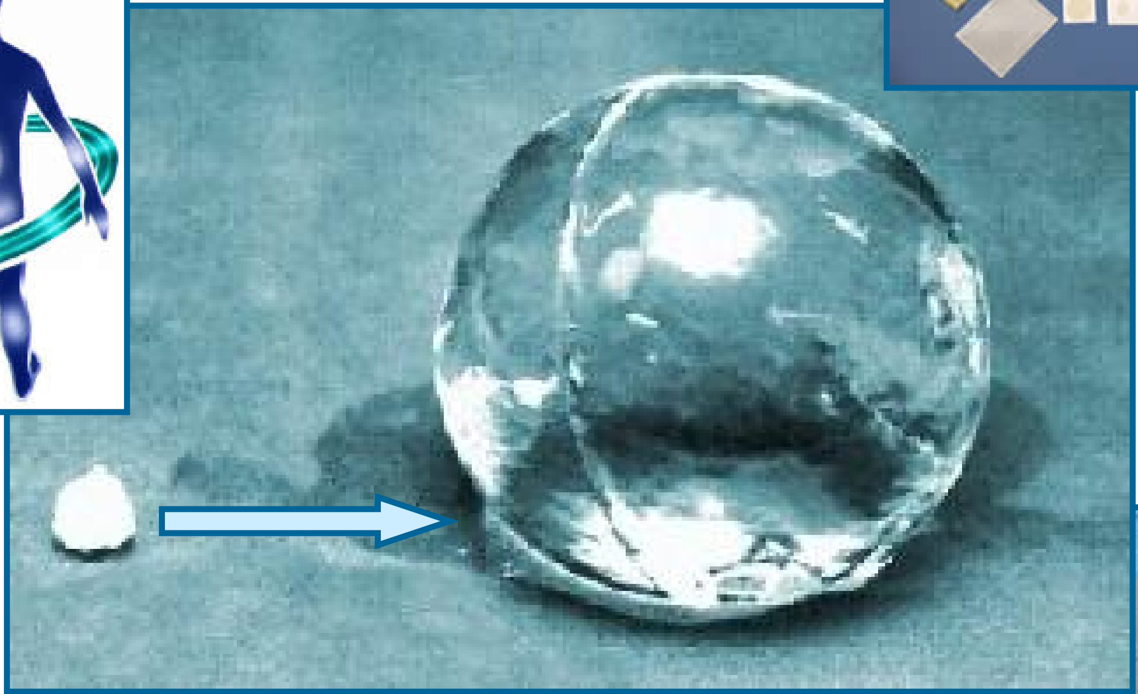
↓

Microspheres

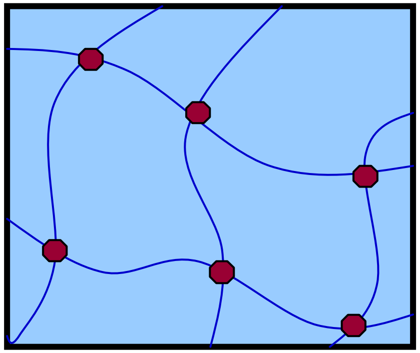
↓

Dextran derivatives

Hydrogels



Hydrogels



Background

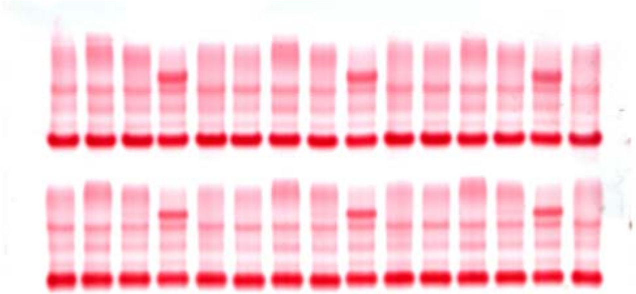
Hydrogels are water-swollen, cross-linked polymeric structures produced by the simple reaction of one or more monomers or by association bonds such as hydrogen bonds and strong van der Waals interactions between chains.

Hydrogels

Applications:

Biotechnology and material fields:

- super-absorbent diapers; water-treatment additives; membranes for separating biological compounds such as proteins; matrix for affinity chromatography and gel electrophoresis.

