GENERAL PHARMACOLOGY

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MPHL - 231

Recommended books

- **Basic and Clinical Pharmacology *by* Katzung**

- **Pharmacology *by* Rang**

Assessment of the course MPHL 231

- CAT- I 10
- Mid-term.....30
- CAT- II..... 15
- Practical 5

- Total 60
- Final 40

100

OUTLINES

- Introduction to pharmacology
- Branches of pharmacology
- Pharmacokinetics.
- Pharmacodynamics.
- Drug nomenclature.
- Sources of Drugs
- Adverse Drug Reactions
- Drug-Drug interactions

Pharmacology

Pharmakon : drug

Logos: Science

Is the science that deals with the drugs names, pharmacokinetics, pharmacodynamics, side effects and uses.

Drug

Drug = Drogue = a dry herb

It is any chemical substance that modify physiological system or pathological state and can be used for diagnosis, prevention or treatment of disease.

Pharmacology is divided into two parts:

- **Pharmacokinetics**

  What the body does to the drug?

- **Pharmacodynamics**

  What the drug does to the body?

Pharmacokinetics

Are studies of the absorption, distribution, metabolism & excretion of drugs.

Pharmacodynamics

Are studies of

- Mechanisms of drug action.
- Pharmacological effects.

Pharmacodynamics

deals with the action of drugs on living cells and mechanisms by which such effects are produced.

Pharmacopia

Pharmakon & Poiein.

Poiein means make.

A pharmacopia or formulary is the book containing a list of drugs with descriptions and formulas which is published by authorized body.

- British Pharmacopia (BP).
- United States Pharmacopia (USP).
- British National Formulary (BNF).

Drug nomenclature

- Full chemical name (Acetyl salicylic acid).
- Official = Generic name (Salicylates).
- Trade name (Aspro).

Sources of Drugs

- **Plants:**
  - Alkaloids (Morphine-Pilocarpine).
  - Glycosides (digoxin).
- **Animals:** Insulin-Vaccines-Vitamins.
- **Minerals:** Iron, gold, aluminium salts.
- **Synthetic:** Sulphonamides-aspirin.
- **Microorganisms:** Antibiotics.

Animal Source:

- Vitamin A from cod liver.
- Insulin from pancreas of bovine or procine.

Mineral Source:

- Iodine = Goiter.
- Iron = Anaemia.
- Gold = Arthritis.
- Aluminum hydroxide and magnesium trisilicate as antiacids.

PHARMACOKINETICS

Absorption of Drugs

OUTLINE

- Mechanisms of drug absorption
- Routes of drug administration
- Factors Affecting Drug absorption
- Bioavailability
- Drug Formulations

Drug absorption

Is the passage of drug through body barriers or cell membranes to reach its site of action.

