UNIT – 3 TRANSDERMAL DRUG DELIVERY SYSTEM

Points to be covered in this topic

- ☐ INTRODUCTION
- ☐ PERMEATION THROUGH SKIN
- ☐ FACTORS AFFECTING PERMEATION
- ☐ PERMEATION ENHANCERS
- ☐ BASIC COMPONENTS OF TDDS
- ☐ FORMULATION APPROACHES OF TDDS

TRANSDERMAL DRUG DELIVERY SYSTEM

INTRODUCTION

• Transdermal drug delivery systems (TDDS), also known as **"patches,"** are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin.

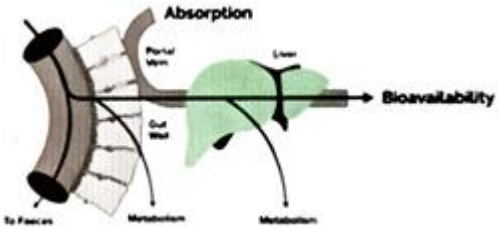
• TDD is a **painless method** of delivering drugs systemically by applying a drug formulation **onto intact and healthy skin**.

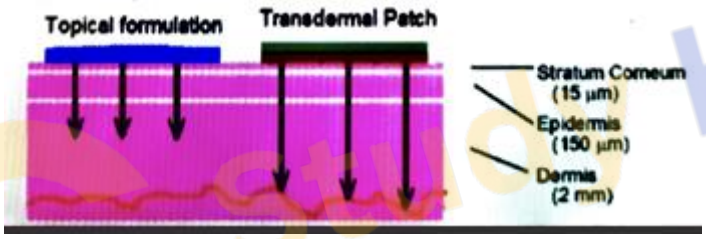
• The drug initially **penetrates through the stratum corneum** and then passes through the **deeper epidermis and dermis** without drug accumulation in the dermal layer.

• When drug reaches the **dermal layer**, it becomes available for **systemic absorption** via the dermal microcirculation.

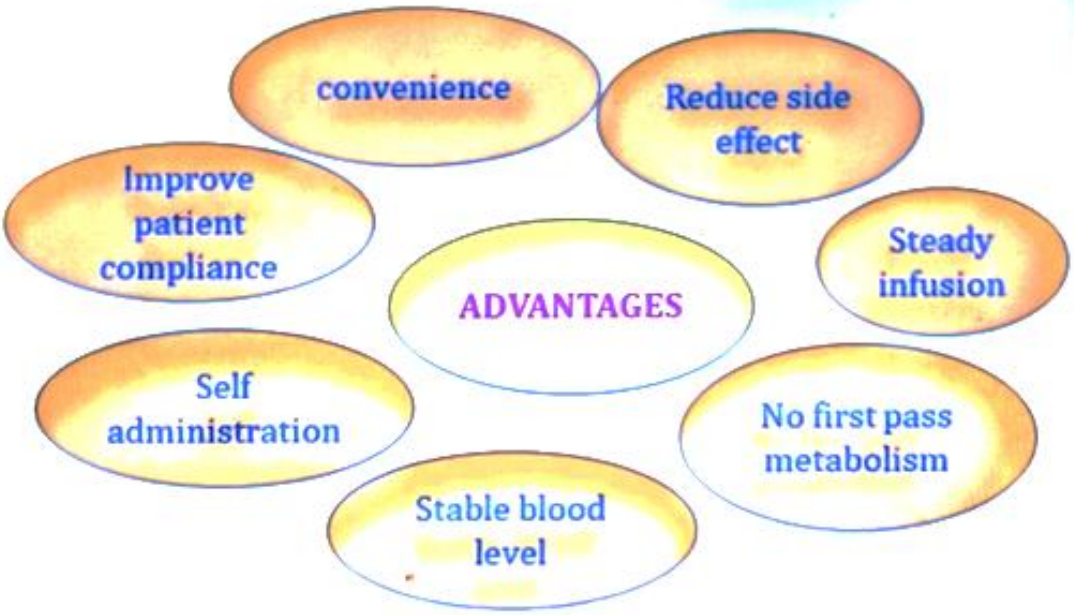
• Transdermal delivery provides a **leading edge over injectable and oral routes** by increasing patient compliance and **avoiding first-pass metabolism**, respectively.

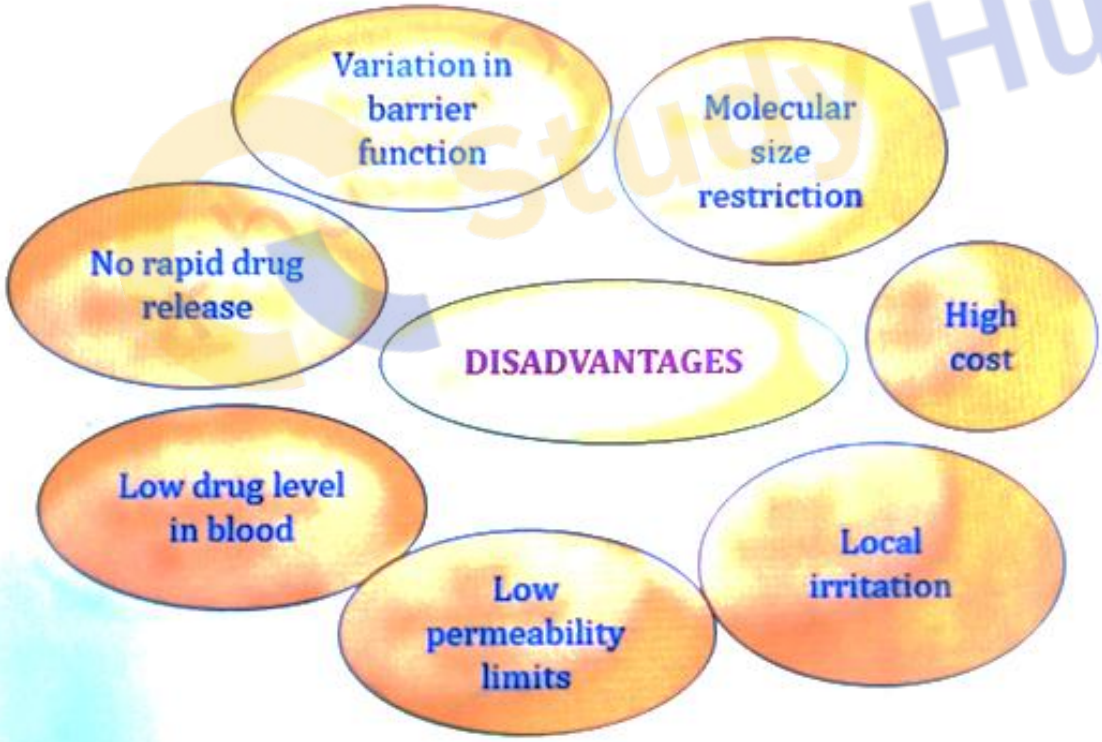
• Transdermal delivery not only provides **controlled, constant administration** of the drug, but also allows continuous input of drugs with **short biological half-lives** and eliminates **pulsed entry into systemic circulation**, which often causes undesirable side effects.