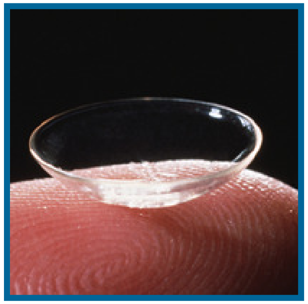


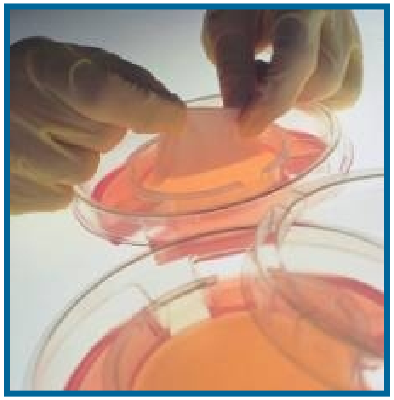
Hydrogels

Applications:

Biomedical field:

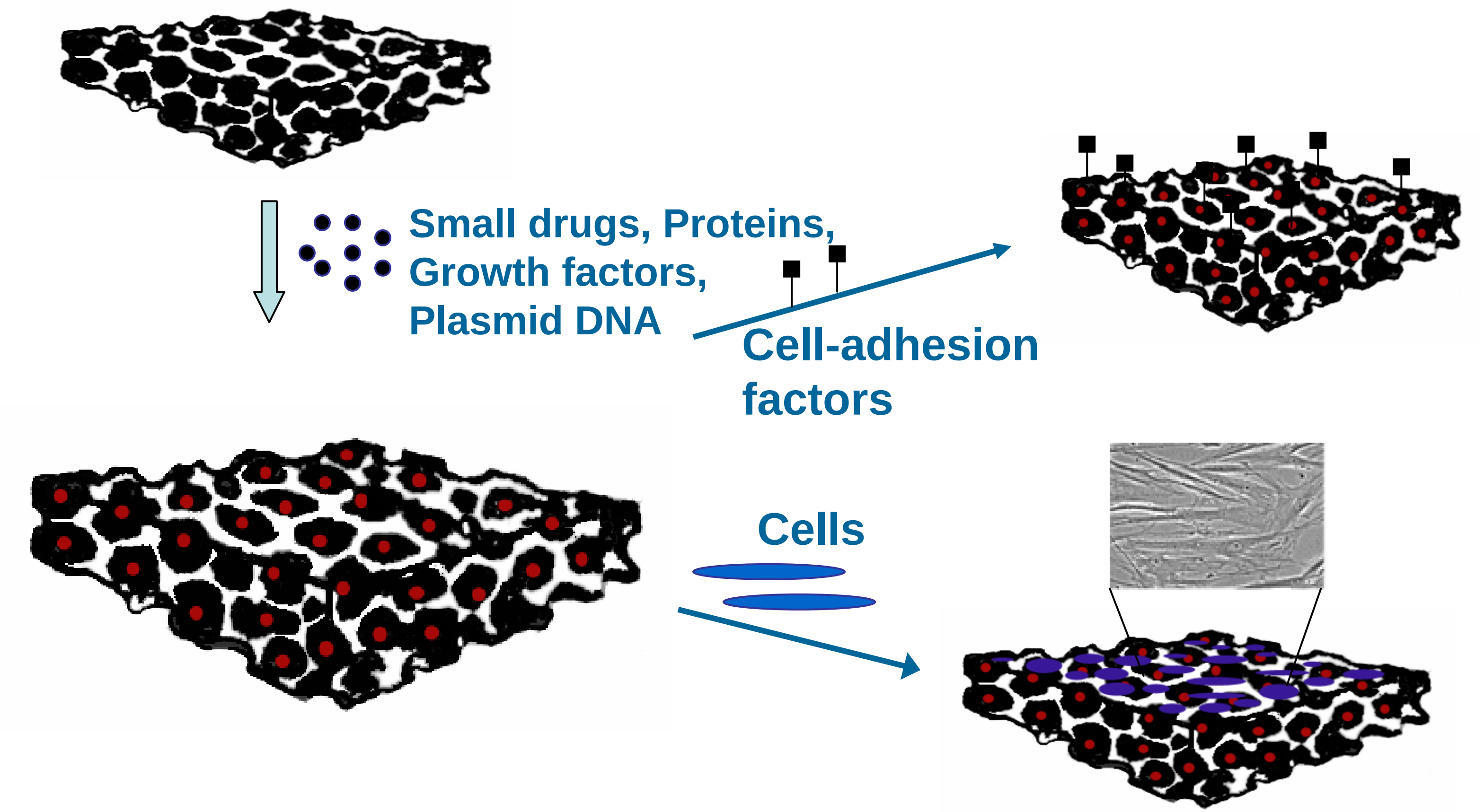
- contact lenses; synthetic joint cartilage; matrix in bone surgery; networks to grow cells for tissue enginnering; small solutes and protein controlled-release systems.