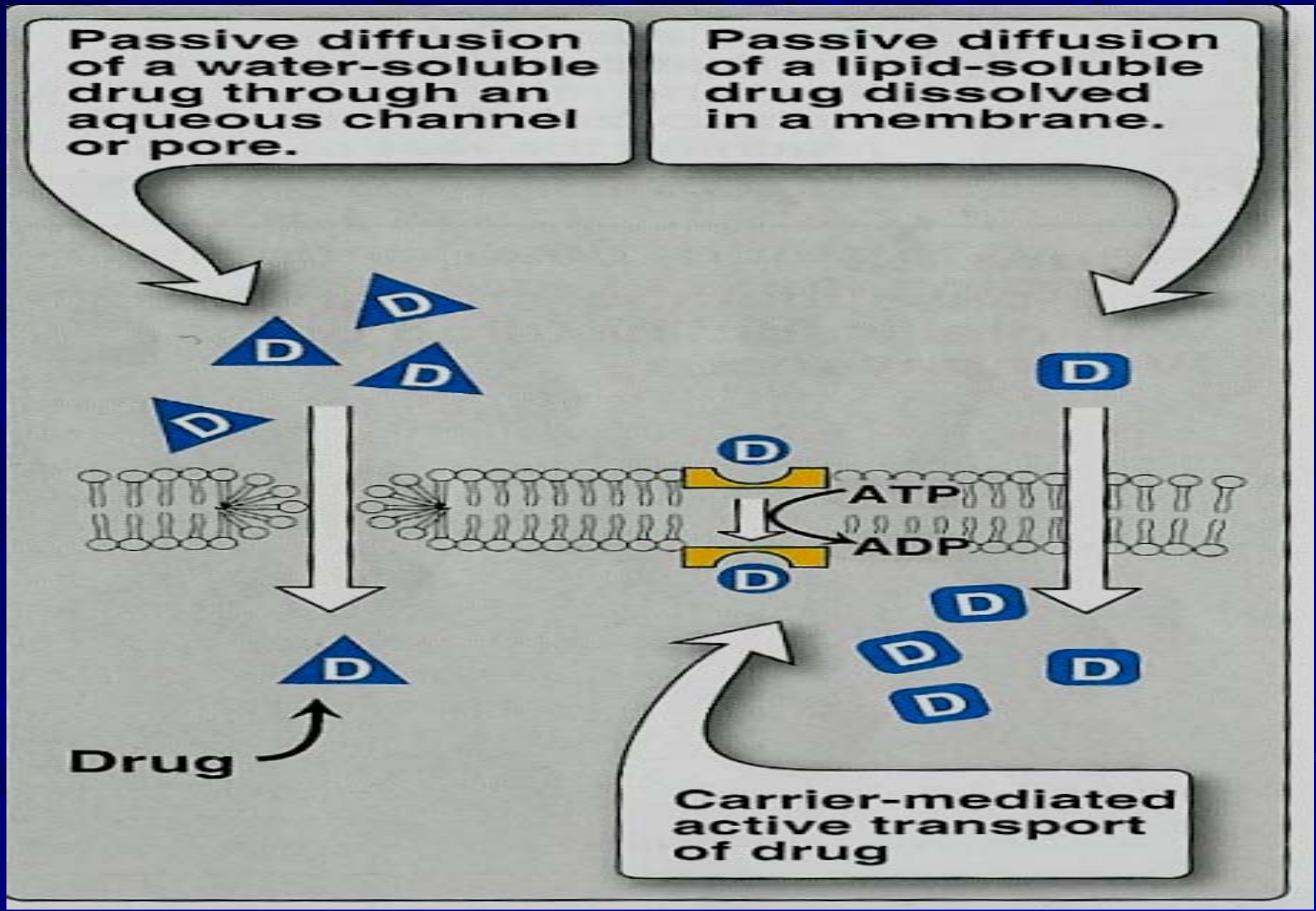
Mechanisms of drug absorption

1. Simple diffusion = passive diffusion.
2. Active transport.
3. Facilitated diffusion.
4. Pinocytosis (Endocytosis).

Simple diffusion

Characters

- Commonest.
- Non selective
- Requires no energy.
- Depends on concentration gradient.
- Depends on Lipid/ Water partition coefficient.
- Depends on pka of drug.
- Depends on pH of environment.


Passive diffusion of a water-soluble drug through an aqueous channel or pore.
Passive diffusion of a lipid-soluble drug dissolved in a membrane.
D
ATP
ADP
Drug
Carrier-mediated active transport of drug

Simple diffusion

PKa

(Dissociation or ionization constant)

PH at which half of the substance is ionized & half is unionized.

PH:

- **ionization of drugs.**
- **Weak acids → best absorbed in stomach.**
- **Weak bases → best absorbed in intestine.**

Active Transport

- Relatively unusual.
- Occurs against concentration gradient.
- Requires carrier and energy.
- Specific e.g. Iodides.
- Saturable.
- Depends on Lipid/Water partition coefficient.
- Iron absorption.
- Uptake of levodopa by brain.

Carrier-mediated Facilitated Diffusion

- Occurs along concentration gradient.
- Requires carriers
- Selective.
- Saturable.
- Does not require energy.
- Is independent of Lipid/Water partition coefficient.

