

Pharmacology Overview



Pharmacology

Field of medicine that specializes in the study of drugs, their sources, appearance, chemistry, actions, and uses.

Pharmacology is the body of knowledge concerned the action of chemicals on biologic systems.

Pharmacology is the study of how drugs exert their effects on living systems.

Pharmacologists work to identify drug targets in order to learn how drugs work. Pharmacologists also study the ways in which drugs are modified within organisms.

In most of the pharmacologic specialties, drugs are also used today as tools to gain insight into both normal and abnormal function.

- **Medical pharmacology** is the area of pharmacology concerned with the use of chemicals in the prevention, diagnosis and treatment of disease, especially in humans.
- **Toxicology** is the area of pharmacology concerned with the undesirable effects of chemicals on biologic systems.

• Divisions of Pharmacology

- Pharmacokinetics
- Pharmacodynamics
- Pharmacogenomics

Medical Pharmacology is divided into 2 major parts:

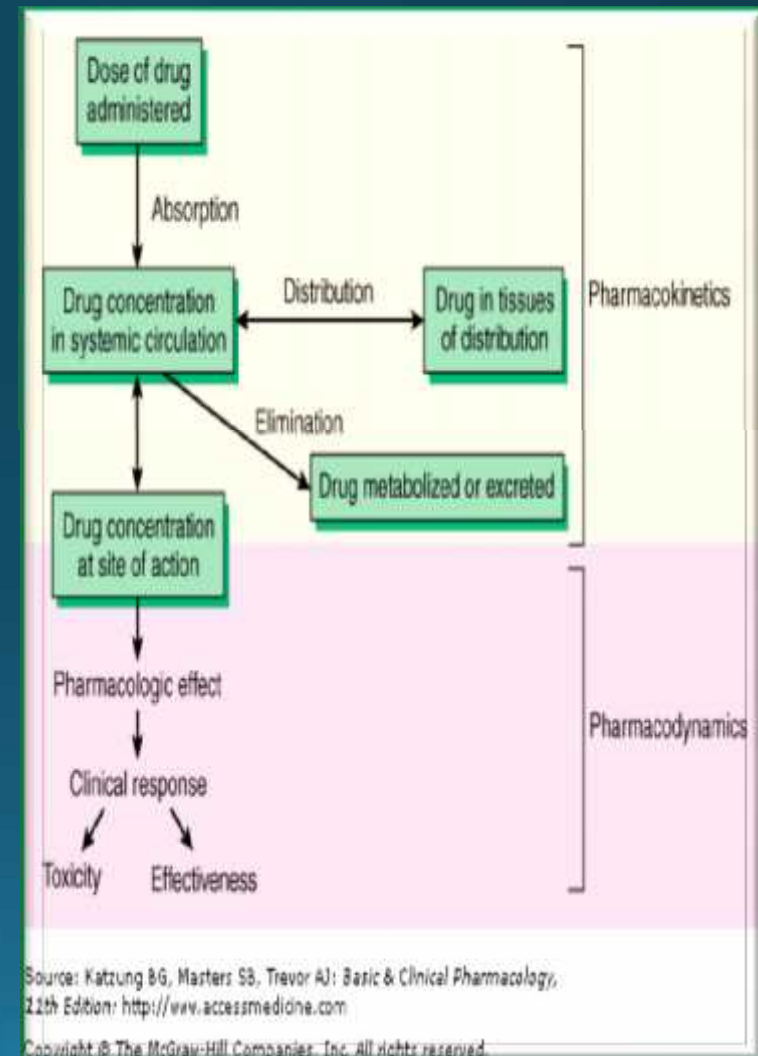
- **Pharmacokinetics and**
- **Pharmacodynamics.**

Pharmacokinetics describes the effects of the body on drugs, example, absorption, excretion, etc.

Pharmacodynamics denotes the actions of the drug on the body, such as mechanism of action and therapeutic and toxic effects.

Pharmacogenomics (Pharmacogenetics) – describes the genetic anomalies of metabolism of the drugs that may lead to hypersensitivity. That is, pharmacogenetics is the study of the genetic variations that cause differences in drug response among individuals or populations.