Applications

Hydrogels as drug delivery systems and scaffolds for tissue engineering



Economic impact

Drug delivery systems: $ 11 billion in 1996 to $42 billion in 2001 (industry estimates)

Tissue enginnering: 8 million surgical procedures in US/year : $ 400 billion/year

DEQ FCTUC

Advantages of hydrogels as Biomaterials

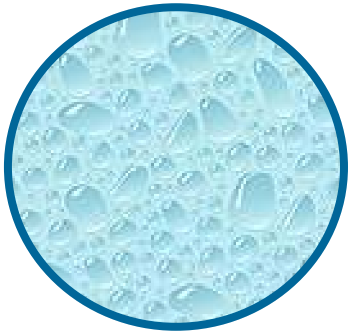
- Permeable for aqueous solids
- Permeable to body fluids
- Soft when hydrated
- Low adherance to tissue and mucuous membranes
- Water absorption , swelling
- Permeable for drug solutions

Hydrogels cathegories by

origin

- Natural
- Synthetic

water content



- Low swelling (20-50%)
- Medium swelling (50-90%)
- High swelling (90-99,5%)
- Super-absorbent (>99,5%)

Hydrogels cathegories by

processing

Thermoset (covalently crosslinked)

Thermoplastic (physicaly cross-linked, solid meltable)