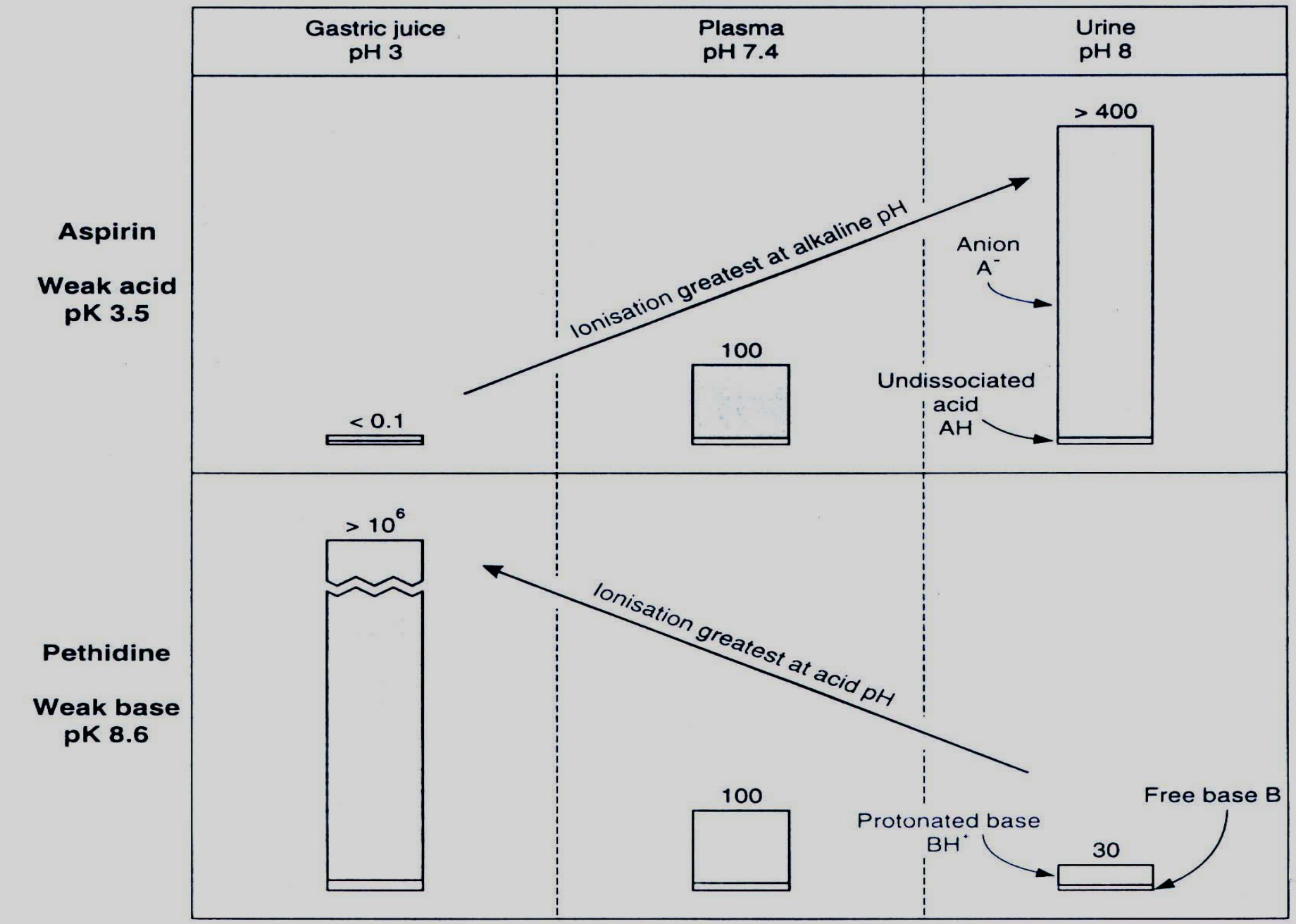
e.g. Uptake of glucose, vit B12 & intrinsic factor.