Pharmacokinetic and pharmacodynamic components of pharmacology



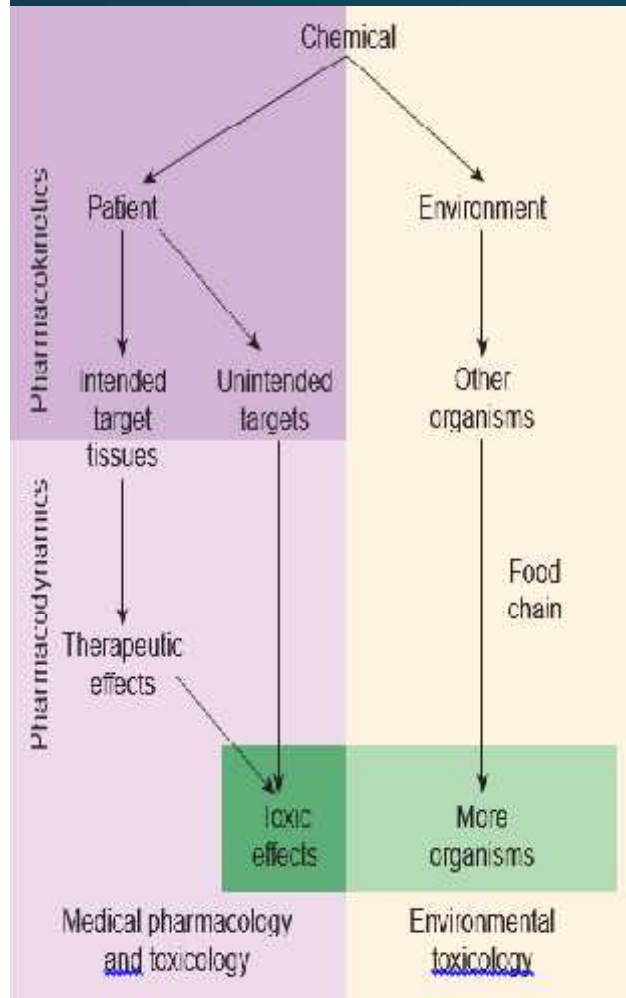
The actions of chemicals can be divided into two large domains.

The first (left side) is that of medical pharmacology and toxicology, which is aimed at understanding the actions of drugs as chemicals on individual organisms, especially humans and domestic animals. Both beneficial and toxic effects are included.

Pharmacokinetics deals with the absorption, distribution, and elimination of drugs.

Pharmacodynamics concerns the actions of the chemical on the organism.

The second domain (right side) is that of environmental toxicology, which is concerned with the effects of chemicals on all organisms and their survival in groups and as species.



Pharmacokinetics

Is what the body does to the drug.

- The magnitude of the pharmacological effect of a drug depends on its concentration at the site of action.
- Absorption
- Distribution
- Metabolism
- Elimination

Pharmacodynamics

Is study of how drugs interact in the human body.

Interaction of drugs with cellular proteins, such as receptors or enzymes, to control changes in physiological function of particular organs.

- Drug-Receptor Interactions
 - *Binding*
- Dose-Response
 - *Effect*
- Signal Transduction
 - *Mechanism of action, Pathways*

Pharmacogenetics

Area of pharmacology concerned with unusual responses to drugs caused by genetic differences between individuals.

- Responses that are not found in the general population, such as general toxic effects, allergies, or side effects, but due to an inherited trait that produces a diminished or enhanced response to a drug.
- Differences in Enzyme Activity
 - *Acetylation polymorphism*
 - *Butylcholinesterase alterations*
 - *Cytochrome P₄₅₀ aberration*

Pharmacist

One who is licensed to prepare and dispense drugs

Drug

Any substance that when taken into the body, may modify one or more of its functions.

Drugs are substances that act on living systems at the chemical (molecular) level and alter their functions.

Medicine is any drug which has a definite form, dose level and is therapeutically used for the treatment of disease in living subject.

The nature of drugs

Drugs are chemicals that modify body functions.

Drugs in common use include ions, carbohydrates, lipids, or proteins.

They vary in size from very small lithium (MW7) to very large proteins (eg, alteplase [tPA], a protein of MW 59.050).

However, most drugs have molecular weights between 100 and 1000. Some drugs are found in plants or animals, but many are partially or completely synthetic.

