Absorption and distribution of drugs

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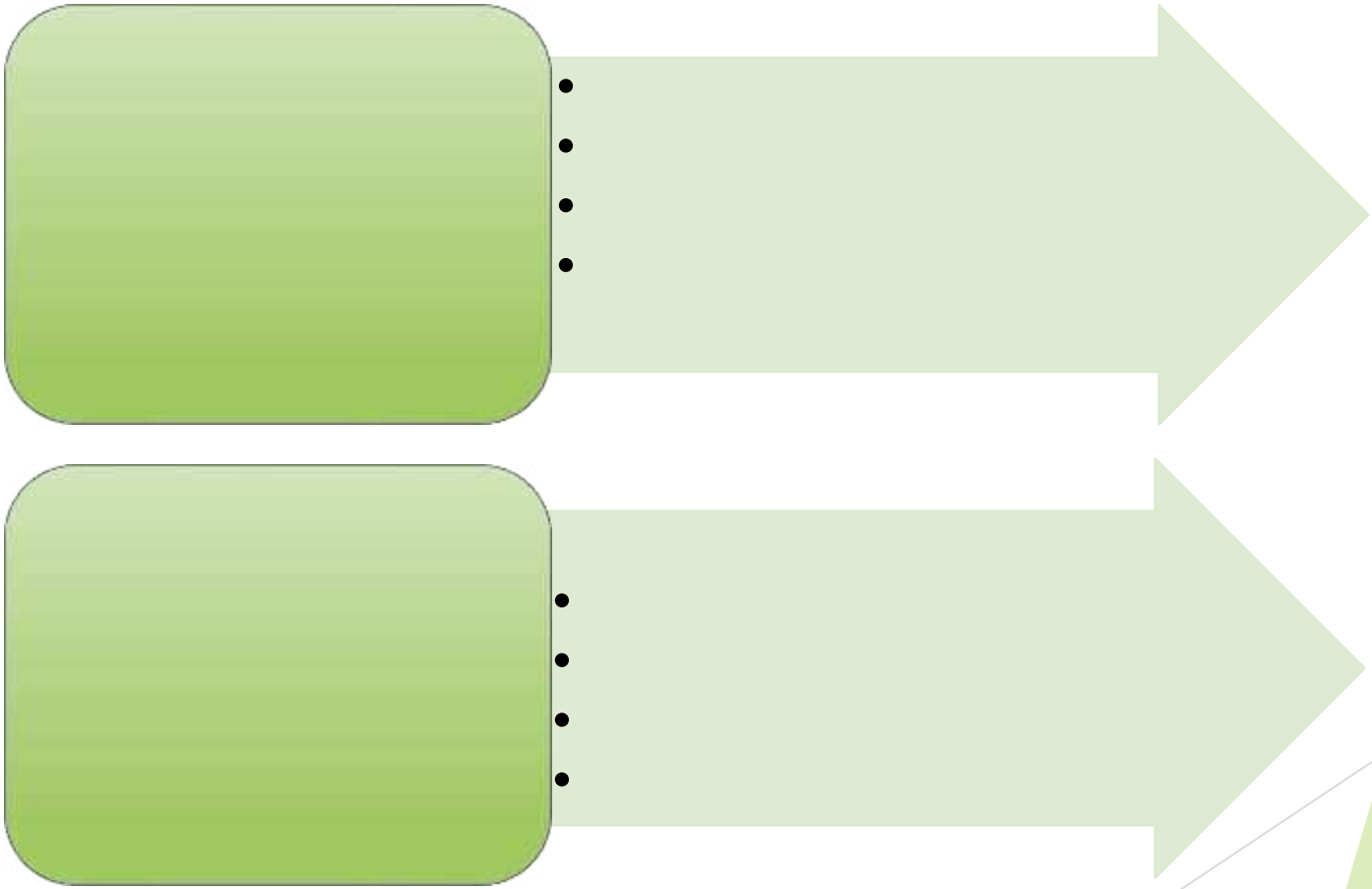
Introduction to Biopharmaceutics

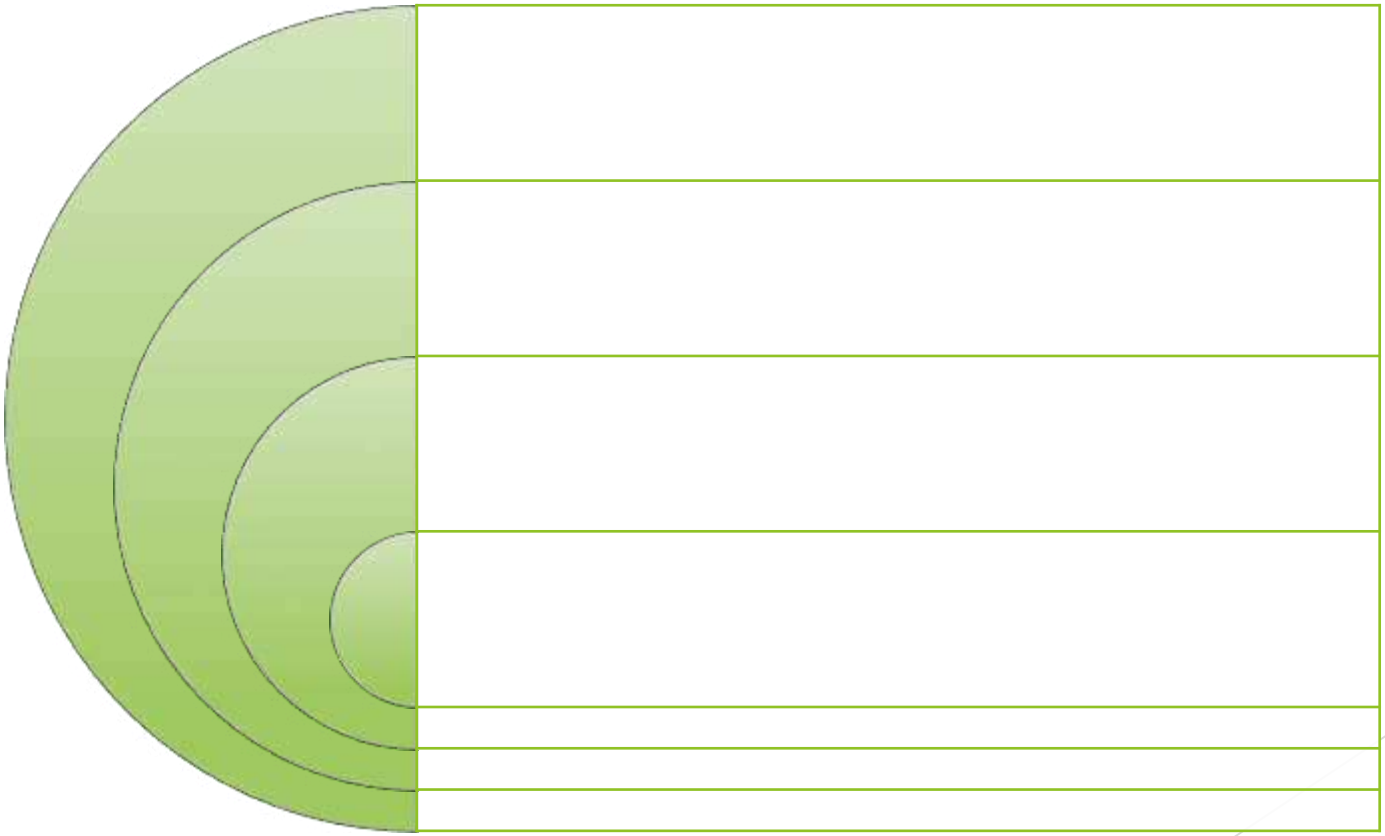
Absorption: Mechanisms of drug absorption through GIT , factors influencing drug absorption though GIT, absorption of drug from Non per oral extra - vascular routes.