❖ Advantages and Disadvantages



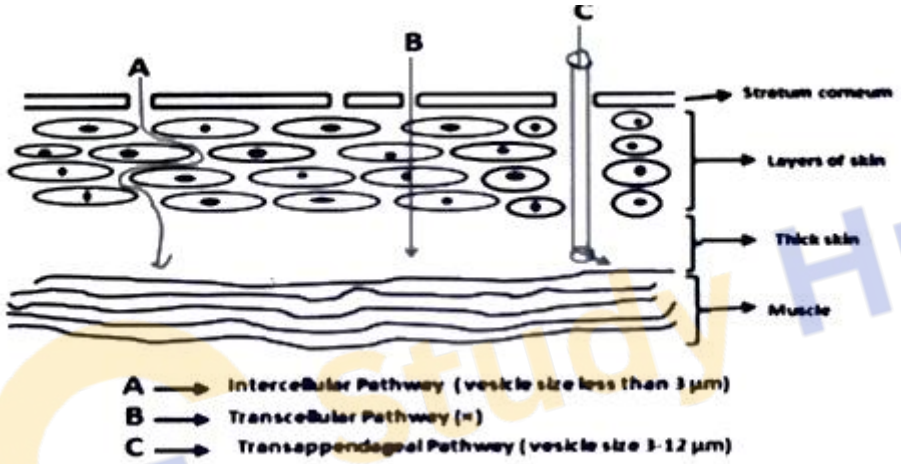


PERMEATION THROUGH SKIN

The permeation through the skin occurs by the following routes:

- **Transepidermal absorption**
- **Transfollicular (shunt pathway absorption)**
- **A clearance by local circulation**

Pathways of permeation through skin

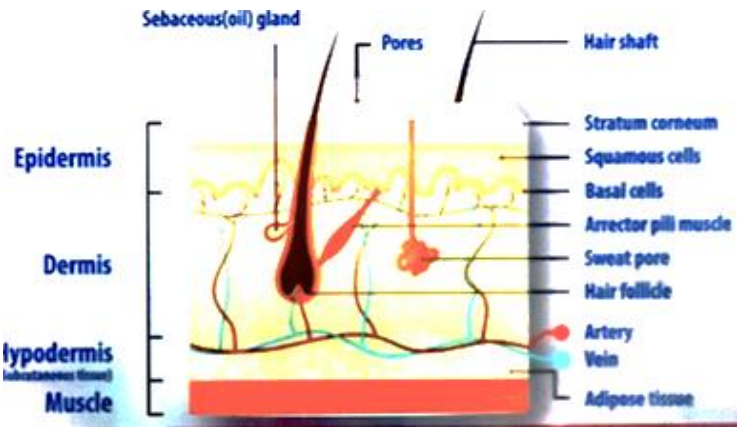


TRANSEPIDERMAL ABSORPTION

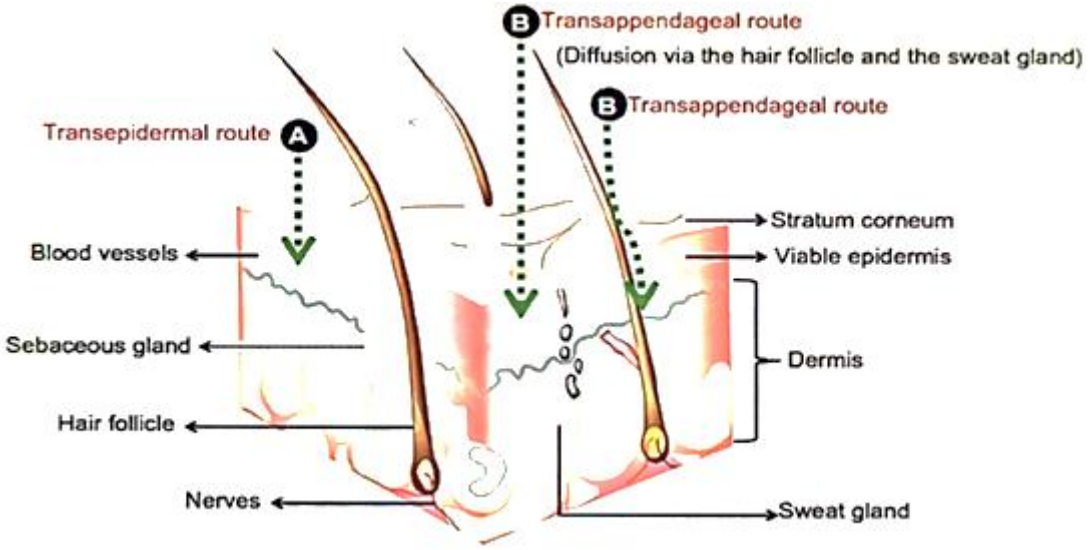
• **Stratum corneum** is the main resistance for absorption through this route. Permeation involves **partitioning of the drug into the stratum corneum**.

• Permeation through the skin depends upon the **o/w distribution tendencies of the drug**.

• **Lipophilic drugs** concentrate in and diffuse with relative ease.



• Permeation through the **dermis** is through the **epidermis interlocking channels of the ground substance**.



❖ Transfollicular Absorption

• The **skin appendages (sebaceous and eccrine glands)** are considered as **shunts** for bypassing the stratum corneum.

• **Follicular route is important for permeation** because the opening of the follicular pore is relatively large and **sebum aids in the diffusion** of the penetrant.

