Hurdles in The Delivery of Ocular Medication

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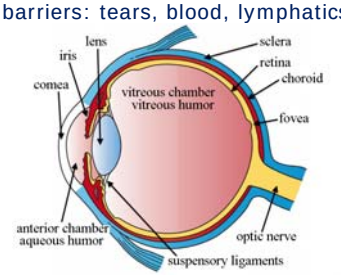
PHARMACODYNAMICS

Pharmacodynamics is the study of bodily absorption, distribution, metabolism, and excretion of drugs.

Challenges to Ocular Drug Delivery

Static barriers: cornea, sclera, retina

Dynamic barriers: tears, blood, lymphatics



Routes of Administration

Topical

Systemic

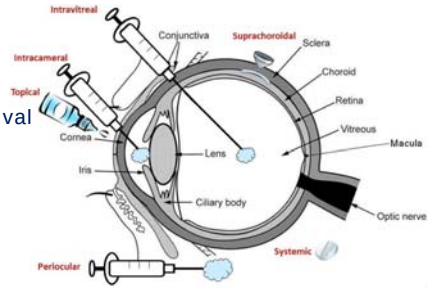
Sub conjunctival

Periorbital

Retro bulbar

Intraocular

Iontophoresis



Topical Delivery

In an ideal world topical delivery would be the method of choice, yet there are challenges associated with topical administration ultimate bioavailability and targeted delivery.

The Barriers:

The container must be opened.

Drug must be released from the container.

Drug must come into contact with the ocular surface.

The recipient must be instructed in the process which involves positioning and sterility maintenance.

The recipient must have the metal and physical capacity to administer (dementia, confusion, arthritis)

Epithelial innervation even in the absence of hypersthesia leads to reflex tearing and blinking resulting in dilution, spillage and excretion.

Contact time of residual drug will depend on specific pharmacodynamics properties, lipophilic, molecule size, static charge, etc.

Allergy and toxicity when present further contribute to reduced bioavailability.

Container must be identified and the label should be understood.

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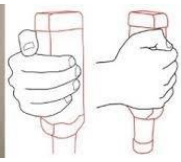

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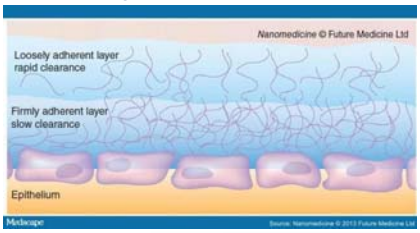

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Crossing The Barriers

Tight epithelial junctions.

Hydrophobicity restrict stroma and endothelium passage.

Conjunctival absorption reduces bioavailability.

Residual available drug can be 1-5%.

Strategy to Increase Residence Time

Gels

Ointments

Liposomes

Contact Lenses

New Strategies:

- Colloidal Dosage: Liposomes, nanoparticles, micro emulsions.
- Soft drug approach: biologically active ingredient which metabolizes to non-toxic drug entity.
- Ion pair drug enhancement
- Chemical drug delivery altered chemical structure to enhance permeability.

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- Colloidal Dosage: Liposomes, nanoparticles, micro emulsions.

Polymeric Micelles target poorly water soluble drugs creating a hydrophobic shell which combined with small size can pass.

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- Soft drug approach: biologically active ingredient which metabolizes to non-toxic drug entity.

Non active compounds which metabolize to active agent.

New Strategies:

- Chemical drug delivery altered chemical structure to enhance permeability.

Prodrugs are inert chemicals which in vivo can be transformed via enzymatic action into active targeting agents.

Increased Residence Time

Reduce the frequency of application.

Improve efficacy.

Improve compliance.

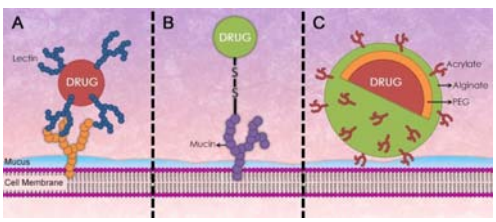
Improve bioavailability – antibiotics/steroids.

New Strategies:

- Ion pair drug enhancement

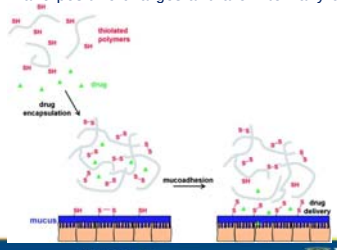
Pairing a positively charged particle with a negatively charged one to accelerate membrane crossing.

The Thiomer Approach



The Thiomer Approach

Thiol is an organic sulfa compound that contains a cobonded sulfhydryl group. Thiolated biopolymers consisting of repetive monomers, containing covalent bonds, which bind with mucus and glycoprotein have positive charges and are internally cross-linked.

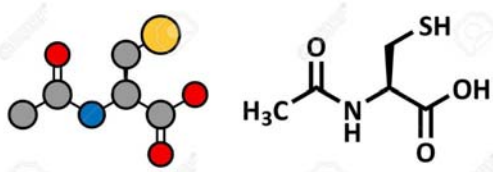


Hyaluronic acid TYPE POLYMERS

Biopolymers such as hyaluronic acid are historically well tolerated. Chitosan, a catatonic biodegradable biopolymer obtained from shellfish exoskeletons, is noted for muco-adhesivity, and has a structure similar to that of Hyaluronic acid.

RESIDENCE TIME

The thiol groups on the surface form disulfide bonds between the biopolymer and the mucin layers thus increasing residence time. A Chitosan N acetylcystine product (Lacrimera) is being evaluated in phase 2 trails in Austria and may show promise in the treatment of keratitis sicca, and cornea erosion.



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