College of Pharmacy
Fifth Stage

Pharmaceutical Biotechnology

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Lectutre 6
Delivery of proteins
Alternative routes of administration

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Alternative Route of Administration

- **Parenteral administration** has disadvantages (needles, sterility, injection skill) compared to other possible routes.

- Therefore, **systemic delivery of recombinant proteins by alternative routes of administration** (apart from the GI tract) has been studied extensively.

Delivery through nose, lungs, rectum, oral cavity, and skin have been selected as potential sites of application.

I. Nasal

Advantage:

1. Easily accessible.
2. Fast uptake.
3. Proven track record with a number of “conventional” drugs.
4. Probably lower proteolytic activity than in the GI tract.
5. Avoidance of first pass effect.
6. Spatial containment of absorption enhancers [osmolarity & pH] is possible (when drugs exhibits poor membrane permeability, large molecular size, lack of lipophilicity and enzymatic degradation by amino peptidases).

Nasal

Disadvantage:

1. Reproducibility (in particular under intranasal pathologies may affect or capacity for nasal absorption).
2. Safety (e.g., cilliary movement that propelled proteins into the throat where it is swallowed and destroyed by the products of the stomach).
3. Low bioavailability for proteins (Because they are large molecular weight polar drugs thus they have low membrane permeability).

II. Pulmonary (intratracheal inhalation or instillation)

Advantage:

1. Relative easy to access (aerosol or syringe).
2. Fast uptake.
3. Proven track record with “conventional” drugs.
4. Substantial fractions of insulin are absorbed.
5. Lower proteolytic activity than in the GI tract.
6. Avoidance of hepatic first pass effect.
7. Spatial containment of absorption enhancer.

Pulmonary

Disadvantage:

1. Reproducibility (in particular under pathological conditions, smoker/non-smoker).
2. Safety (e.g., inhaled human insulin [powder or liquid] has been shown to be more immunogenic than comparator insulin given by S.C. routes; however, adverse effects of antibody formation demonstrated).
3. Presence of macrophages in the lung with affinity for particulates.

III. Rectal

Advantage:

1. Easily accessible.
2. Partial avoidance of hepatic first pass.
3. Probably lower proteolytic activity than in the upper parts of GI tract.
4. Spatial containment of absorption enhancers is possible.
5. Proven track record with a number of “conventional” drugs.

Disadvantage:

Low bioavailability for proteins.

IV. Buccal

Advantage:

1. Easily accessible.
2. Avoidance of hepatic first pass.
3. Probably lower proteolytic activity than in the lower parts of the GI tract.
4. Spatial containment of absorption enhancer is possible.

Disadvantage:

Low bioavailability of proteins.

V. Transdermal

Advantage:

1. Easily accessible.
2. Avoidance of hepatic first pass.
3. Removal of formulation if necessary is possible.
4. Spatial containment of absorption enhancers.
5. Proven track record with “conventional” drugs.
6. Sustained/controlled release possible.

Disadvantage:

Low bioavailability of proteins.


Thank You