Distribution: Tissue permeability of drugs, binding of drugs, apparent, volume of drug distribution, plasma and tissue protein binding of drugs, factors affecting protein-drug binding. Kinetics of protein binding, Clinical significance of protein binding of drugs.

Overview



Pharmacokinetics



Absorption

Movement of drug from its site of administration to central compartment & extent to which it occurs

sor on o ro
o on ro s o r
n s r on

n r

- s n
- r
-

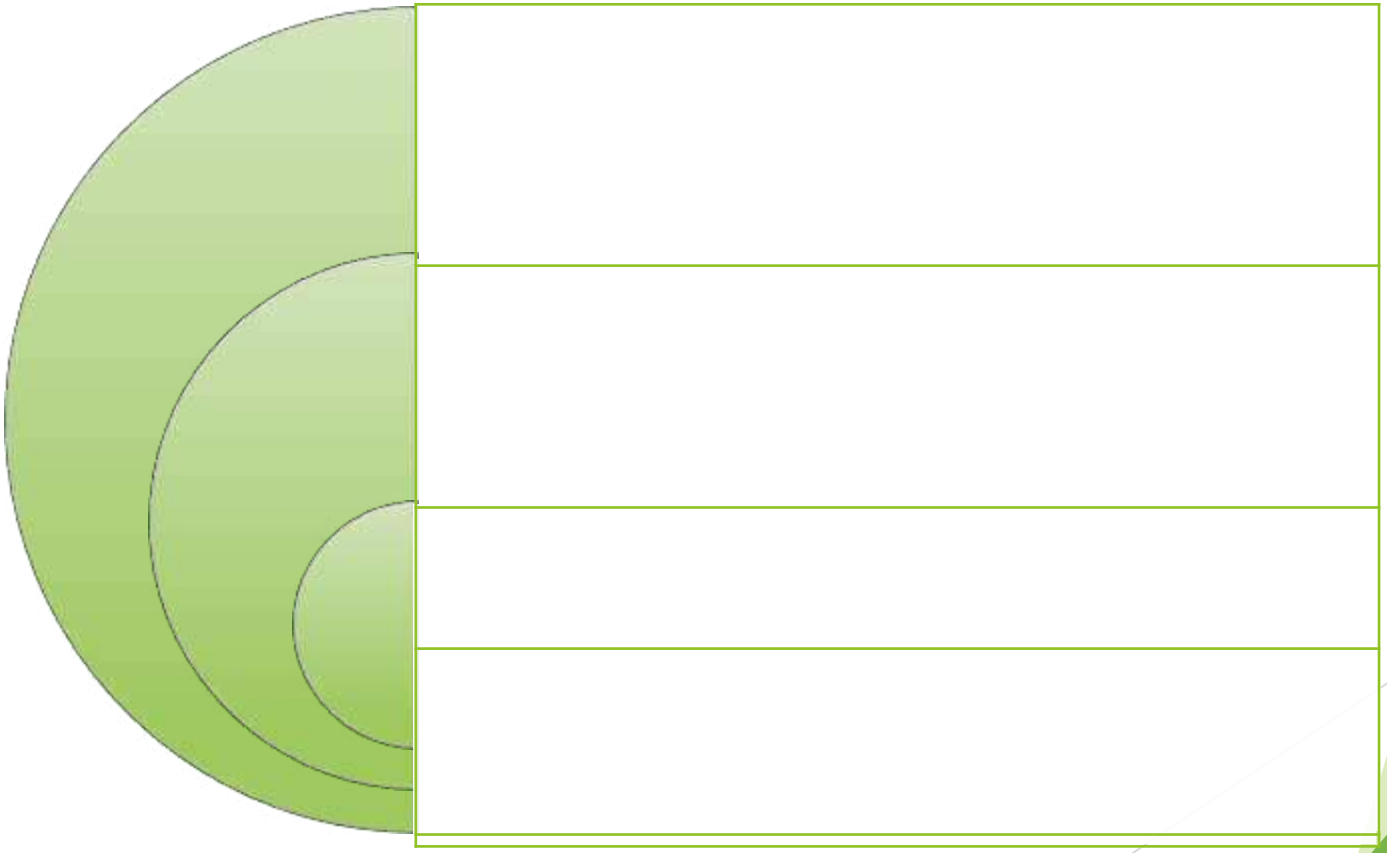
r n r

- n r no s
- n r s r
- n o s
- nh on

o

- r ns r
- o s r n
- r

Absorption via gastrointestinal tract



h n s o r
sor on