• **Partitioning into the sebum followed by the diffusion to the depth of the epidermis** is the mechanism.

(Diagram labels):

- Transepidermal route
- Transappendageal route (Diffusion via the hair follicle and the sweat gland)
- Stratum corneum

- Viable epidermis
- Dermis
- Blood vessels
- Sebaceous gland
- Hair follicle
- Nerves
- Sweat gland

❖ Clearance by Local Circulation

• The earliest point of entry of drugs into the systemic circulation is **within the papillary plexus in the upper epidermis**.

• The process is thus regarded as **the end point**.

❖ FACTORS AFFECTING PERMEATION

❖ Physicochemical Properties of the Permeate Molecule

➤ Partition Co-efficient

• Drug possessing both **water and lipid solubility** are favorably absorbed through the skin.

• **Transdermal permeability co-efficient shows a linear dependence on partition co-efficient.**

➤ Molecular Size

• There is an **inverse relationship** existed between **transdermal flux** and **molecular weight** of the molecule.

• The drug molecules selected as candidates for transdermal delivery tend to lie within **narrow range of molecular weight (100–500 Dalton).**

➤ pH Condition

• According to **pH partition hypothesis**, only the **unionized form** of the drugs can permeate through the lipid barrier in significant amounts.

➤ Solubility / Melting Point

• **Lipophilicity is a desired property** of transdermal candidates as lipophilic molecules tend to permeate through the skin faster than more hydrophilic molecules.

• Drugs with **high melting points** have relatively **low aqueous solubility** at normal temperature and pressure.

❖ Physicochemical Properties of the Drug Delivery System

➤ Affinity of the Vehicle for Drug Molecules

• It can influence **the release of the drug molecule** from the carrier.

• **Solubility in the carrier** determines the release rate of the drug.

➤ Composition of Drug Delivery System

• Composition of drug delivery system may affect not only the **rate of drug release** but also the **permeability of the SC** by means of hydration.

➤ Enhancement of Transdermal Permeation

• Due to the dead nature of the SC, the **release of the drug from the dosage form is less**.

• **Penetration enhancers** thus can cause the physicochemical or physiological changes in SC and **increase the penetration of the drug through the skin**.

❖ Physiological and Pathological Condition of the Skin

➤ Skin Age

• Foetal and infant skin appears to be **more permeable** than mature adult skin.

• Therefore **percutaneous absorption of topical steroids** occurs more rapidly in children than in adults.

➤ Lipid Film

• The thin lipid film on skin surface is formed by the **excretion of sebaceous glands** and cell lipids like sebum, help in **maintaining the barrier function of the SC**.

➤ Skin Hydration

• Hydration of SC can **enhance transdermal permeability**.

➤ Skin Temperature

• Raising skin temperature results in an **increase in the rate of skin permeation**.

• Which are in contact with skin leading to an **increase in percutaneous absorption**.

➤ Cutaneous Drug Metabolism

• After crossing the SC barrier, some of the drug reaches the **general circulation in active form** and because of the presence of **metabolic enzymes present in the skin layers**.

• It was reported that **more than 95% of testosterone absorbed was metabolized** as it present through the skin.

❖ PERMEATION ENHANCERS

• These are compounds which **promote skin permeability** by altering the skin as a barrier to the flux of the desired penetrant.

• The flux of the drug (J) is given by:

$$J = D\left(\frac{dc}{dx}\right)$$

Where:

- **D = diffusion coefficient**
- **C = concentration of the diffusing species**

- **x = spatial coordinate**

❖ Classification of Permeation Enhancers

➤ Chemical Enhancers

Chemical permeation enhancers can work by **one or more of the following three principles**:

✓ Relaxation of the extremely ordered **lipid structure of the stratum corneum**.

✓ Interacting with **aqueous domain of bilayer of lipid**.

✓ Enhanced **partition of the drug**, by addition of co-enhancer solvent into the stratum corneum.

❖ Types of Chemical Enhancers

a. Solvents

b. Surfactants

- **Anionic surfactants:** Dioctyl sulphosuccinate, Sodium lauryl sulphate
- **Non-ionic surfactants:** Pluronic F127, Pluronic F68
- **Bile salts:** Sodium taurocholate, Sodium deoxycholate

c. Binary systems:

- Propylene glycol, oleic acid

d. Miscellaneous chemicals:

- Urea, Calcium thioglycholate

BASIC COMPONENTS OF TDDS

1. Polymer Matrix:

The polymer controls the release of the drug from the device. Possible useful polymers for transdermal devices are:

a. Natural Polymers:

e.g., cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.

b. Synthetic Elastomers:

e.g., polybutadiene, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene-butadiene rubber, Neoprene etc.

c. Synthetic Polymers:

e.g., polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinyl pyrrolidone, Polymethylmethacrylate, Epoxy etc.

2. Drug:

For successfully developing a transdermal drug delivery system, the drug should be chosen with great care.

Physicochemical properties:

- Should have a molecular weight less than **1000 Daltons**
- Should have affinity for both **lipophilic and hydrophilic phases**
- Should have **low melting point**

3. Permeation Enhancers:

- These are compounds which **promote skin permeability** by altering the skin as a barrier to the flux of a desired penetrant.
- Improve the **diffusivity and solubility of drugs** through the skin that would reversibly reduce the barrier resistance of the skin.
- These include water, pyrrolidones, fatty acids and alcohols, zone and its derivatives, alcohol and glycols, essential oils, terpenes and derivatives, sulfoxides like **DMSO** and their derivatives, urea and surfactant.

4. Pressure Sensitive Adhesives (PSA):

- Fastening of all transdermal devices to the skin can be done by using a PSA.
- The first approach involves the **development of new polymers**, which include hydrogel hydrophilic polymers and polyurethanes.
- The second approach is to **physically or chemically modify the chemistries of the PSAs** in current use (such as silicones and acrylates).

5. Backings Laminates:

- Backings laminates are selected for **appearance, flexibility and need for occlusion**.
- Examples of backings are **polyester film, polyethylene film and polyolefin film**.

- It causes the TDDS to lift and may possibly irritate the skin during long-term use.