chemical stability

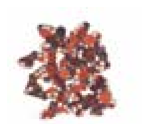
Biodegradable

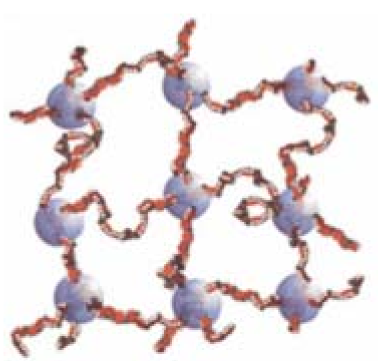
Bioerodible

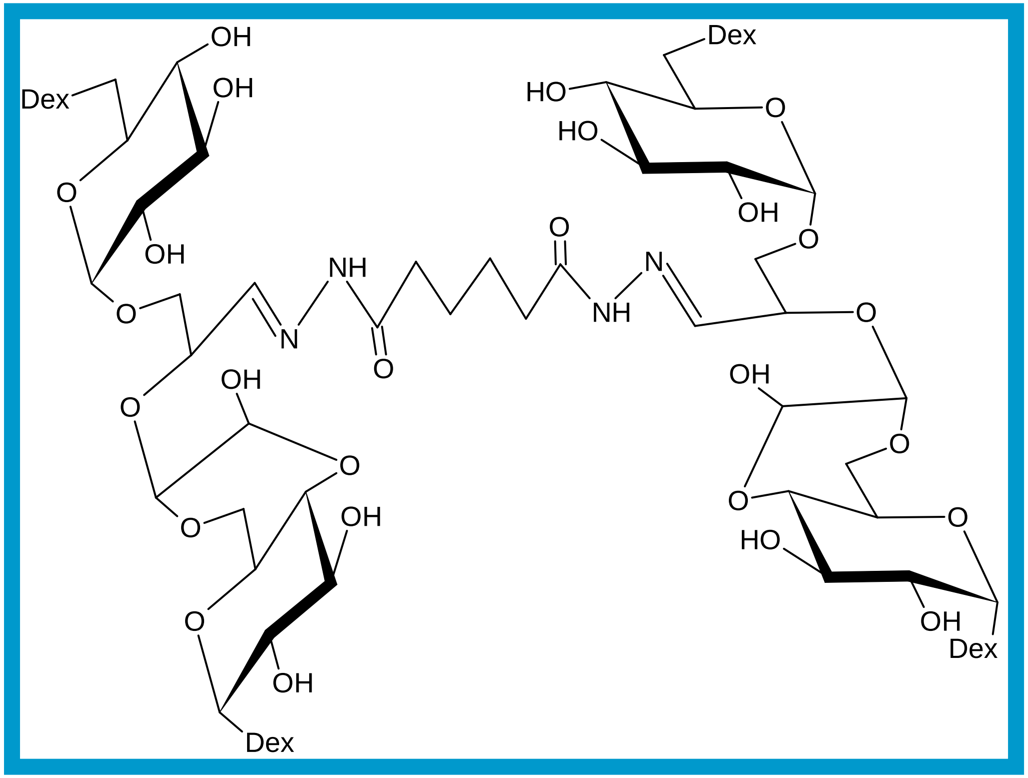
Non-degradable

Injectable and Degradable Dextran-Based Hydrogels

Oxidized dextran Cross-linked with AAD



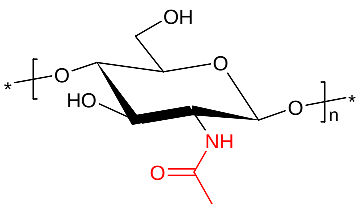




Biomaterials

extraction

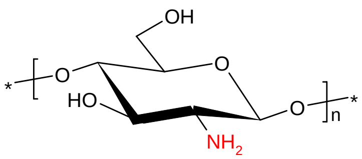
chitin
the second most abundant natural polysaccharide



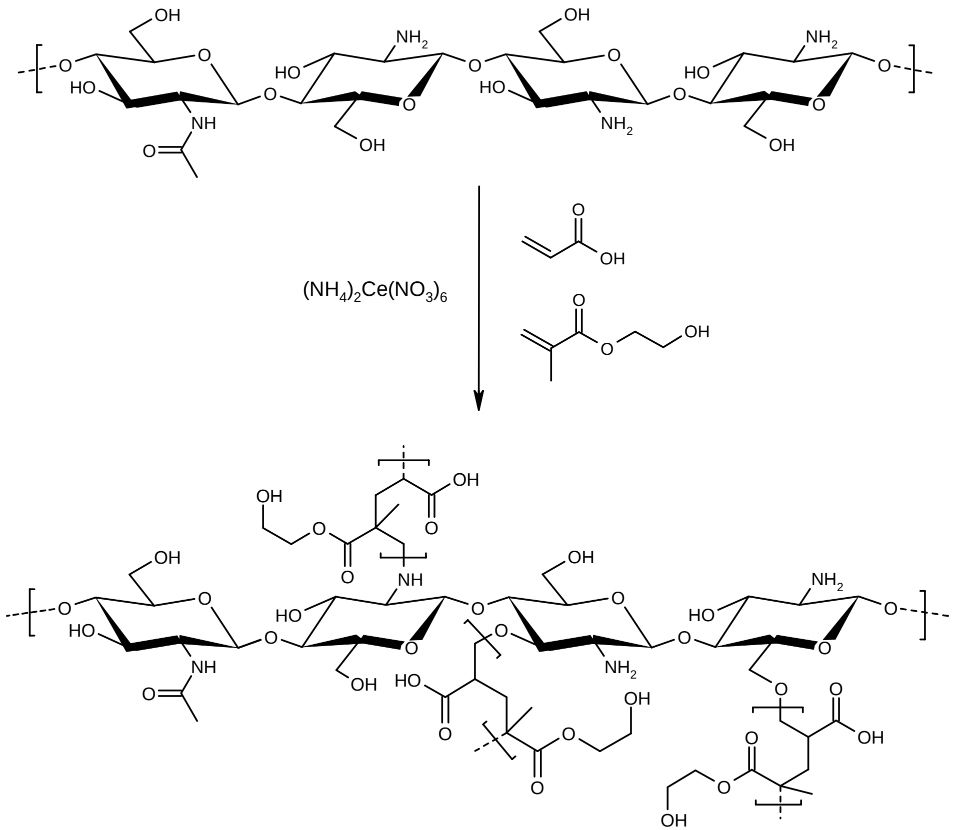
after cellulose

partial deacetylation

chitosan
medical and pharmaceutical applications



biocompatibility
biodegradability
adsorption properties
film-forming ability
antimicrobial activity
haemostatic effect
non-toxicity
bioadhesivity