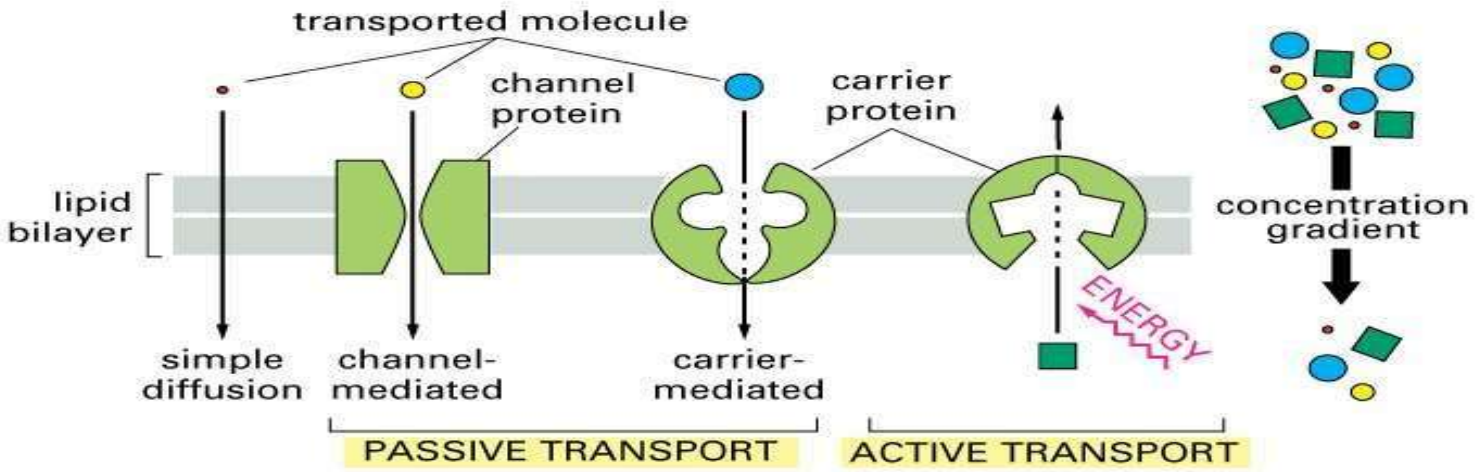


Figure 12-4 Essential Cell Biology, 2/e. (© 2004 Garland Science)

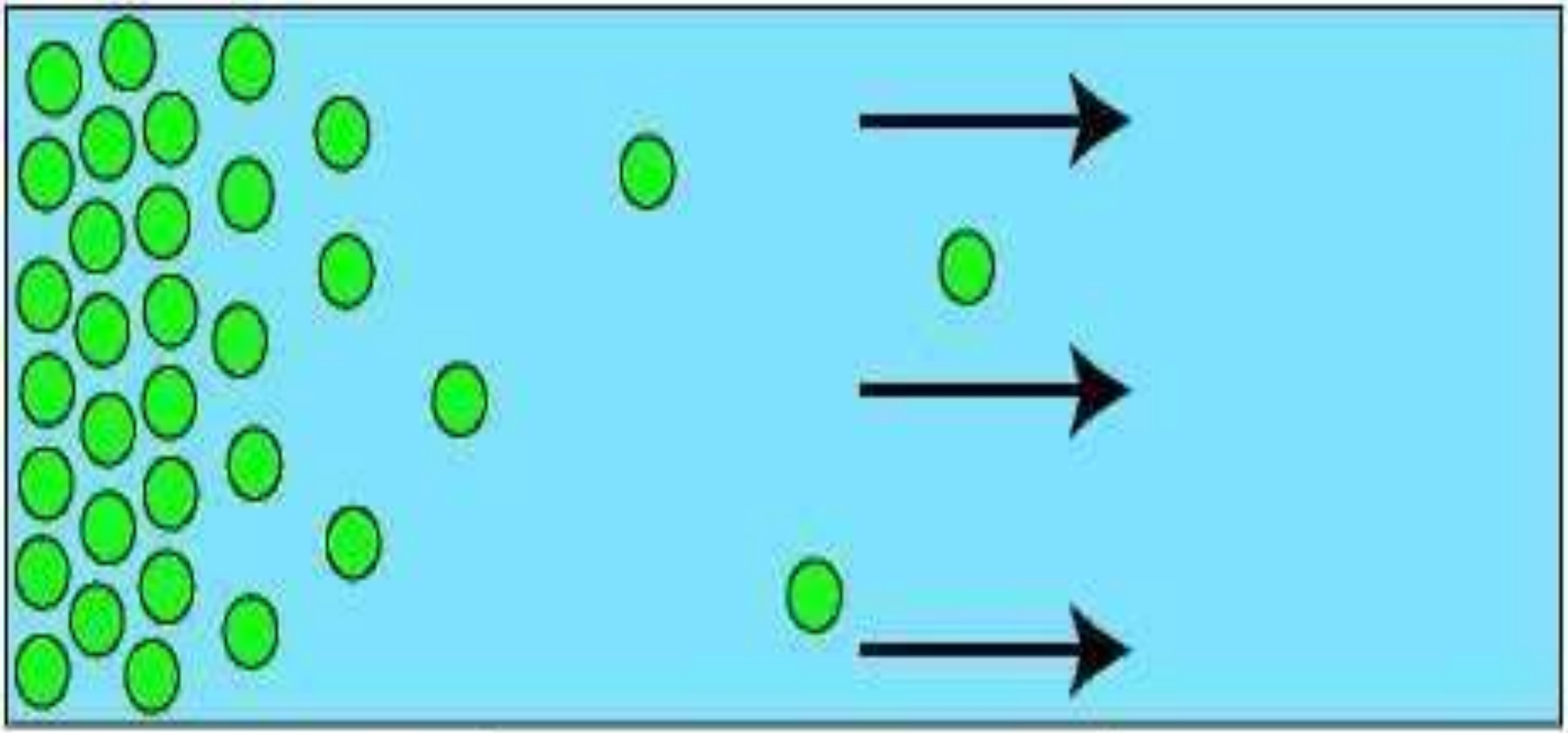
ss s on

- on - on s on
- or ro ss or sor on o o r s
- r n or Con n r on or ro h r n
- o o s **Fick s first law of diffusion**

r o s s ro r on o h h r on n r on o on o r on n r on n r s n n h h r o s on s r ro or on o on n r on r n ross r n

C - C

Diffusion



high concentration → low concentration

solute

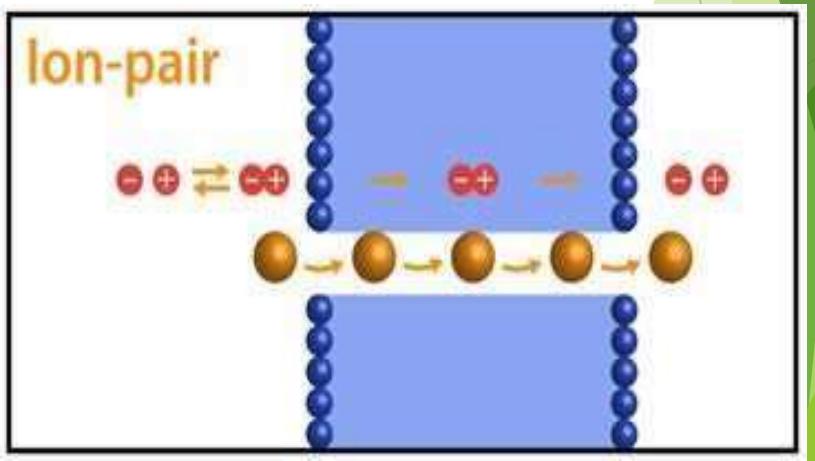
or r ns or

- Con r ns or o or r on
- s ons or r ns or o o s n o s
- r n or h ros or or os o r n s ross r n
- or n n sor on o o o r h 1 o o r s h n n r o o n s o r h o ons