- **Drugs** have double names – generic and brand names.
- Generic name (official) is the legal, noncommercial name for a drug.
- Brand (trade) name is the commercial name for a drug, normally the property of the drug manufacturer.
- Chemical name is the chemical formula for a drug.

Drug Names

- **Chemical name**

- Describes chemical structure of the drug

- Formula that indicates composition of the drug

Drug Names

- **Generic name**

- Name that was established when drug was first manufactured

- **Written in lowercase letters**

- Official name of a drug

- Each drug has only one generic name

- Original manufacturer is only company that can use generic name for the first 17 years

Drug Names

- **Brand name**

Name under which the drug is sold by a specific manufacturer

Spelling always begins with a capital letter

Also known as the Trade Name

Name is owned by the drug company and no other company may use that name

Each brand name carries a registered trademark symbol ®

Drug forms:

Solid dosage forms.

- Powders.
- Tablets

Soft dosage forms.

- Ointment
- Pasta.
- Candles.

Liquid dosage forms.

- solution.
- Infusions.
- Broth.
- Sleazy.
- Suspensions
- extracts.
- Potions.

Placebo - An inactive "dummy" medication made up to resemble the active investigational formulation as much as possible but lacking therapeutic effect.

Orphan drugs - Drugs developed for diseases in which the expected number of patients is small. Some countries bestow certain commercial advantages on companies that develop drugs for uncommon diseases.

- . a pharmaceutical that remains commercially undeveloped owing to limited potential for profitability.
- "These drugs are called orphan drugs and are allowed to have less premarketing testing."

Pharmacy

Drug store

Toxicology

Study of poisons, their detection, their effects

Establishing antidotes and methods of treatment for conditions they produce

PRESCRIPTION

A written prescription is the prescriber's order to prepare or dispense a specific treatment - usually medication — for a specific patient.

PARTS OF PRESCRIPTION:

Superscription – This is simply R_x , the abbreviation for *recipe*, the imperative of *recipere*, meaning “take thou”.

Inscription – This represents the ingredients and their amounts. If a prescription contains several ingredients in a mixture, it is customary to write them in the following order: (1) basis or principal ingredient, (2) adjuvant, which may contribute to the action of the basis, and (3) corrective, which may eliminate some undesirable property of the active drug or the vehicle, which is the substance used for dilution.

Subscription – This contains directions for dispensing. Often it consists only of *M.*, the abbreviation for *misce*, meaning “mix”.

Signature – This is often abbreviated as *Sig.* And contains the directions to the patient, such as “Take one teaspoonful three times a day before meals.” The signature should indicate whether the medicine is intended for external application and whether it has some special poisonous properties. Wherever possible, instructions of a general nature, such as “take as directed”, should be avoided since the patient may misunderstand verbal directions given by the physician.

In addition to the basic parts of a prescription, it should have the patients name and the physician’s signature, followed by the abbreviation M.D.

RATIONAL PRESCRIBING & PRESCRIPTION WRITING:

Once a patient with a clinical problem has been evaluated and a diagnosis has been reached, the practitioner can often select from a variety of therapeutic approaches. *Medication, surgery, psychiatric treatment, radiation, physical therapy, health education, counseling, further consultation, and no therapy* are some of the options available. Of these options, drug therapy is by far the one most frequently chosen. In most cases, this requires the writing of a prescription.

THE PRESCRIPTION

Although a prescription can be written on any piece of paper, it usually takes a specific form. A typical printed prescription form for outpatients is shown in this figure:

① JOHN B. DOE, MD 1234 SOUTH NORTHEAST DR ③ WEST CITY, CA 94099 (234) 555-6789 ④	
FOR: ⑥	DATE: ⑤
ADDRESS: ⑦	
Rx ⑧ (DRUG NAME AND STRENGTH) ⑨ (QUANTITY) ⑩	
SIG: ⑪	
REFILL	TIMES
OR UNTIL ⑫	
NO CHILDPROOF CONTAINER ⑬	
WARNING: ⑭	⑮, MD
	AD1234567 ⑯
	STATE LICENSE NO. ⑰

Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology*, 11th Edition: <http://www.accessmedicine.com>

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This is the common form of outpatient prescription.

In the hospital setting, drugs are prescribed on a particular page of the patient's hospital chart called the **physician's order sheet (POS)** or **chart order**.