6. Release Liner:

- During storage the patch is covered by a protective liner that is **removed and discarded before the application** of the patch to the skin.
- The release liner is composed of a base layer which may be **non-occlusive** (e.g., paper fabric) or **occlusive** (e.g., polyethylene, polyvinyl chloride).
- The liner should be **chemically inert**.

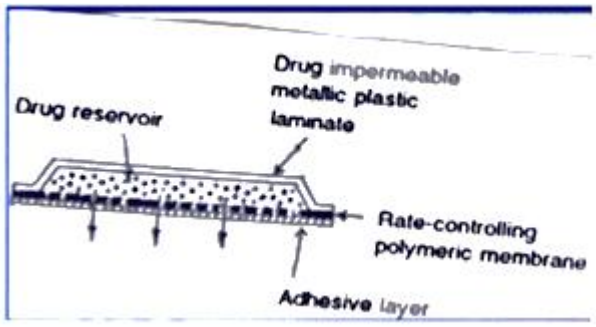
FORMULATION APPROACHES OF TDDS

1. Polymer Membrane Permeation Controlled TDDS System:

- Drug reservoir sandwiched between **drug impermeable backing laminate** and **rate controlling polymeric membrane**.
- In drug reservoir compartment drug is **dispersed homogeneously in a solid polymeric matrix** (e.g., polyisobutylene),
- Suspended in an unleachable viscous liquid medium (e.g., silicon fluid) to form a paste-like suspension.
- Rate controlling membrane is either a **micro-porous or a nonporous polymeric membrane** (e.g., ethylene-vinyl acetate copolymer).

Examples:

- **Estraderm** (twice a week in treatment of postmenopausal syndrome)



- **Duragesic** (management of chronic pain for 72 hrs)

Intrinsic rate of drug release:

$$\{dq/dt\} = Cr\left(\frac{1}{Pm} + \frac{1}{Pa}\right)$$

Where:

- **Cr** = Concentration of drug in the drug reservoir
- **Pa** = Permeation co-efficient of adhesive layer
- **Pm** = Permeation co-efficient of rate controlling membrane

For any microporous rate-controlling membrane, **Pm approximately represents the sum of permeability co-efficient across the pores and polymeric material**.

2. Polymer Matrix Diffusion Controlled TDDS System:

- In this the drug reservoir is prepared by **homogeneously dispersing drug particles** in a hydrophilic (or) lipophilic polymer matrix.
- The resulting polymer matrix is then **moulded into discs** with defined surface area and controlled thickness.
- The medicated disc is then **moulded onto an occlusive base plate** in a compartment made up of a drug impermeable backing.
- Finally **adhesive polymer is spread along the circumference** of the film.

Example:

- **Nitroglycerine releasing transdermal therapeutic system** at a daily dose of **0.5 g/cm²** for angina pectoris.

Rate of drug release equation:

$$dq/dt = \{ACpDp/2t\}^{1/2}$$

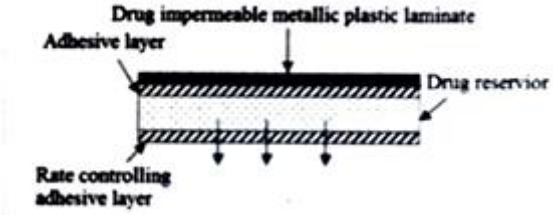
Where:

- **A** = Initial drug loading dose dispersed in polymer matrix
- **Cp** = Solubility of drug in polymer
- **Dp** = Diffusivity of drug in polymer
- Since Cp is equal to Cr

3. Adhesive Dispersion – Type Systems:

- This is a **simplified form of membrane** permeation-controlled systems.
- In this system, drug and other selected excipients are directly **incorporated into the adhesive solution**.
- They are then mixed and casted as thin films and finally the solvent is **evaporated by drying the film**.
- The drug reservoir (film) is then **sandwiched between the backing laminate and rate-controlling** adhesive polymer membrane.

Rate of drug release:



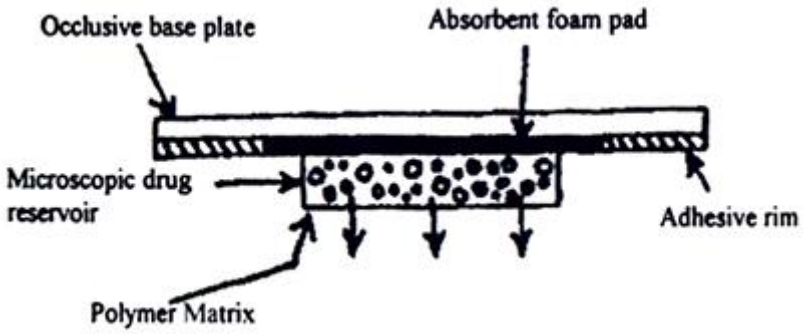
$$dq/dt = Cr \cdot Ka/r \cdot Da/ha$$

Where:

- **Ka/r** = Partition co-efficient for interfacial partitioning of drug from reservoir layer to adhesive layer

4. Micro-Reservoir Dissolution Controlled TDDS System:

- It is considered as the **hybrid system of reservoir and matrix dispersion type drug delivery**.
- In this system the drug reservoir is formed by **first suspending the drug solids in aqueous solution** of water-miscible drug solubiliser (e.g., polyethylene glycol).
- Then **homogeneously dispersing the drug suspension** with controlled aqueous soluble lipophillic polymer by high shear mechanical force to form **thousands of un-leachable microscopic drug reservoirs**.



UNIT–3 GASTRO RETENTIVE DRUG DELIVERY SYSTEM (PART - 2)

Points to be covered in this topic

➞ ☐ **INTRODUCTION**

➞ ☐ **ADVANTAGES OF GRDDS**

➞ ☐ **DISADVANTAGES**

➞ ☐ **APPROACHES**

➞ ☐ **APPLICATION**

GASTRO RETENTIVE DRUG DELIVERY SYSTEM

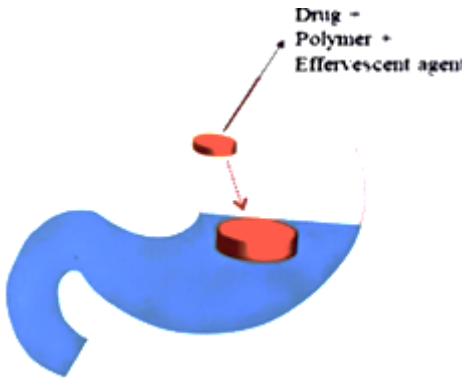
INTRODUCTION

• Gastro retentive drug delivery is an **approach to prolong gastric residence time**, thereby targeting **site-specific drug release in the upper gastrointestinal tract (GIT)** for local or systemic effects.