on r r ns or

- n r on o r n or n
  r rs n r o s h
  n o no s ons o n

- ro r no o h o



Carrier mediated transport

- C rr r o on n o r n n s r rs or non o n h so o s n o r rs s o o h r s o r n

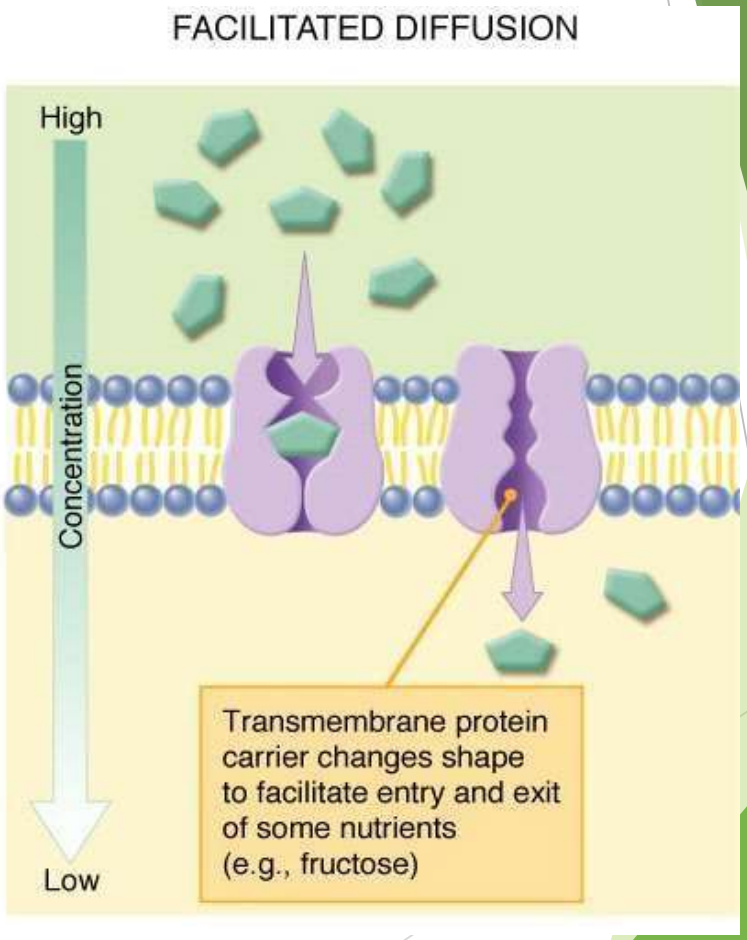
1. C rr rs- n r on

   r r s

   C

s on

- C rr r
  r ns or o r s
  o n h
  on n r on
  r n o nh
  r ns or
- r n or -
  Con n r on
  r n
- o n r
  n r
- n 1