The patient's name is typed or written on the form; therefore, the orders consist of the name and strength of the medication, the dose, the route and frequency of administration, the date, other pertinent information, and the signature of the prescriber.

A typical chart order might be as follows:

11/15/08

10:30 a.m.

(1) Ampicillin 500 mg IV q6h x 5 days

(2) Aspirin 0.6 g per rectum q6h prn temp over 101

[Signed] Janet B. Doe, MD

Thus, the elements of the hospital chart order are equivalent to the central elements of the outpatient prescription.

ELEMENTS OF THE PRESCRIPTION

✓ *The first four elements* (see circled numerals in Figure 1) of the outpatient prescription establish the identity of the prescriber: name, license classification (ie, professional degree), address, and office telephone number. Before dispensing a prescription, the pharmacist must establish the **prescriber's bona fides** and should be able to contact the prescriber by telephone if any questions arise.

✓ *Element [5]* is the date on which the prescription was written. It should be near the top of the prescription form or at the beginning (left margin) of the chart order. Since the order has legal significance and usually has some temporal relationship to the date of the patient prescriber interview, a pharmacist should refuse to fill a prescription without verification by telephone if too much time has elapsed since its writing.

- ✓ *Elements [6] and [7]* identify the patient by name and address. The patient's name and full address should be clearly spelled out.
- ✓ *The body of the prescription contains the elements [8] to [11]* that specify the medication, the strength and quantity to be dispensed, the dosage, and complete directions for use. When writing the drug name (element [8]), either the brand name (proprietary name) or the generic name (nonproprietary name) may be used. The strength of the medication [9] should be written in metric units. However, the prescriber should be familiar with both systems now in use: metric and apothecary.

For practical purposes, the following approximate conversions are useful:

- **1 grain (gr) = 0.065 grams (g), often rounded to 60 milligrams (mg)**
- **15 gr = 1 g**
- **1 ounce (oz) by volume = 30 milliliters (mL)**
- **1 teaspoonful (tsp) = 5 mL**
- **1 tablespoonful (tbsp) = 15 mL**
- **1 quart (qt) = 1000 mL**
- **1 minim = 1 drop (gtt)**
- **20 drops = 1 mL**
- **2.2 pounds (lb) = 1 kilogram (kg)**

Drug Standards

- Rules established to control strength, quality, and purity of medications prepared by various manufacturers
- Require all preparations called by the same drug name to be of a uniform strength, quality, and purity

Drug Standards

- Pharmacopeia/National Formulary (P/NF)
 - Contains formulas and information that provide standards for preparation and dispensation of drugs
 - Recognized by government as the official listing of standardized drugs in the United States
 - specifies a drug is official when it is listed in P/NF

Drug References

- Available for health professionals responsible for safe administration of medications

- Provide the following information:

- Composition, action, indications for use, contraindications for use, precautions, side effects, adverse reactions, route of administration, dosage range, and what forms are available

Drug References

- **Hospital formulary**
 - Lists all drugs commonly stocked in the hospital pharmacy
 - Provides information about the characteristics of drugs and their clinical use

Drug References

- Physicians' Desk Reference

- Published yearly by Medical Economics Company

- Manufacturers pay to list information about their products in the PDR





- Same information that appears on Package Inserts (as required by the FDA)

- Generic name, indications, contraindications, adverse effects, dosage, and route of administration

Drug References

- Drug facts and comparisons
 - Loose-leaf binder reference that provides information on drugs according to their therapeutic classification
 - Same basic facts as other drug references
 - Particularly helpful in comparing the various drugs within each category to other products
 - In reference to effectiveness, content, and cost

Drug Sources

Source	Example	Drug name	Classification
Plants 	cinchona bark purple foxglove	quinidine digitalis	antiarrhythmic cardiotonic
Minerals 	magnesium gold	Milk of Magnesia Solganal; auranofin	antacid, laxative anti-inflammatory used to treat rheumatoid arthritis
Animals 	pancreas of cow, hog thyroid gland of animals	insulin thyroid, USP	antidiabetic hormone hormone
Synthetic 	meperidine diphenoxylate	Demerol Lomotil	analgesic antidiarrheal

Drug Actions – Drug Interactions

○ Drug actions

- How drugs produce changes within the body

○ Drug effect

- Changes that take place in the body as a result of drug action

- Slowing down or speeding up processes

- Destroying certain cells or parts of cells

- Replacing substances that the body lacks or fails to produce

Drug Actions – Drug Interactions

Desired effect

Effect of drug in the body that was intended

Side effect

Additional effect on the body by the drug that was not part of the goal for that medication

Not usually severe enough to warrant discontinuing the medication

Drug Actions – Drug Interactions

Adverse reaction

One in which the body reacts to a drug in an unexpected way that may endanger a patient's health and safety.