M1 = chitosan

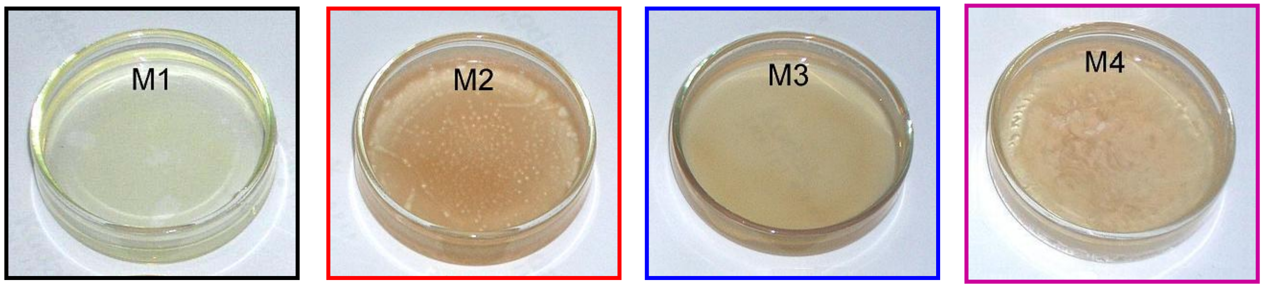
M2 = chitosan-*g*-HEMA

M3 = chitosan-*g*-AA

M4 = chitosan-*g*-HEMA-*g*-AA

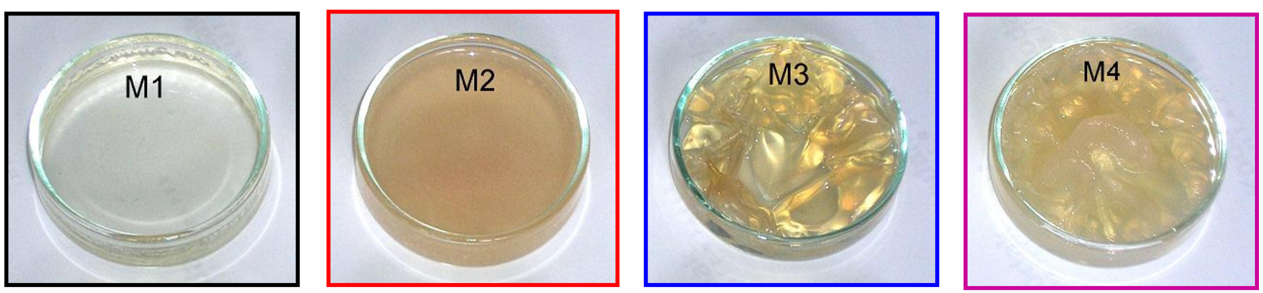
M1 = chitosan

M3 = chitosan-*g*-AA



DRIED MEMBRANES

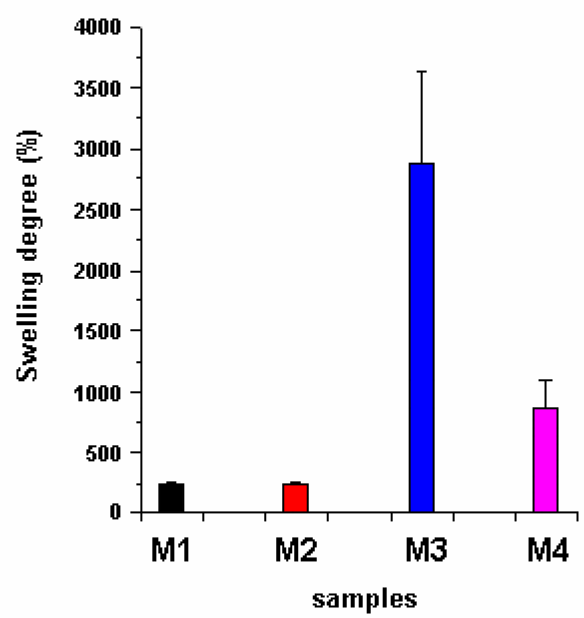
SWELLED MEMBRANES



M3 = chitosan-*g*-HEMA

M4 = chitosan-*g*-HEMA-*g*-AA

Biomaterials

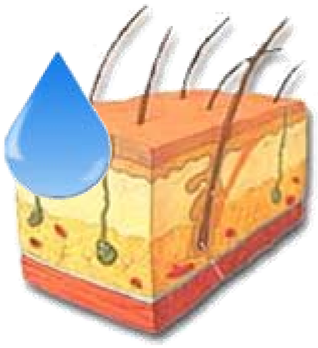


M1 = chitosan
M2 = chitosan-*g*-HEMA
M3 = chitosan-*g*-AA
M4 = chitosan-*g*-HEMA-*g*-AA

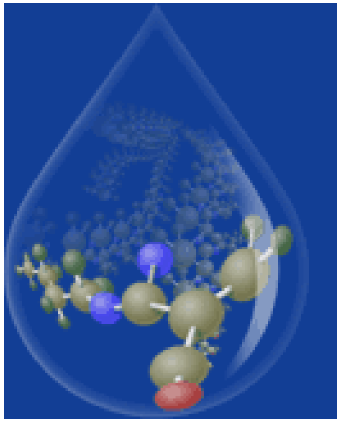
Swelling Assay

- **M2** had almost the same swelling degree (220%) of **M1** (223%);
- **M3** showed the highest swelling degree (2860%);
- **M3** was about 14 fold more water absorbent than **M1**;
- **M4** had swelling properties (870%) balanced according to the composition of each monomer;
- **M4** was able to absorb 4 fold more water than **M1**, despite its content in HEMA.