• Gastro retentive dosage forms can **remain in the gastric region for long periods** and hence significantly **prolong the gastric retention time (GRT)** of drugs.

• Gastro-retentive drug delivery systems provide efficient means of **enhancing the bioavailability and controlled delivery of many drugs**.

• Drugs which require increase in bioavailability and controlled delivery can be formulated by utilizing the novel concept **GRDDS**.



Need for gastro-retention:

✓ Drugs that are absorbed from the **proximal part of the GIT**.

✓ Drugs that are **less soluble or that degrade at alkaline pH**.

✓ Drugs that are absorbed due to **variable gastric emptying time**.

✓ Treatment of **peptic ulcers caused by H. Pylori infections**.

ADVANTAGES OF GRDDS

• This system offers **improved bioavailability**.

• It reduces **dose and dosing frequency**.

• This system minimizes **fluctuation of drug concentration in blood**.

• This system helps in **targeting of drugs**.

• Local action can be achieved in **GIT (Eg. Antacids)**.

• This system **reduces the side effect**.

• **Sustained release** can be achieved.

• **Safest route of administration**.

• It is **economic** and can be used for **wide range of drugs**.

DISADVANTAGES

• This system should be administered with **plenty of water**.

• Drugs with **solubility or stability problem in GIT** can't be administered.

• Drugs which undergo **first pass metabolism** are not suitable (e.g. **Nifedipine**).

• Drugs which are **irritant to gastric mucosa** are not suitable (e.g. **Aspirin & NSAID**).

• Drugs that absorb equally well throughout GIT (e.g. **Isosorbide dinitrate, Nifedipine**).

APPROACHES

Floating system or Low density system

• Floating Drug Delivery Systems (**FDDS**) have a **bulk density lower than gastric fluids** and thus **remain buoyant in the stomach for a prolonged period of time**.

• Without affecting the **gastric emptying rate**, the drug is released slowly at a desired rate from the system.

• Results in an **increase in the gastric residence time**.

• Provides **better control of fluctuations in plasma drug concentrations**.

• **Minimal gastric content** needed to allow proper achievement of buoyancy retention.

• A **minimal level of floating force (F)** is required to keep the dosage form reliably buoyant on the surface of the meal.

Floating force measurement

• The floating force kinetics is measured using a **novel apparatus** by determining the resultant weight (**RW**).

• The object floats better if **RW is on the higher positive side**.

$$RW \text{ or } F = F_{buoyancy} - F_{gravity}$$

$$= (Df - Ds)\, gV$$

Where,

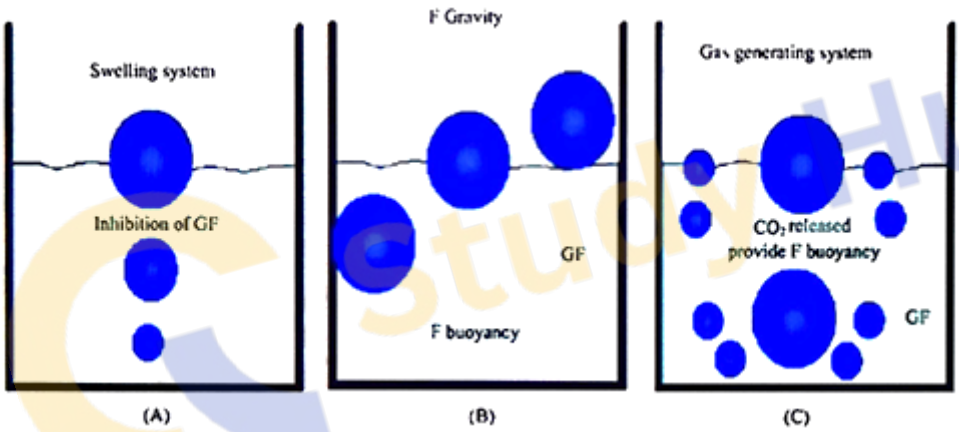
RW = total vertical force

Df = fluid density

Ds = object density

V = volume

g = acceleration due to gravity



Based on the mechanism of buoyancy

Two different technologies have been used in development of floating drug delivery systems. These include:

a) Non-Effervescent system

b) Effervescent system

• The **non-effervescent FDDS** is based on the mechanism of **swelling of polymer** or **bio-adhesion to mucosal layer in GI tract**.

• A drug delivery system can be made to float in the stomach by incorporating a **floating chamber**, which may be filled with **vacuum, air or inert gas**

• The gas in floating chamber can be introduced either by **volatilization of an organic solvent** or by **effervescent reaction between organic acids and bicarbonate salts**.

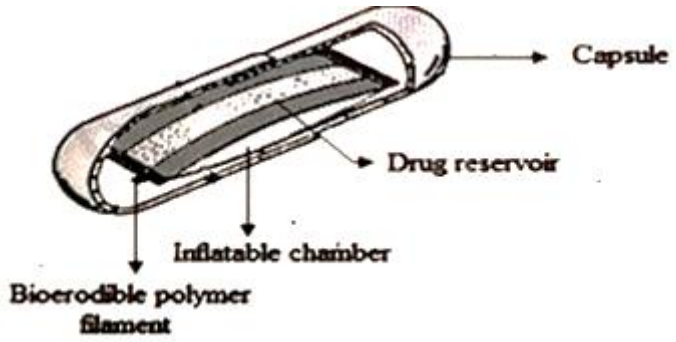
❖ Inflatable Gastrointestinal Delivery Systems

- These systems are incorporated with an **inflatable chamber**, which contains **liquid ether** that gasifies at **body temperature** to inflate the chamber in the stomach.
- These systems are fabricated by loading the inflatable chamber with a **drug reservoir**, which can be a **drug impregnated polymeric matrix**, then encapsulated in a **gelatin capsule**.
- After oral administration, the capsule dissolves to release the **drug reservoir together with the inflatable chamber**.
- The inflatable chamber **automatically inflates and retains the drug reservoir compartment in the stomach**.
- The drug is released continuously from the reservoir into **gastric fluid**.