Contraindication

Any special symptom or circumstance that indicates that the use of a particular drug or procedure is dangerous, not advised, or has not been proven safe for administration.

Drug Actions – Drug Interactions

Local effect

Response to a medication that is confined to a specific part of the body.

Systemic effect

Generalized or widespread response to a drug by the body because it is absorbed into the bloodstream.

Drug Actions – Drug Interactions

Cumulation

Occurs when a drug is not completely excreted from the body before another dose is given.

Drug starts to accumulate in the body tissues when repeated doses are given.

Toxic effects may occur.

Drug Actions – Drug Interactions

Idiosyncrasy

An unusual, inappropriate response to a drug or to the usual effective dose of a drug.

Anaphylactic Shock = severe idiosyncratic reaction.

Acute respiratory distress, hypotension, edema, tachycardia, cool pale skin, cyanosis, and possible convulsions shortly after administration of the medication.

Drug Actions – Drug Interactions

○ Potentiation

○ Occurs when two drugs administered together produce a more powerful response than the sum of their individual effects

○ Tolerance

○ Resistance to effect of a drug

○ A characteristic of drug addiction

ROUTES OF DRUG ADMINISTRATION

Drugs are usually administered by one of the following routes of administration:

- oral;
- buccal;
- sublingual;
- rectal;
- topical;
- intravitreal (Fig.6);
- transdermal;
- intravenous;
- intramuscular;
- intraossal;
- subcutaneous;
- by inhalation.

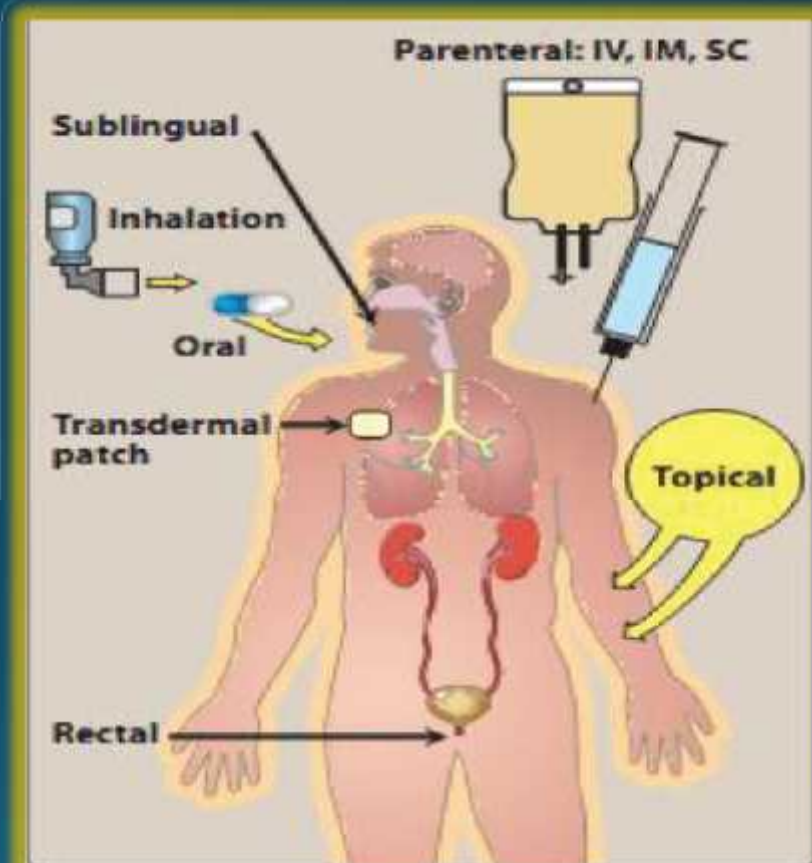


Figure 1.2

Commonly used routes of drug administration. IV = intravenous; IM = intramuscular; SC = subcutaneous.