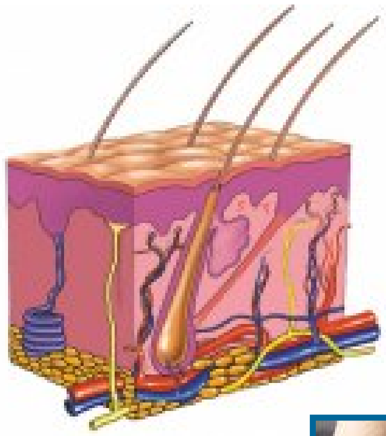
Biological glues

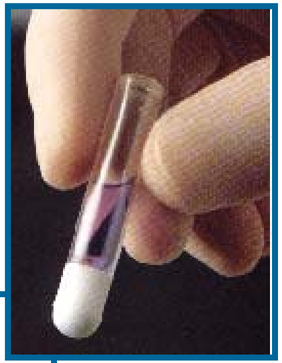


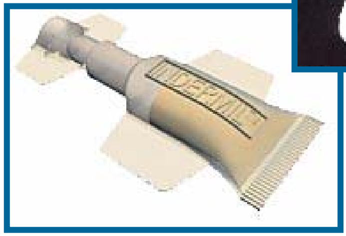
The idea of using an adhesive goes back to 1787 when it was verified that lots of construction workers glued their injuries with solid glues solubilized in water" (Haring, 1972).



Adesivos mais utilizados







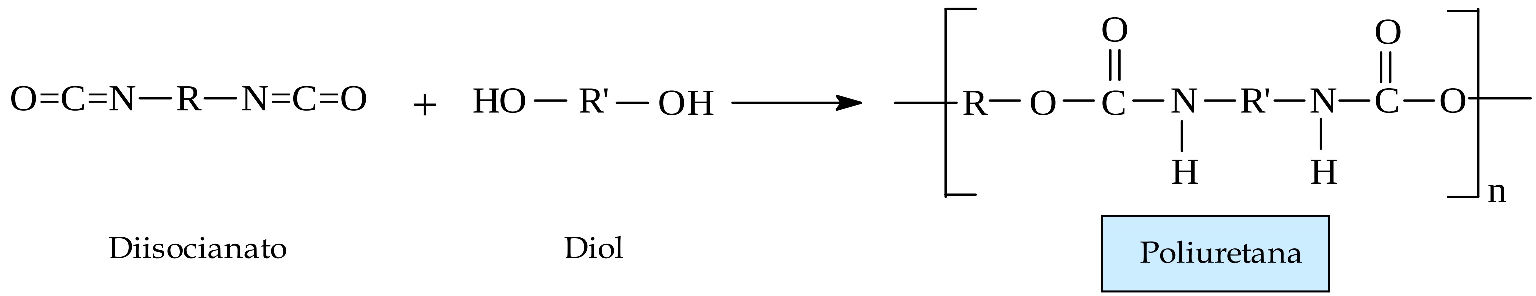
-cianoacrilatos

-fibrina

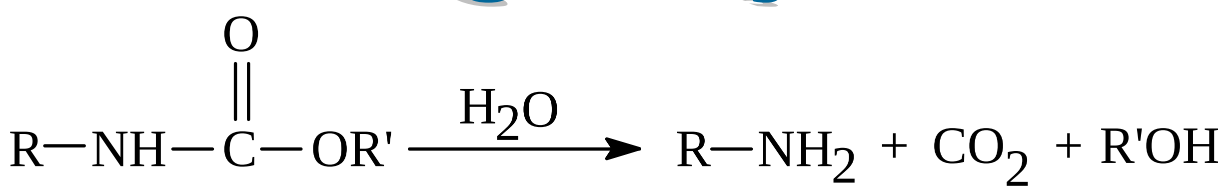
- gelatinas reticuladas

Colocados no mercado

♦ Reacção de polissacarídeos com diisocianato



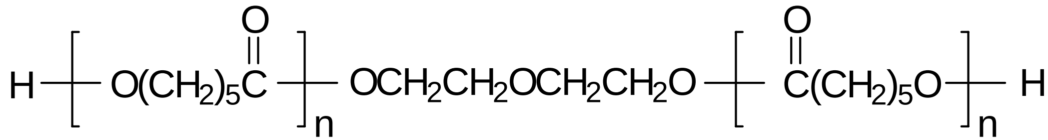
Degradação



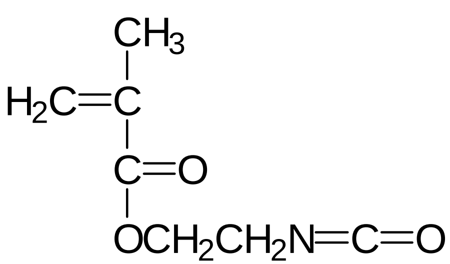
À reacção de hidrólise segue-se a reabsorção pelas células fagocitárias