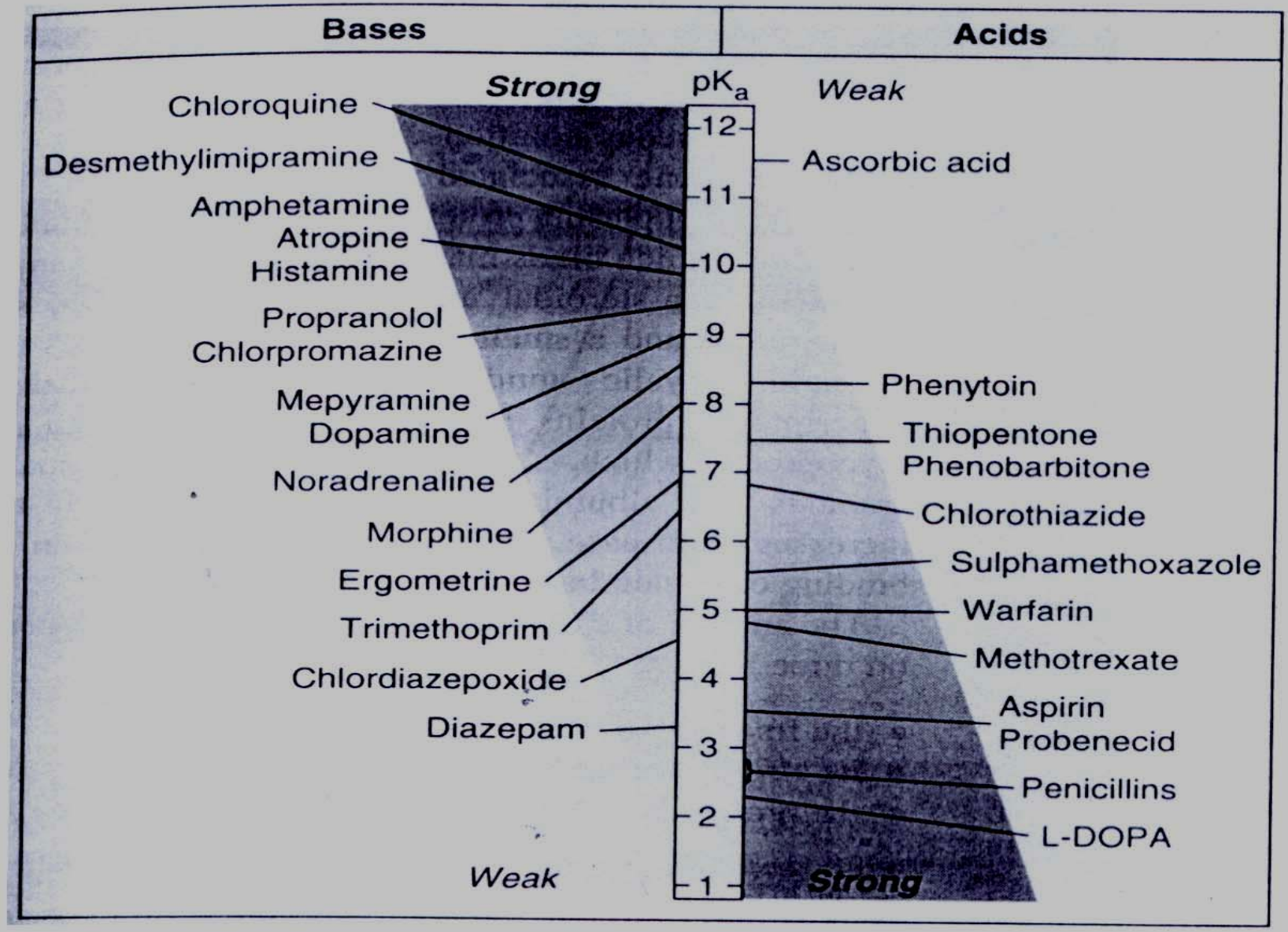
Endocytosis

High molecular weight drugs

Engulfment of the substrate by the cell.

Vit A & D & E & K absorbed by this way.


Gastric juice
pH 3
Plasma
pH 7.4
Urine
pH 8
Aspirin
Weak acid
pK 3.5
> 400
Anion
A⁻
Ionisation greatest at alkaline pH
100
Undissociated
acid
AH
< 0.1
Pethidine
Weak base
pK 8.6
> 10⁶
Ionisation greatest at acid pH
100
Free base B
Protonated base
BH⁺
30


Bases
Acids
Strong
pKa
Weak
Chloroquine
Desmethylimipramine
Amphetamine
Atropine
Histamine
Propranolol
Chlorpromazine
Mepyramine
Dopamine
Noradrenaline
Morphine
Ergometrine
Trimethoprim
Chlordiazepoxide
Diazepam
12
11
10
9
8
7
6
5
4
3
2
1
Ascorbic acid
Phenytoin
Thiopentone
Phenobarbitone
Chlorothiazide
Sulphamethoxazole
Warfarin
Methotrexate
Aspirin
Probenecid
Penicillins
L-DOPA
Weak
Strong

Routes of drug administration

- Gastrointestinal tract (GIT).
  - Oral
  - Sublingual
  - Rectal
- Parenteral administration = injections.
- Topical application

Oral administration

Advantages

Easy

Self use

Safe

Most convenient

cheap.