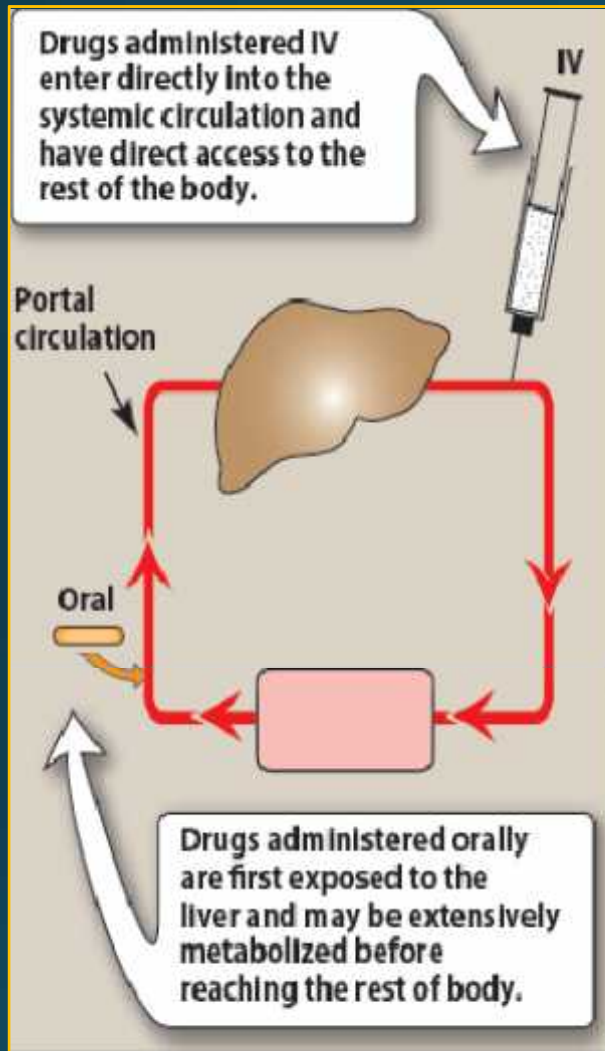


Figure 1.11

First-pass metabolism can occur with orally administered drugs. IV = intravenous.

1. Oral (swallowed) –The oral route offers maximum convenience, but absorption may be slower and less complete than when parenteral routes are used. Ingested drugs have low bioavailability.

The bioavailability of a drug is the fraction (or percentage) of the administered dose that reaches the systemic circulation.

After administration part of the oral dose is lost because of metabolism in the gut (intestine) and the liver before it enters the systemic circulation. This is the first-pass effect. So, ingested drugs are subject to the first-pass effect.

Bioavailability is defined as unity (or 100%) in the case of intravenous administration.

NOTE!

First-pass metabolism by the intestine or liver limits the efficacy of many drugs when taken orally. For example, more than 90 percent of nitroglycerin is cleared during a single passage through the liver, which is the primary reason why this agent is administered via the sublingual route when the first-pass effect is avoided.

Routes of Administration

Oral

Given by mouth and swallowed

Advantage

Easiest and safest method

Most economical method

Disadvantage

Slow method of absorption

Possibility of being destroyed by gastric juices

Routes of Administration

Sublingual - *The sublingual route (under the tongue) permits direct absorption into the systemic venous circulation, by passing the first-pass metabolism and hepatic portal circuit. This process may be fast or slow, depending on the physical formulation of the product.*

Placed under the tongue – dissolves in saliva

Advantage

More rapid absorption rate than oral

Higher concentration of medication reaches bloodstream

Disadvantage

Not convenient route of administration for bad-tasting medications or irritating medications

Routes of Administration

○ **Buccal** - The buccal route (in the pouch between the gums and cheek) offers the same features as the sublingual route.

○ Placed in mouth next to cheek (tablet form)

○ Advantage

○ More rapid absorption rate than oral

○ Higher concentration of medication reaches bloodstream

○ Disadvantage

○ Possibility of swallowing the pill

Routes of Administration

Inhalation - In the case of respiratory diseases (for example, asthma or chronic obstructive pulmonary disease), the inhalation route offers delivery closest to the target tissue. This route often results in rapid absorption because of the large and thin alveolar surface area. Examples of drugs administered via this route include bronchodilators, such as albuterol, and corticosteroids, such as fluticasone.