r ns or

- r s n r n or o

  r r r ns or

  r s r n r

  s

1 on r ns or rs

  r ns or n on n or o s

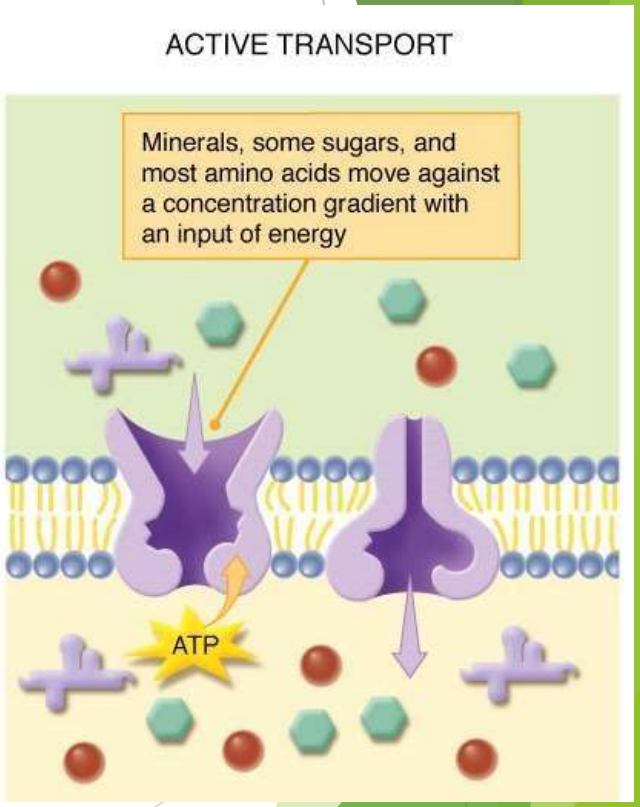
  r n on s ro on

  C n n ss r ns or rs

  s ons or r ns or n s or n
  o s o o s sor on

  - o ro n r r s s n
  ro n

  C r ns or rs n r n r s



on r r ns or

o r n r r r n

1 or o - r ns or

r ns or o o h o s n
s r on

o

r ns or r 1

n n s n

r ns or o

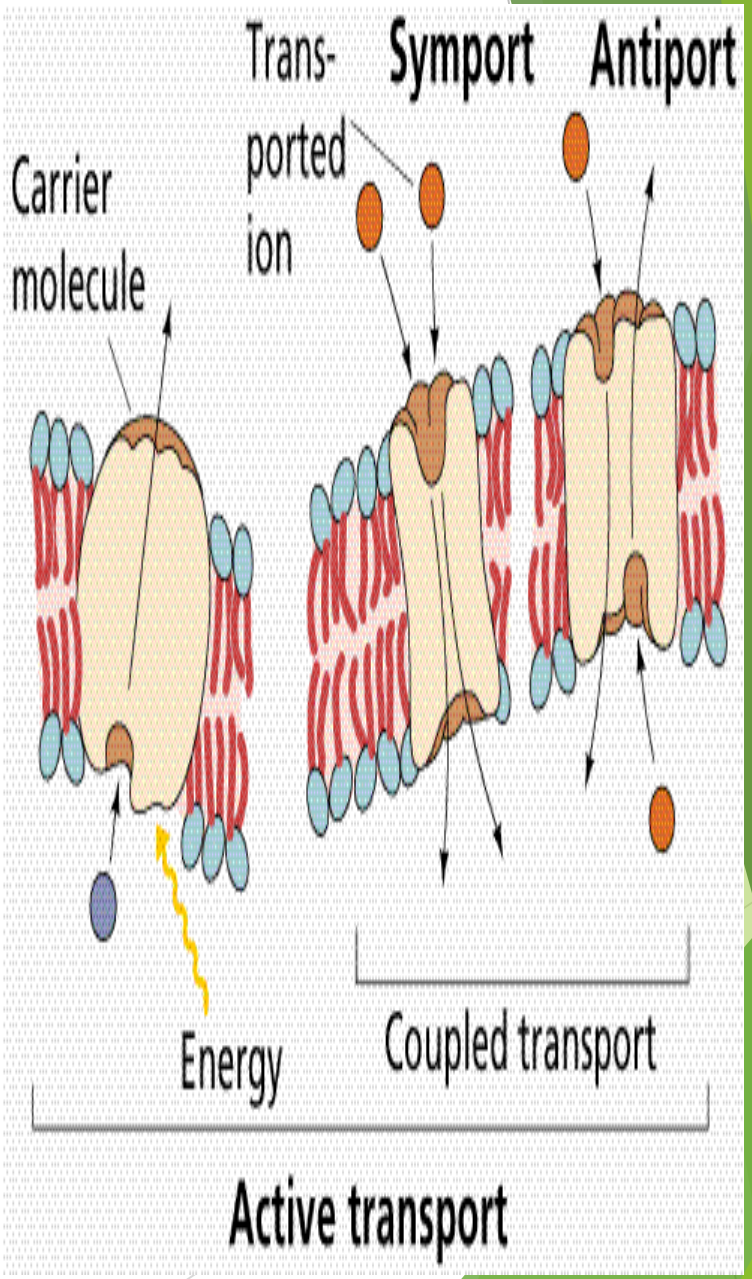
n o s

n or o n r -
r ns or

o n o o s n
o os r on

s on s n

r n n n s



- r o n s n n s

1 n r s r on n s s

n n n

o o n r n r s

s r h os s

os o sor

- r n o s on

o oso r s

- o s n n

œ o sor -

Bioavailability of drugs

h h n n o h h
on n r on o r s
s r s o on
oo s r

Bioavailability - immaterial in drugs with higher safety margin
example water soluble vitamins , antacids

Difference in bioavailability – Concern in drugs with steep dose response curve

Example - Drugs with zero order kinetics or mixed order kinetics and drugs with narrow safety margin

Factors influencing absorption and bioavailability

h r ors

h r o o ors

Pharmaceutical factors

or on o r o ↓

n o o n or r

so on s s ns on s
o

1s s s n r on

n s sso on

Particle size

r sso s r s r r s ↑
↓ r s

Poorly soluble and slowly dissolving drugs marketed in microfine or fine particles

Salt form

sso on r o r r s
r n ro h o r n o o n

Salts of weakly acidic drugs are highly water soluble

Water of hydration

o sso on n o
n s on or o h r on h r
or nh ro s

Anhydrous forms of caffeine , theophylline, Ampicillin - faster dissolution and better bioavailability

r o on s on

on on s so r s

Better absorbed

ron or s r s or h h
on s r s

1] ↓ Bioavailability from GIT
2] Examples - Streptomycin, neostigmine , acetylcholine and its analogue ,d-tubocurarine

Pharmacological factors

s r n n o ors

h r s r n ↑

o o r s

Gastric emptying promoted by

1) Fasting
2) Anxiety
3) Lying on right side
4) Hyperthyroidism
5) Gastro kinetic drugs

Gastric emptying retarded by

1) Fatty diet
2) Endogenous depression
3) Lying on left side
4) Pyloric stenosis
5) Hypothyroidism
6) Drugs - Atropine

s r n

ss o r r sso on ro s o h
o s n s n

s r n s s

1 ons o on s s r - s

sso on o r o rs n n s n n r
o s

r s no s n s r - n n
r hro n

r s sor ro s r o n s n
n 1

n s r n s r o n

1 oo ro o s r sso on sor on-
r s o n

s n r on sso on o os or s
ro o s r s

r s sso s o r s o n

r s rr s r os s r n
h n on n ro r n o n

5 r s sor ro ro r o s
n s n - n C

s ro n s n s s s

C s s

sor on o

Crohn's s s

hron n on o

s ro n r s

oo n o h r s s n s

1 sor on o r

s o h

sor on r ↓ r n s on o

oo

sor on o r n ↓ h n

n h or ro s

sor on o n n r s ↑ h n

n h

5 n ↑ sor on o ron

rs ss o s

- " *The loss of drug as it passes through GIT membrane, liver for the first time during the absorption process* "

- o r r r s s s h h r s s
  o s o r s

1. L n n s
   n s or os n s
   r n s
   n s

- **Luminal enzymes:** h s r n s r s n n
  s n n n s ro n s n n
  n r s r ons h ro s s
- **Gut wall enzymes:** so os n s h
  r r s n n n n s n o on oho
  h ro n s
- **Bacterial enzymes:** ro or s n r s n n
  s o h n s n s n n s r h n o on
  s h s n → s h r n 5
- **Hepatic enzyme:** s r r n r o rs ss
  h o s h h r on s n
  so r n n n ro r n or h n