No need for sterilization.

Disadvantages of oral

- Delayed effect (Slow effect).
- Not suitable for vomiting, unconscious, emergency.
- No complete absorption (Low bioavailability).
- Destruction by GIT.
- First pass effect.
- GIT irritation.
- Food–Drug interactions.
- Drug-Drug interactions.

Formulation

Capsules

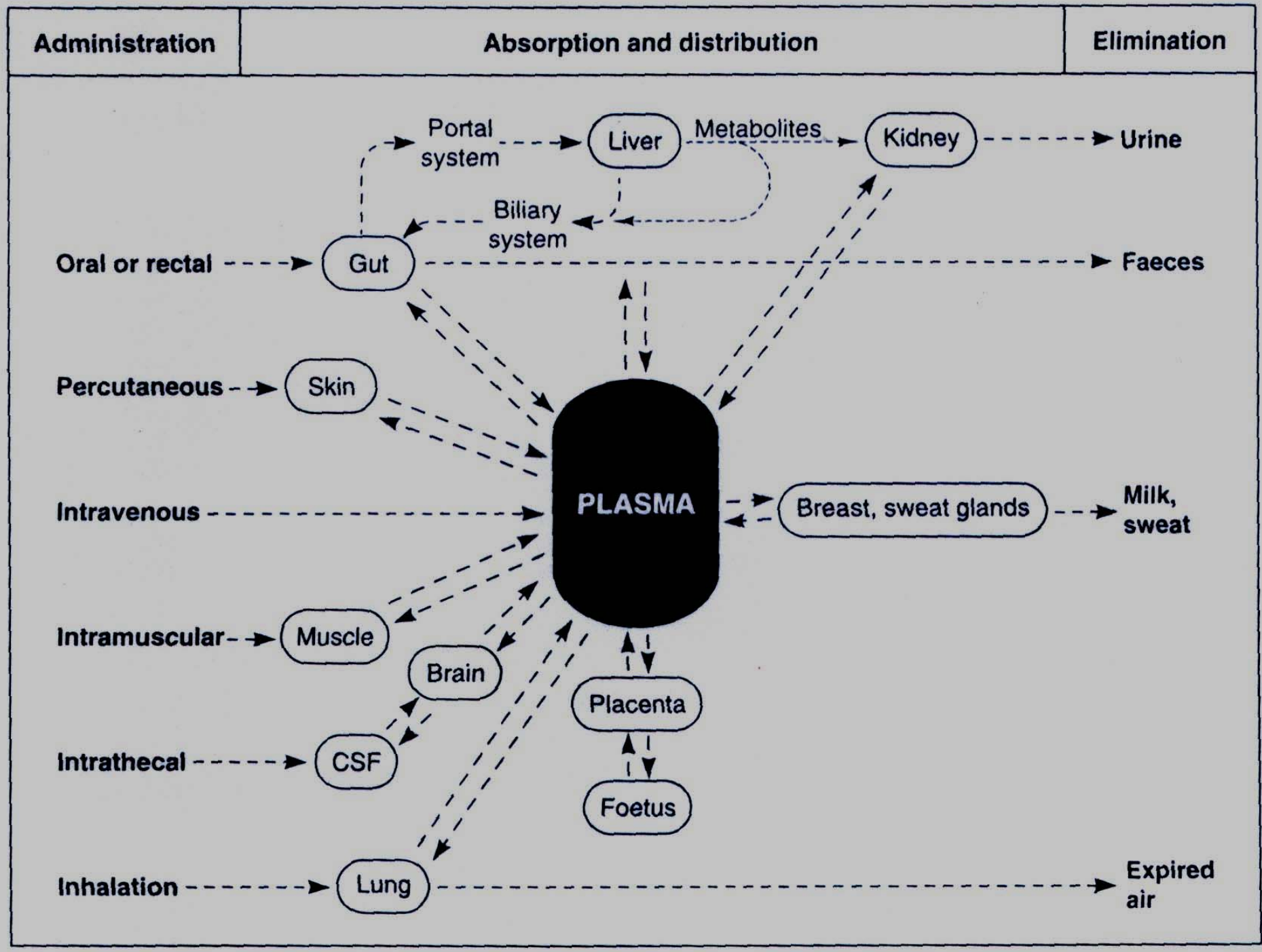
Tablets

Granules

Syrup

Suspension

Emulsion


Administration
Absorption and distribution
Elimination
Portal system
Liver
Metabolites
Kidney
Urine
Biliary system
Oral or rectal
Gut
Faeces
Percutaneous
Skin
PLASMA
Intravenous
Breast, sweat glands
Milk, sweat
Intramuscular
Muscle
Brain
Placenta
Intrathecal
CSF
Foetus
Inhalation
Lung
Expired air