Diagram labels:

- Capsule
- Drug reservoir

- Inflatable chamber
- Biodegradable polymer filament



❖ Bioadhesive Systems

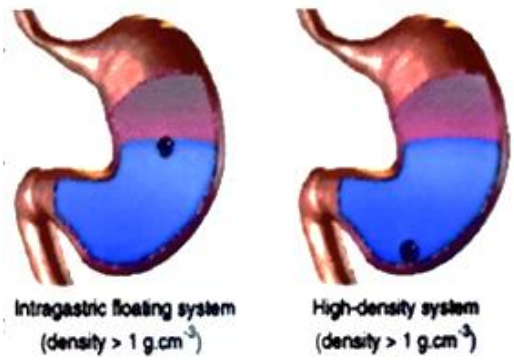
- Bio/mucoadhesive systems are those which **bind to the gastric epithelial cell surface or mucin**.
- Serve as a potential means of **extending the gastro-retention of drug delivery system (DDS) in the stomach**.
- Increase the **intimacy and duration of contact of drug with the biological membrane**.
- A bio/muco-adhesive substance is a **natural or synthetic polymer** producing an adhesive interaction based on:
    - **Hydration-mediated adhesion**
    - **Bonding-mediated adhesion**
    - **Receptor-mediated adhesion**
- Adhesion occurs with a **biological membrane** or **mucus lining of GI mucosa**.

Classification of polymer binding to mucin-epithelial surface:

1. Hydration-mediated adhesion
2. Bonding-mediated adhesion
3. Receptor-mediated adhesion

❖ High Density Systems

- These systems with a **density of about 3 g/cm³** are retained in the **antrum part of the stomach** and are capable of withstanding **peristaltic movements**.
- The only major drawback with such systems is that it is **technically difficult to manufacture formulations with high amount of drug (>50%)** and to achieve a density of about **2.5 g/cm³**.
- This approach involves formulation of dosage forms with a **density that must exceed density of normal stomach content**.
- These formulations are prepared by **coating drug on a heavy core** or mixed with inert materials such as:
    - **Iron powder**
    - **Barium sulphate**



- A density close to **2.5 g/cm³** seems necessary for significant prolongation of **gastric residence time**.

Diagram captions:

- Intragastric floating system (density > 1 g/cm³)
- High-density system (density > 1 g/cm³)

❖ APPLICATION

Gastro-retentive drug delivery system offer several applications as follows:

➤ Bioavailability

- The bioavailability is **significantly enhanced** in comparison to the administration of **non-GRDDS controlled release polymeric formulations**.

➤ Site Specific Drug Delivery Systems

- These systems are particularly advantageous for drugs that are **specifically absorbed from intestine**, e.g. **Furosemide**.
- The controlled, slow delivery of drug to the stomach.
- It reduces the side effects.
- Prolonged gastric availability from a **site-directed delivery system** may also reduce the dosing frequency.

➤ Sustained Drug Delivery

- In this system, dose large and passing from **pyloric opening is prohibited**.

- New sustained release floating capsules of **nicardipine hydrochloride** were developed and were evaluated **in vivo**.
- Plasma concentration–time curves show a **longer duration of administration (16 hours)** in sustained release floating capsules as compared.

➤ **Minimize adverse activity at the colon**

- Retention of the drug in the **HBS systems at the stomach** minimizes the amount of drug that reaches the colon.
- Thus, undesirable activities of the drug in colon may be prevented.

UNIT–3 NASOPULMONARY DRUG DELIVERY SYSTEM (PART - 3)

Points to be covered in this topic

➤ INTRODUCTION TO NASAL ROUTES OF DRUG DELIVERY

➤ INTRODUCTION OF PULMONARY ROUTES OF DRUG DELIVERY

➤ FORMULATION OF INHALERS

➤ NASAL SPRAYS

➤ NEBULIZERS

NASOPULMONARY DRUG DELIVERY SYSTEM

INTRODUCTION TO NASAL ROUTES OF DRUG DELIVERY

• Nasal route of drug delivery has been considered as a potential administration route to **achieve faster and higher level of drug absorption**.

• It is permeable to more compounds than the gastrointestinal tract due to **lack of enzymatic activity**.

• It is a useful delivery method for drugs that are **active in low doses** and show **minimal oral bioavailability**, such as proteins and peptides.

• For many years, drugs have been administered nasally for both **topical and systemic action**.

• Topical administration includes the treatment of **congestion, rhinitis, sinusitis and related allergic or chronic conditions**.

• The intranasal administration of drugs is an effective way for the **systemic availability of drugs** as compared to oral and intravascular routes of administration.

• It provides **fast and extended drug absorption** than oral and parenteral administration.

• Therapeutic classes of drugs delivered include **analgesics (morphine), cardiovascular drugs, hormones**.

Advantages

• Drug degradation that is absent.

• Hepatic **first pass metabolism is avoided**.

• **Rapid drug absorption** and quick onset of action can be achieved.

• The **bioavailability of larger drug molecules** can be improved.

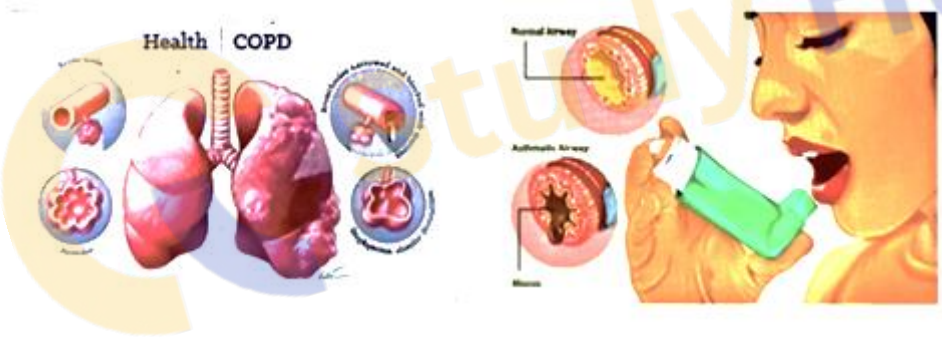
• Drugs that are **orally not absorbed** can be delivered by nasal drug delivery.