1s ss

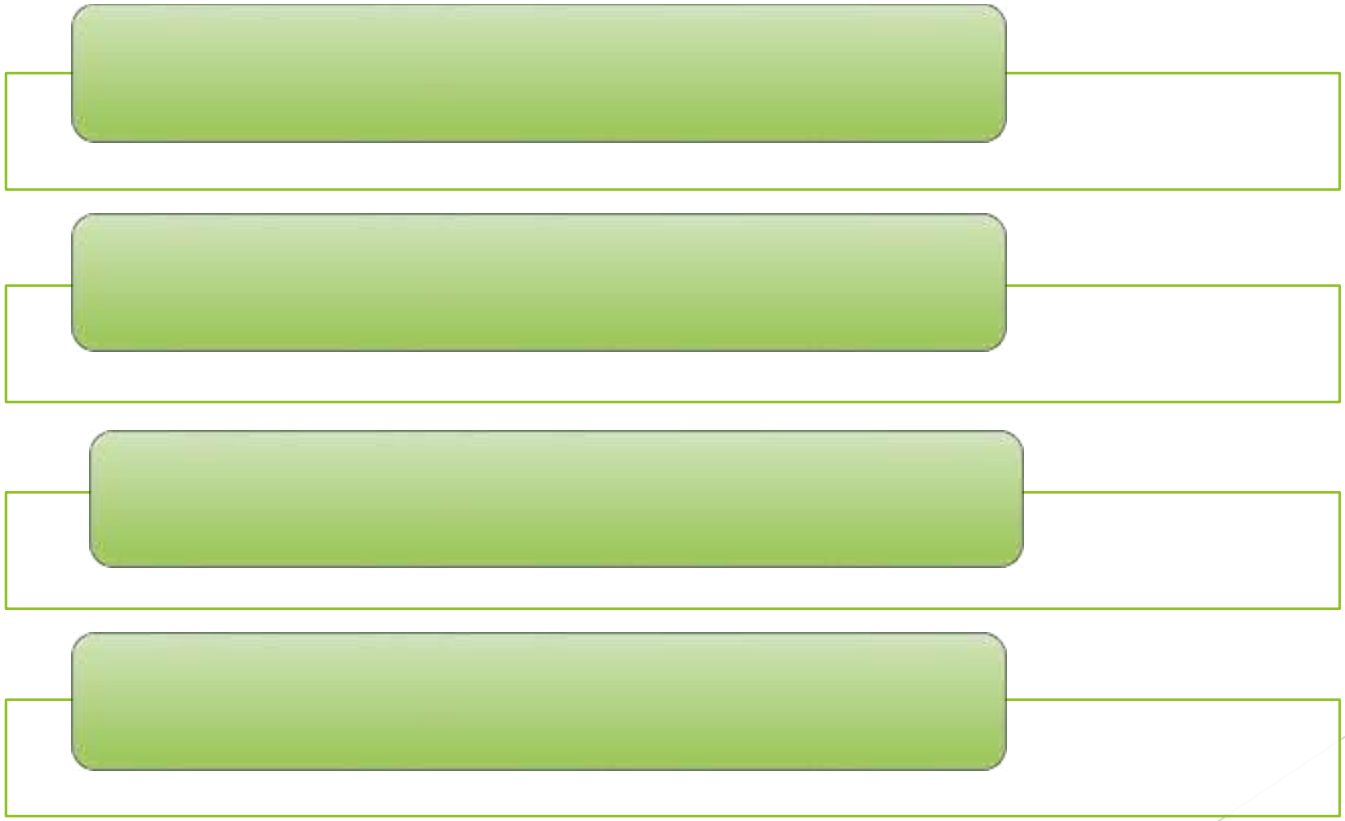
↓ o n h r

s ons

s

1] Morphine
2] Nitroglycerine
3] Isosorbide nitrate
4] Propranalol

Equivalence types

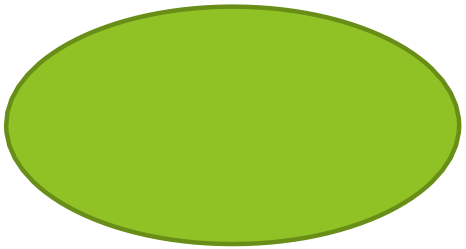


Distribution of drugs

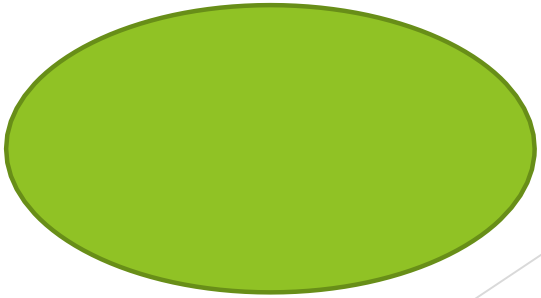
Distribution of drugs

o n o r ro oo n o ss

1s s r o

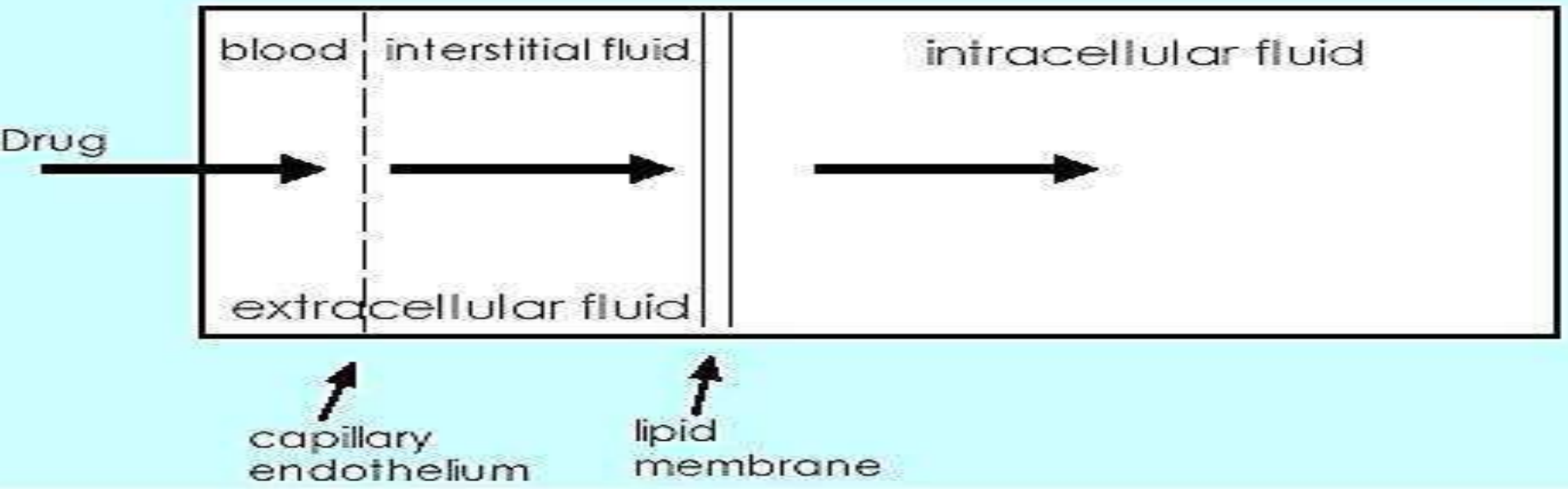


n s r on h s n o
hrs



Distribution

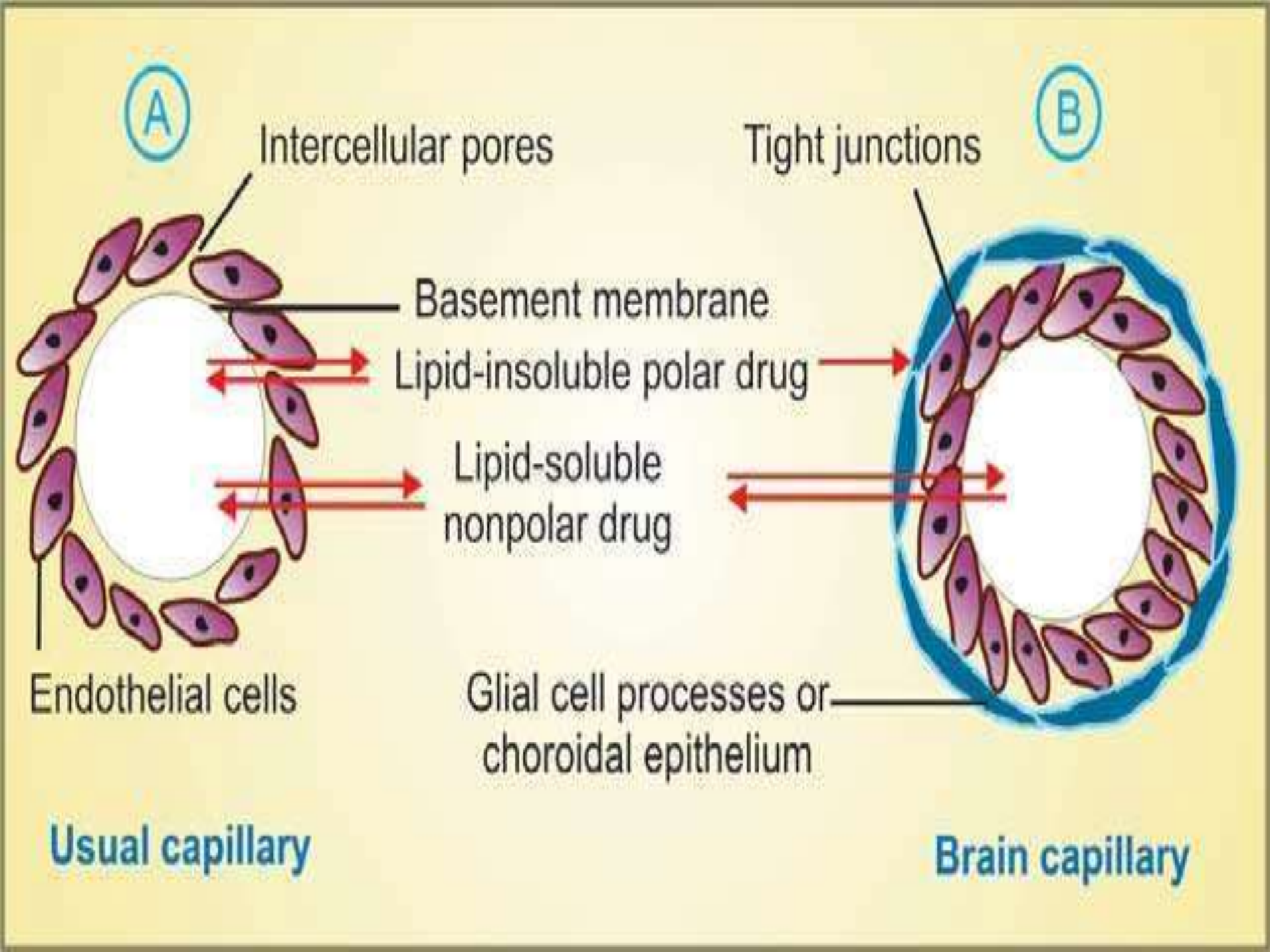
- rs r ns r o r s n
  on o r n n no h r n
  oo r s r s ss s



- s r on s r o n n ss
  ro ss h r n or s h
  on n r on r n n h
  oo n r s r ss s

- ro ss o rs h s on o
  r r n r s
  s sh

- s h h r o o on o r
  n s on s on n r on h
  s o on s r on s
  s n n ro n h _ons n ns
  n r on o on
- s r on o r s no n or
  hro ho h o s r n
  ss s r h r ro s
  r n r s n o r n
  n s


A
Intercellular pores
Basement membrane
Lipid-insoluble polar drug
Lipid-soluble
nonpolar drug
Endothelial cells
Usual capillary
B