Sublingual Administration

Advantages

- Rapid effect (Emergency)
- No first pass metabolism.
- No destruction by GIT (PH).
- No food drug interaction.

Sublingual Administration

Disadvantages

- Limited drugs.
- Smaller doses than oral.
- Dosage form (friable tablets).

Sublingual Administration

- Not for
  - irritant drugs.
  - Frequent use.
  - Vasoconstrictors for buccal BVS.

Rectal Administation

Advantages

Suitable for

- **vomiting & unconsciousness, children.**
- **Irritant & Bad taste drugs.**
- **For Local action e.g. piles**
- **Avoid first pass metabolism.**

Rectal Administation

Disadvantages

- Irregular absorption & bioavailability.
- Irritation of rectal mucosa.
- Inconvenience.

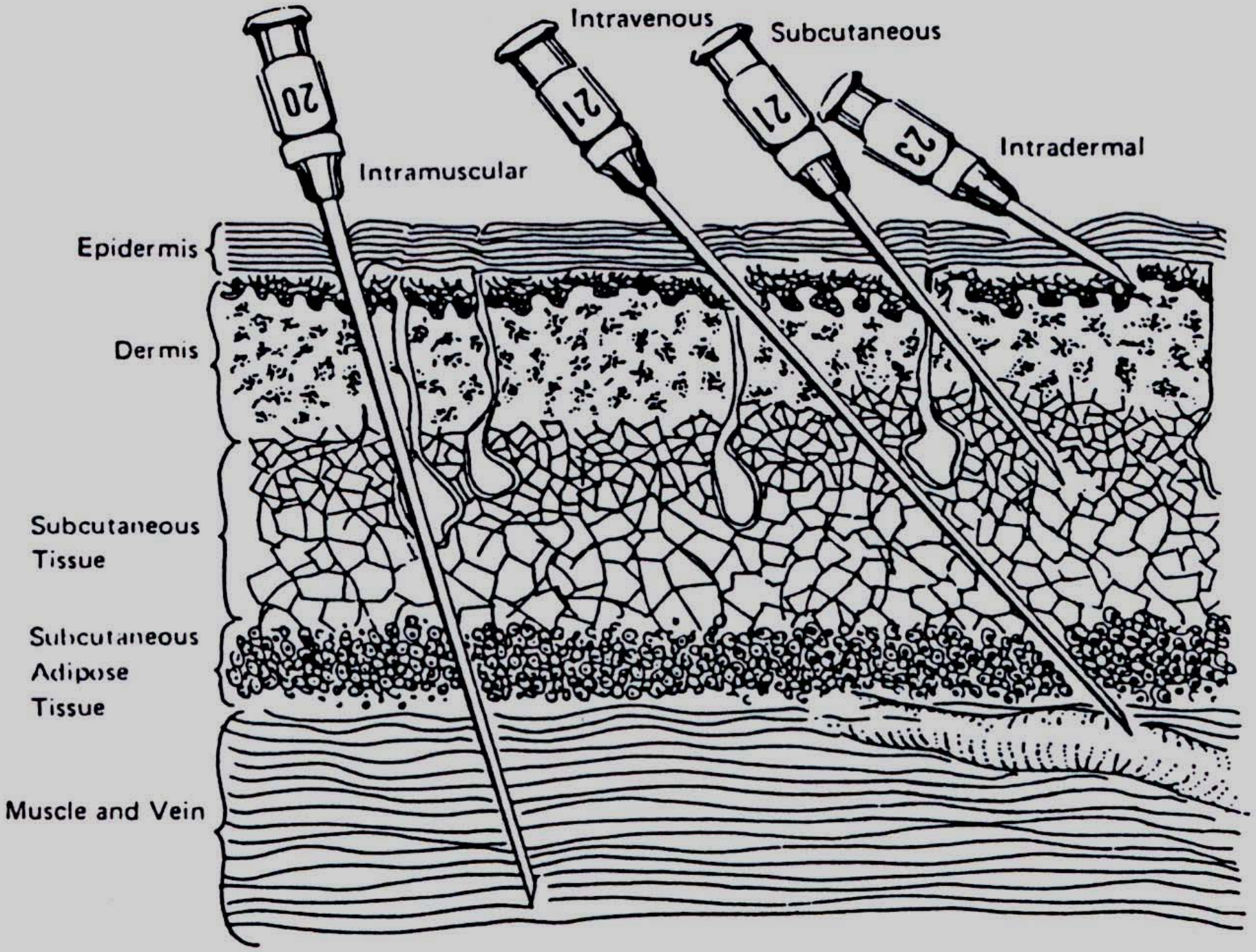
Formulation

Enema or suppository

e.g. aminophylline - phenobarbitone.

Parenteral administration

- Intradermal (I.D.)
- Subcutaneous (S.C.)
- Intramuscular (I.M.)
- Intravenous (I.V.)
- Intra-arterial (I.A.)
- Intrathecal (I.T.) (subarachnoid space)
- Intraperitoneal (I.P.) (peritoneum)
- Intra - articular (Synovial fluids)


Intravenous
Subcutaneous
20
21
21
23
Intramuscular
Intradermal
Epidermis
Dermis
Subcutaneous Tissue
Subcutaneous Adipose Tissue
Muscle and Vein

Intradermal Injection

- Between dermis & epidermis (0.1 ml).