Polyurethanes

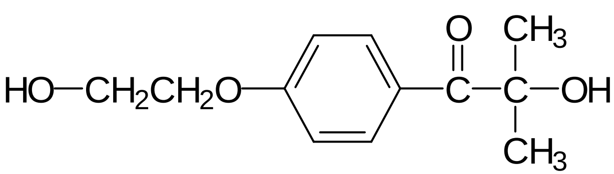
Polycaprolactone diol



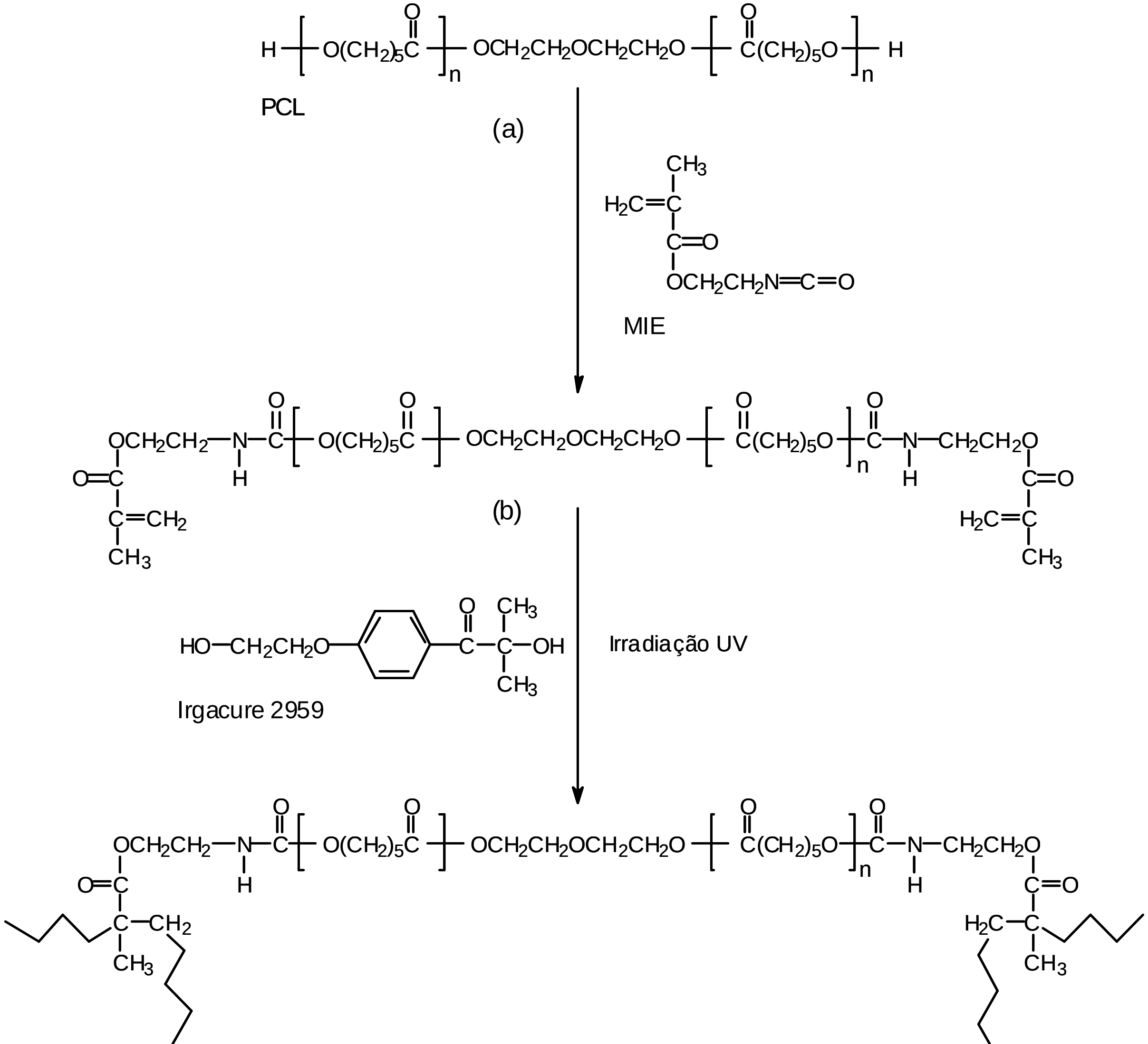
2-Isocyanatoethyl methacrylate



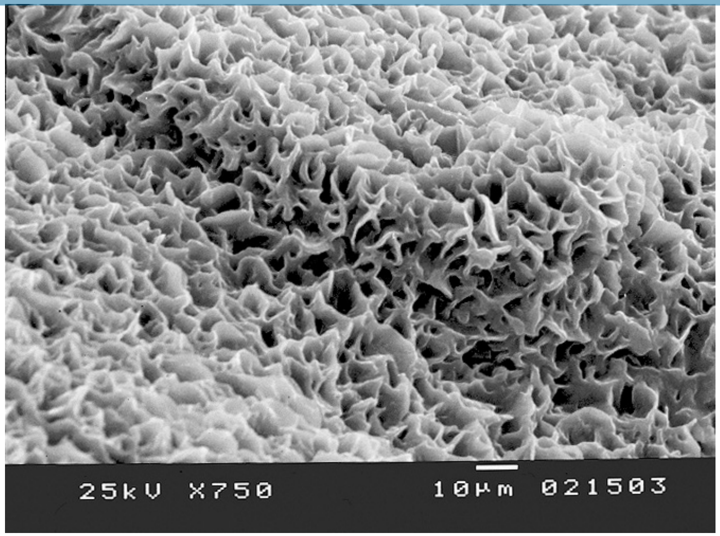