Tight junctions
Glial cell processes or
choroidal epithelium
Brain capillary

Blood brain barrier

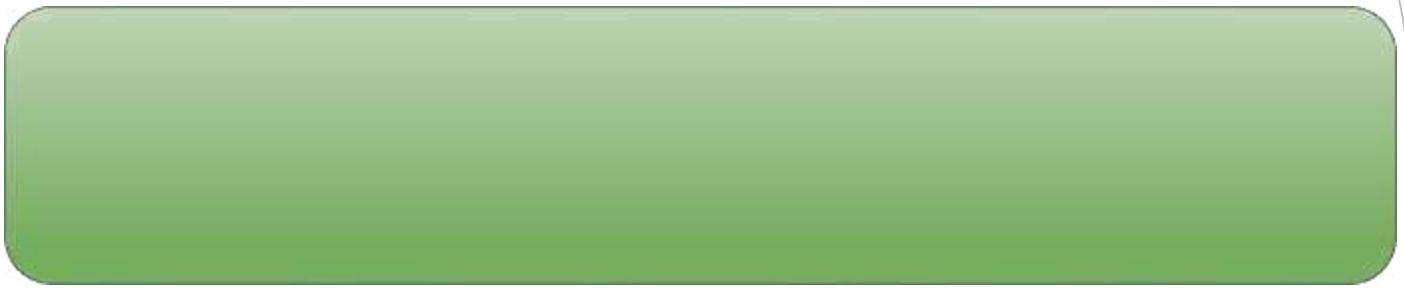
Cons r n s ss o r o r n n
C

r r ns or rs
o r rr r

C n or n ro s r n
ss

1 o s s n s n oo

r h r n ro r ns rs



n or on ons nn s r
n on o r n h s r ss
r r o

Penicillin
Chloramphenicol
Ampicillin

C r n rr r s r o
r o s ro C o r n

C n n
r n o r n s ss n n s

Placental barrier

- L n n r

  o r ns r o non o r so
  s s n s ss s on

- h r h n s s

1. r ns or no n
   os

   no os s rn no o n

o r o o os r o o r
r n r s

Drug administration should be severely restricted

r o n r rs r s r

Thalidomide
Phenytoin
Trimethadione streptomycin
Methotrexate

r n s r n s r s r
n on o s

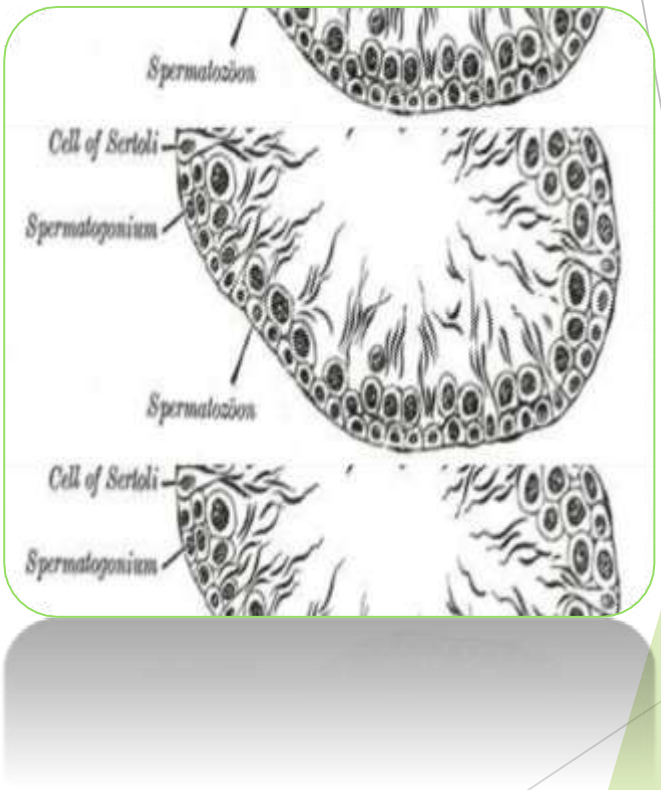
or h n s h

n h ro r s on o r

o n r s n r
or r s

Blood testis barrier

- Lo h
  s r o s r o
  n on
- h n on
  n n h or n
  s r o s h
  s rr r
- s r h ss
  o r s o
  s r o n
  s r s