- Vaccinations-Sensitivity test.

Subcutaneous Injection

- Under the skin (0.1 ml – 1 ml).
- Sustained release effect. e.g. insulin zinc preparation

Intramuscular Injection

- Larger amount of fluid (3-5 ml).
- Avoid first-pass metabolism.
- Onset of action more rapid than oral.
- Prolonged duration of action
- Solubility of drug is not important.
- Used for Oily preparation.

Disadvantages

- Pain – Abscess –Tissue necrosis.

Intravenous (I.V.)

Advantages

- The most rapid absorption.
- Rapid effect (in emergency).
- High bioavailability (100%)
- No destruction by GIT.
- No gastric irritation.
- No First pass metabolism.
- No food-drug interaction.
- Used in coma, convulsion
- Used for irritant drugs.

Disadvantages

- Only water soluble drugs (clear solution should be given).
- Anaphylaxis.
- Infection e.g. Viral hepatitis.
- Thrombophlebitis.
- Sterilization.
- Pain at site of injection.
- Needs skill & Training.
- More expensive.

Intraperitoneal Injection

Dialysis e.g. rabies vaccine.

Intracardiac Injection

In cardiac arrest e.g epinephrine.

Intra-arterial Injection

- Diagnosis ⟶ arteriography.
- Treatment ⟶ dissolution of coronary thrombosis.

Intra-thecal Injection

- CNS infections.
- Spinal anesthesia.
- Drugs that do not cross BBB.