Medication is sprayed or inhaled into nose, throat, and lungs

Advantage

Good absorption due to large surface contact area

Provides rapid treatment

Disadvantage

Sometimes difficult to regulate dose

Not suitable method for medications that irritate mucous membrane lining

Routes of Administration

○ **Rectal** - The rectal route offers partial avoidance of the first-pass effect because suppositories tend to migrate upward in the rectum and part of the administered dose enters the portal circulation. Larger amounts of drug and drug with unpleasant tastes are better administered rectally than by the buccal or sublingual routes. Rectal administration is often used in patients who are vomiting or if the patient is unconscious. Furthermore, this route is often used in pediatrics. Some drugs irritate the rectal mucosae.

○ Medication inserted into rectum and is slowly absorbed into mucous membrane lining of rectum (suppository)

○ Advantage

○ One method of choice when patient is nauseated or cannot take medications orally

○ Disadvantage

○ Absorption is slow and irregular

Routes of Administration

Vaginal - Medication is inserted into the vagina in the form of a suppository, cream, foam, or tablet

Advantage

Easiest method for treating the specific area

Disadvantage

Medications sometimes stain underwear

No other disadvantages

Routes of Administration

Topical - This route includes application to the skin or to the mucous membrane of the eye, ear, nose, throat, airway, or vagina for local effect. The rate of absorption varies with the area of application and the drug's formulation but is usually slower than any of the routes listed previously. For example, clotrimazole is applied as a cream directly to the skin in the treatment of dermatophytosis.

Medication is applied directly to the skin or mucous membrane for a local effect to area

Advantage

Easy method, convenient

Disadvantage

Slow absorption through skin

Intravitreal injections:



Routes of Administration

Transdermal

Method of applying a pre-measured amount of medicine to unbroken skin through an adhesive-backed disk

Advantage

Good method for administering medications slowly into bloodstream over a period of time

Disadvantage

Units can be dangerous if they come in contact with skin of children or pets

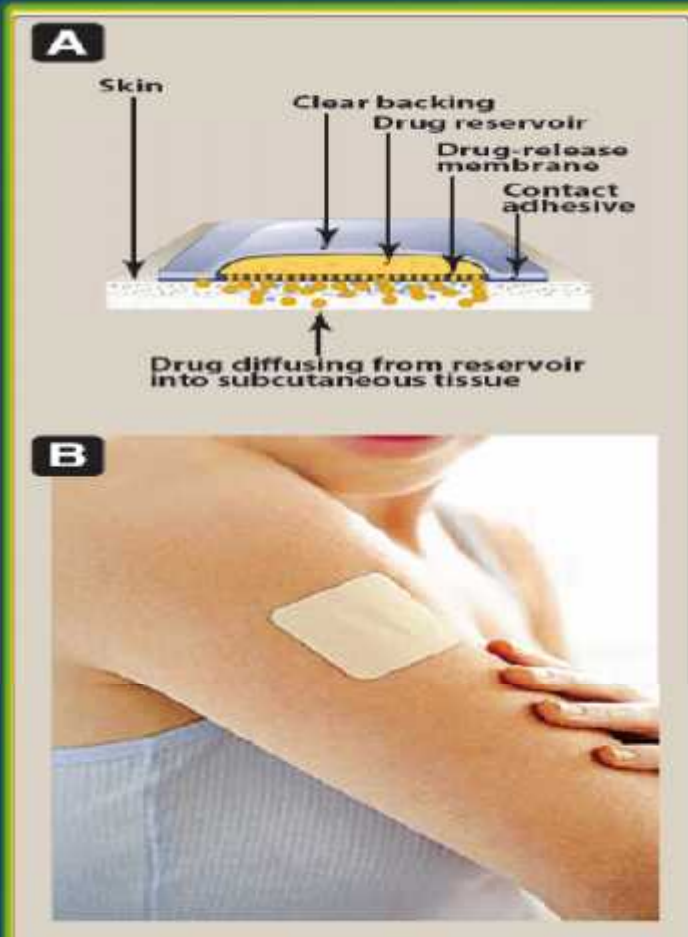


Figure 1.4
A. Schematic representation of a transdermal patch. B. Transdermal nicotine patch applied to arm.