INTRODUCTION OF PULMONARY ROUTES OF DRUG DELIVERY

• Pulmonary drug delivery (PDD) systems are known to be able to deliver the drug directly to the required site in the body or to other distant sites through the bloodstream.

• The **lungs provide a huge surface area of alveoli with rich capillary network**, which acts as an excellent absorbing surface for administration of drugs.

• Throughout the past several years, **rapid onset of action and higher efficiency** has been responsible for the success of pulmonary delivery systems for symptomatic relief in the treatment of **asthma and chronic obstructive pulmonary disease (COPD)**.



Advantages

• Have very negligible side effects.

• Onset of action is very quick with pulmonary drug delivery.

• Degradation of drug by liver is avoided in pulmonary drug delivery.

• Ability to **nebulize viscous drug formulations**, thereby overcoming drug solubility issues.

• Increased drug delivery efficacy due to **size-stable aerosol droplets**.

• **Liposomal drug formulations remain stable** when nebulized.

• Ability to nebulize **protein-containing solutions**.

• Inhaled drug delivery places drug **where it is needed**.

FORMULATION OF INHALERS

Dry Powder Inhalers (DPIs)

• Dry powder inhalers are designed to **deliver drug/excipients powder to the lungs**.

• Dry powder inhalers (DPIs) are devices through which a dry powder formulation of an active drug is delivered for **local or systemic effect via the pulmonary route**.

• Dry powder inhalers are **bolus drug delivery devices** that contain solid drug, suspended or dissolved in a **non-polar volatile propellant** or in dry powder inhaler that is fluidized when the patient inhales.

• These are commonly used to treat respiratory diseases such as **asthma, bronchitis, emphysema and COPD**, and have also been used in the treatment of **diabetes mellitus**.

• Excipients used in DPI are used as carrier for Active Pharmaceutical Ingredient (API).

• Most commonly used carrier is **Lactose Monohydrate**.

Formulation of DPI mainly includes the following three steps

a. API Production

✓ The important requirement of API in case of DPI is **particle size**.

✓ Particle size of drug should be **less than 5 µm**.

✓ It should be in the range of **2–5 µm**.

b. Formulation of API with or without carriers

✓ The role of carrier in DPI is **enhancing the flow property of powder**.

✓ After drug and carrier have separately been brought to their desired forms, they are **combined in the blending process**.

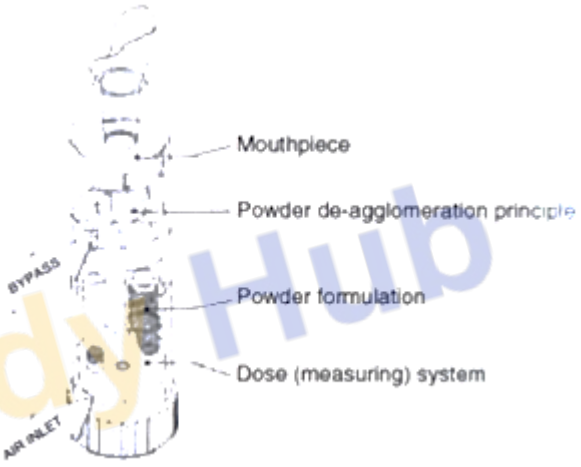
c. Integration of the formulation into device

✓ After the formulation has been blended, it is **filled into capsules**.

Currently there are two types

➤ Unit dose devices

➤ Multi dose devices



Pressurized Metered Dose Inhalers (MDIs)

• A metered-dose inhaler (MDI) is a device that **delivers a specific amount of medication to the lungs**.

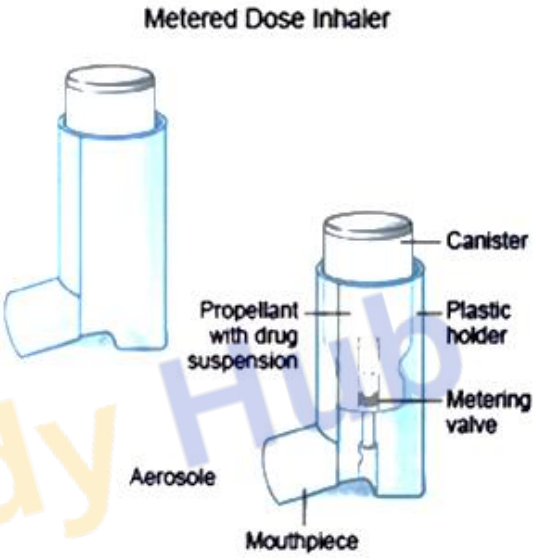
• It is the most commonly used delivery system for treating **asthma, chronic obstructive pulmonary disease (COPD)** and other respiratory diseases.

• The medication in a metered dose inhaler is most commonly a **bronchodilator, corticosteroid**, or a combination of both for the treatment of asthma and COPD.

● **Pressurized Metered Aerosols**

- Pressurized metered aerosols may be formulated as **either solutions or suspensions of drug** in the liquefied propellant.
- Compared with suspension formulations, **solution MDIs offer the benefits of homogeneous formulation**.
- The basic requirements for formulation of MDIs are **containers, propellants, and metering valve**.

Filling Metered Dose Inhaler:



- Filled by liquefying the propellant at **reduced temperature or elevated pressure**.
- In **cold filling**, active compound, excipients and propellant are chilled and filling at about **−60°**.
- Additional propellant is then added at the same temperature.

☐ NASAL SPRAYS

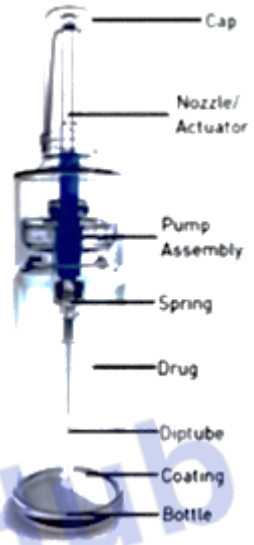
- Most of the pharmaceutical nasal preparations on the market containing **solutions, emulsions or suspensions** are delivered by **metered-dose pump sprays**.
- Nasal sprays, or nasal mists, are used for the nasal delivery of a drug or drugs, either locally to generally **alleviate cold or allergy symptoms** such as nasal congestion or systemically.

- Although delivery methods vary, most nasal sprays **function by instilling** **a fine mist into the nostril** by action of a hand-operated pump mechanism.