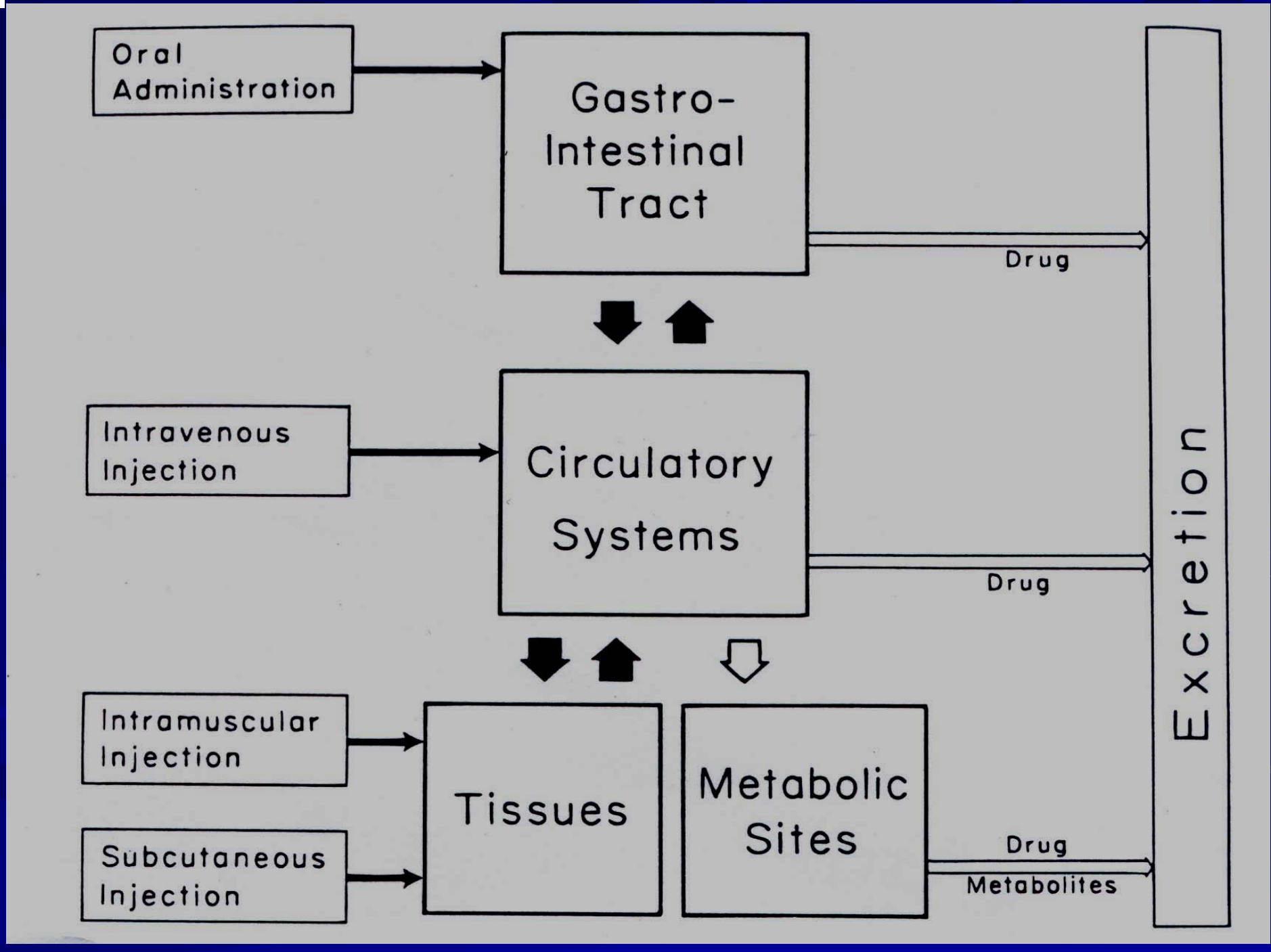
Topical application

- **Topical:**
  - Skin (percutaneous).
    adhesive plasters
  - Ear.
  - Nose.
  - Respiratory tract (Inhalation)
  - Eye.
  - Vagina

- Provide local action.
- Lipid soluble drugs.
- Prolonged drug action.
- Avoids first pass metabolism.

Inhalation

- Local action in respiratory tract.
- Rapid effect due to large surface area
- Inhalation anesthetics & bronchodilators.
- Drugs given as
  - Gases.
  - Volatile liquids e.g. halothane
  - Solution (aerosol, nebulizer)
  - powder (very fine).
  - NOT irritant.


Oral Administration
Gastro-Intestinal Tract
Drug
Intravenous Injection
Circulatory Systems
Drug
Intramuscular Injection
Subcutaneous Injection
Tissues
Metabolic Sites
Drug
Metabolites
Excretion

Bioavailability

- Is the fraction of unchanged drug that enters systemic circulation after administration and becomes available for biological effect.
- It may be less than the dose (unity).
- I.V. provides 100% bioavailability.

Factors Affecting Bioavailability

- Molecular Weight.
- Lipid/Water Partition Coefficient.
- Pka.
- Drug Formulation.
- First pass metabolism
- pH of gut.
- Rate of gastric emptying.
- Intestinal motility (Transit Time).
- Surface area available for absorption.
- Drug interactions
- Food

Food

Reduces absorption

aspirin, penicillin V,

tetracycline, erythromycin.

Increases absorption

Propranolol, diazepam, dicoumarol.