Transdermal - This route involves application to the skin for systemic effect usually via a transdermal patch.

Absorption usually occurs very slowly, but the first-pass effect is avoided. This route is most often used for the sustained delivery of drugs, *such as the*

- *antianginal drug nitroglycerin,*
- *the antiemetic scopolamine, and*
- *nicotine transdermal patches, which are used to facilitate smoking cessation.*

Routes of Administration

Parenteral - Administered by injecting medication into body using a needle and syringe

Must be in liquid form

Administered by one of following methods

Intradermal

Intramuscular

Intravenous

Subcutaneous

Routes of Administration

Intradermal

- Small amount of medication is injected just beneath epidermis
- Used for allergy testing, tuberculin skin testing, and some vaccinations

Needle Angle: 10 to 15-degree

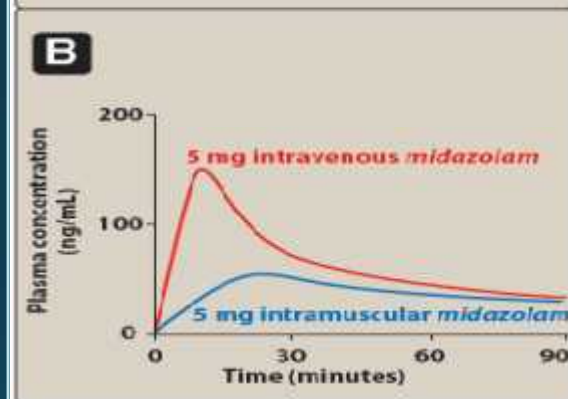
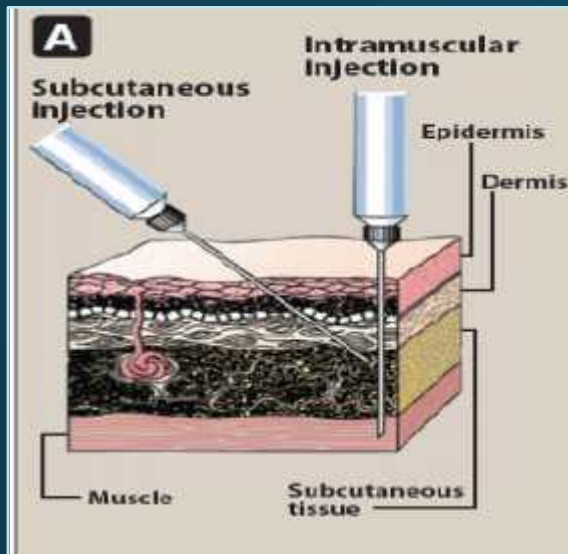


Figure 1.3

A. Schematic representation of subcutaneous and intramuscular injection.
 B. Plasma concentrations of *midazolam* after intravenous and intramuscular injection.

Intravenous – The intravenous route offers instantaneous and complete absorption. Bioavailability is 100%.

This route is potentially more dangerous because of the high blood levels reached when the dose is large or administration is too rapid.

Intramuscular - Absorption from an intramuscular injection site is often faster and more complete (higher bioavailability) than with oral administration. Large volumes (eg, >5ml into each buttock) may be given if the drug is not too irritating. First-pass metabolism is avoided, but anticoagulants such as heparin cannot be given by this route because they may cause bleeding (hematomas) in the muscle.

Routes of Administration

Intramuscular

Medication is injected directly into muscle
Used for administering antibiotics, medications that might be irritating to layers of the skin, and medications that require dosages larger than amount allowed for subcutaneous injections

Needle Angle: 90-degree

Routes of Administration

Intravenous

Medication is injected directly into the vein, entering the bloodstream immediately

Used when medication is needed quickly

Used for infusing medication over a period of time, by adding the medication to a bag of intravenous fluids

Needle Angle: 25-degree

Routes of Administration

Subcutaneous - The subcutaneous route offers slower absorption than the intramuscular route. Large-volume bolus doses are less feasible, but heparin does not cause hematomas when administered by this route. First-pass metabolism is also avoided.

Medication is injected into subcutaneous layer, or fatty tissue of skin.

Used for administering insulin, hormones, and local anesthetics.

Needle Angle: 45-degree

Parenteral Routes of Administration