Types for Local Effect:

- **Antihistamines**
- **Corticosteroids**
- **Topical decongestants**

Components of Metered-Dose Pump Sprays:



- The **container**
- The **pump with the valve**
- The **actuator**
- The dose accuracy of metered-dose pump sprays is dependent on the **surface tension and viscosity** of the formulation.
- For solutions with higher viscosity, **special pump and valve combinations** are on the market.

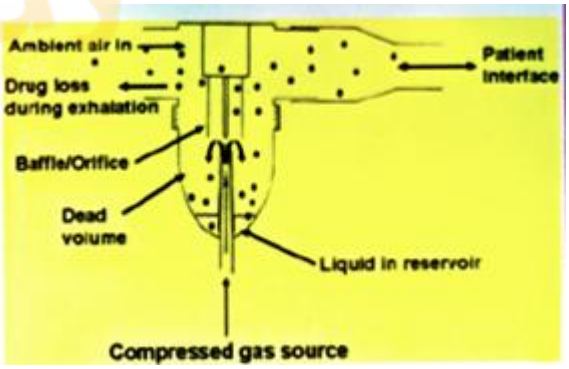
☐ NEBULIZERS

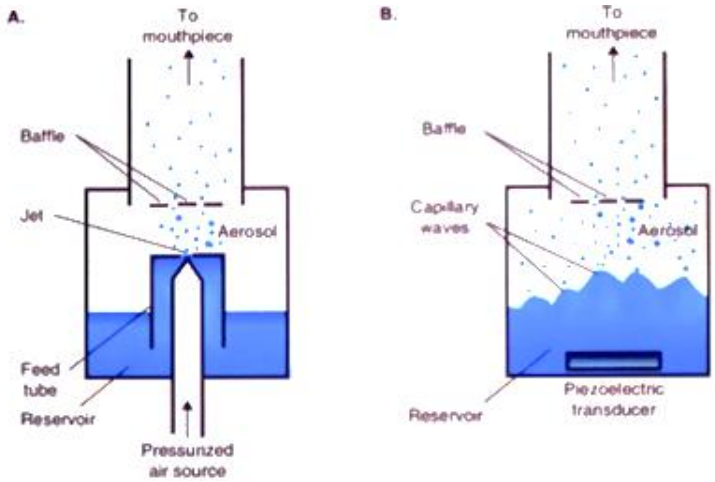
- A device **converts liquids into aerosols** that can be inhaled into the lower respiratory tract.
- Nebulizers are used in aerosol drug delivery to produce a **poly-disperse aerosol** where the drug delivered in the **particle size range 1–5 µm in diameter**.

- Most nebulizers use **compressed air for atomization**, but some use **ultrasonic energy**.
- There are following **three main types of nebulizers** commercially available.

◆ Jet Nebulizer:

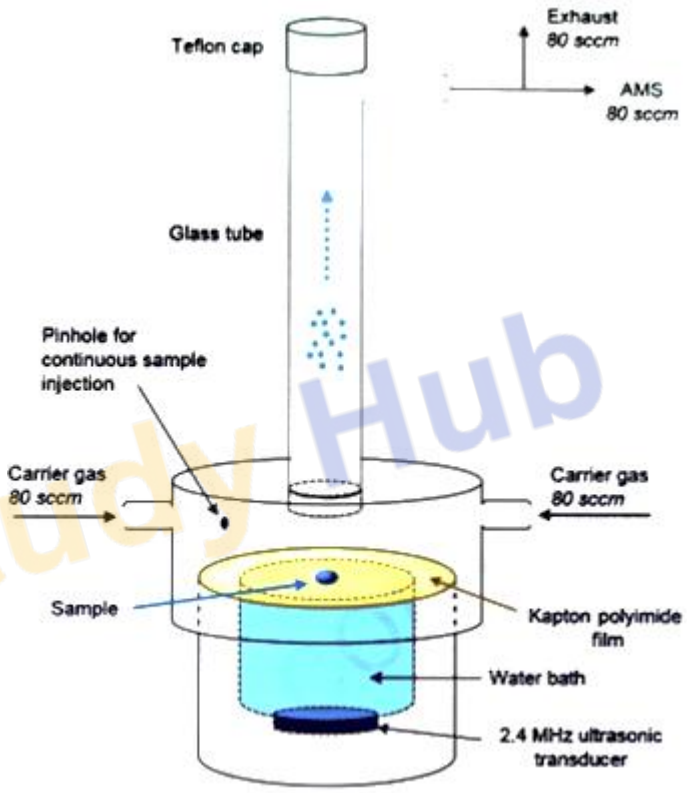
- This uses **compressed gas** to make an aerosol (tiny particles of medication in the air).
- Jet nebulizers are applicable for **acute and domiciliary treatment** of various respiratory diseases, pediatric and adult medical practices.
- These types of nebulizers require **2–10 L/min** withdraw medication via a capillary tube from the reservoir of the nebulizer.
- It may cause generation of a **wide range of particles** which are blasted into one or more baffles (to convert larger particles to smaller particles) out of suspension and return them to nebulizer.





◆ Ultrasonic Nebulizer:

- This makes an aerosol through **high-frequency vibrations**.
- The particles are **larger than with a jet nebulizer**.
- Ultrasonic nebulizers incorporate a **piezoelectric crystal** vibrating at high frequencies (**1–3 MHz**) to produce an aerosol.
- Ultrasonic nebulizers work on the **principle that converts electrical energy to high-frequency vibrations using a transducer**.
- This nebulizer generates vibrations, which are transferred to solution surface that would **create waves**, and those waves produce aerosol.
- These types of nebulizers are **large volume nebulizers** to deliver hypertonic saline for sputum inductions.



◆ Mesh Nebulizer:

- Mesh nebulizers contain **apertures or aperture plate**; when force is applied, it will generate aerosol.

- They force liquid medications through **multiple apertures in a mesh or aperture plate** to generate aerosol.
- Comparisons of mesh and ultrasonic nebulizers demonstrated **similar drug delivery** in simulated ventilator-dependent patients.
- Mesh nebulizers are **more efficient than jet nebulizers** and can provide **higher drug doses** to patients.
- The efficiency of mesh nebulizers is affected by various factors like **size**.