Plasma protein binding as drug reservoir

r s n o s ro ns or r
ro ns n r rs n n
r

- ro n o n r no ss

Capillary diffusion
Metabolism
Excretion

- or n ro ns h
  on r o r n n

Plasma albumin
(acidic drugs)
1. Warfarin
2. Penicillin
3. Sulfonamides
4. Tolbutamide
5. Salycylic acid

Alpha 1 acid
glycoprotien
Acute phase reactant
(basic drugs)
1. Quinidine
2. Imipramine
3. Lidocaine
4. Chlorpromazine
5. Propranalol

Drugs bound to tissue proteins and nucleoproteins (High aVd) Example

1. Digoxin

2. Emetine

3. Chloroquine

Miscellanous protein binding

1. Corticosteroid - Transcortin globulin

2. Thyroxine- Alpha globulin

- C n or n s s o
  s ro n n n

1 h s ro n o n r
  o r

  h ro n o n

Difficult to remove by dialysis

n n o r s o s ro ns
  n s r

S S S

Disease	Influence on plasma protein	Influence on protein drug binding
n r r	 n on n	r s n n o r n r or s r r n
r	 n s n h s s	r s n n o r n n o s r s nor or r n n on
n or s r rn n on	 s	n r s n n o s r n r n r n

or h n on r n n o s s o
n r s o s n r on

- C n or n s n

Salicylates, Indomethacin, Phenytoin, Tolbutamide displace warfarin

Phenylbutazone, Salicylates, Sulfonamides displace tolbutamide

Sulfonamides, Vitamin k displace billirubin

Salicylates displace methotrexate

Apparent volume of distribution

o s h h sho n
o o on n no n o n o r

$$\frac{o \quad o\ n\ o \quad r}{Con\ \ n\ r \quad on\ o \quad r \quad n \quad s}$$

- o so r s s h or h n
  o o
- s r n o
- o n r n h no r on
  n o s o or h n
- o r o s s
  o o rs

r s oo n s or ss- r s h
o o s ro n o n

- C n s n n o r
  o o s r on
- r r o n os n
  or ons o on
- h oro n s n r
- Ch oro n s s
  o n os o o
  r hrs h n or
  n s

5L

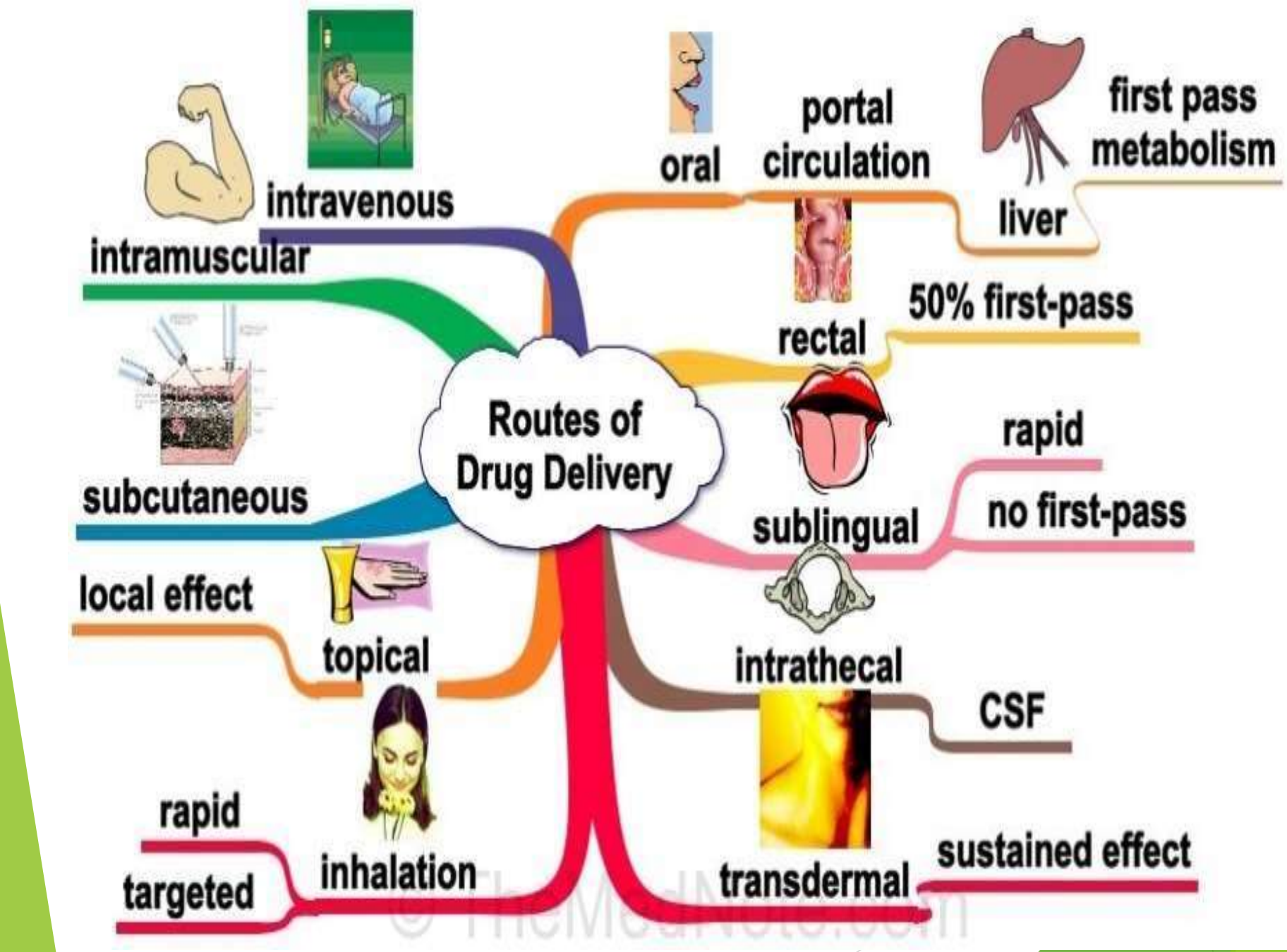
- r s r n n s r
  o r n
- r n ns n r r n
  ros

≈15L

- r s r s r o r r
- s r n o n n
  o r r n

L

- r s s r hro h o
  o r h no h n o n
  h o h o h n or
- n r on n r o s ss s
  o n r n
  or h n h oro n


Routes of Drug Delivery
intravenous
intramuscular
subcutaneous
local effect
topical
rapid
targeted
inhalation
oral
portal circulation
first pass metabolism
liver
rectal
50% first-pass
rapid
no first-pass
sublingual
intrathecal
CSF
transdermal
sustained effect

Thanks