Photoinitiator Irgacure® 2959



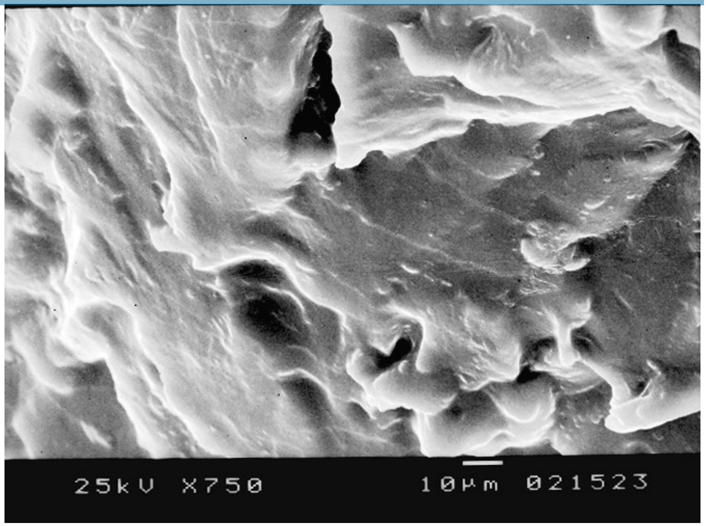
Biomaterials



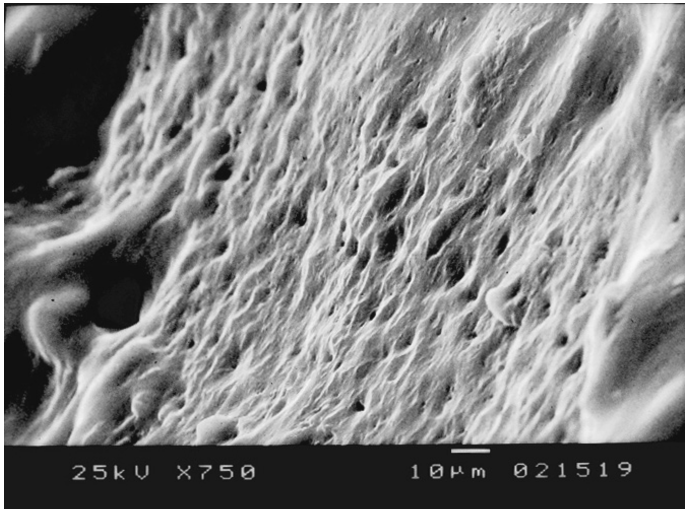
Biomaterials



4% Irgacure 60s UV



4% Irgacure 70s UV



4% Irgacure
80s UV

Biomaterials