UNIT-3

TRANSDERMAL DRUG DELIVERY SYSTEM

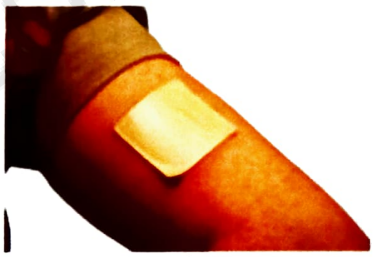
Points to be covered in this topic

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

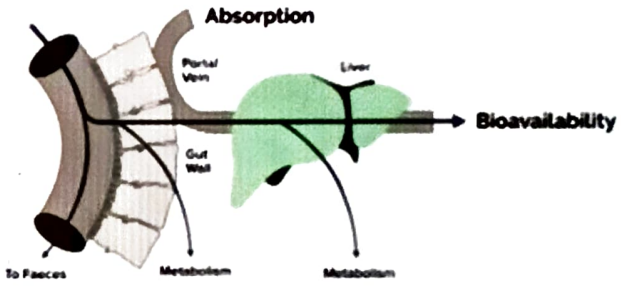
TRANSDERMAL DRUG DELIVERY SYSTEM

❑ INTRODUCTION

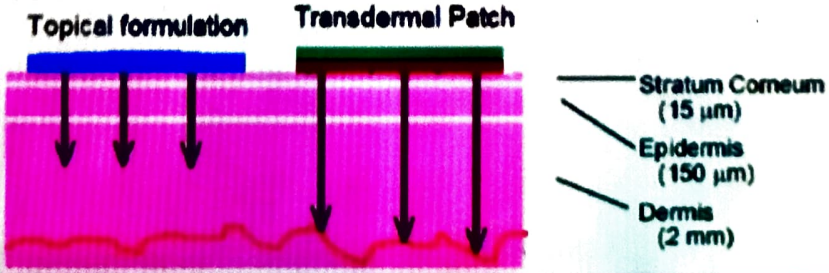
- Transdermal drug delivery systems (TDDS), also known as **"patches,"** are dosage forms designed to deliver a therapeutically effective amount of **drug across a patient's skin.**
- TDD is a **painless method** of delivering drugs systemically by applying a drug formulation **onto intact and healthy 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.



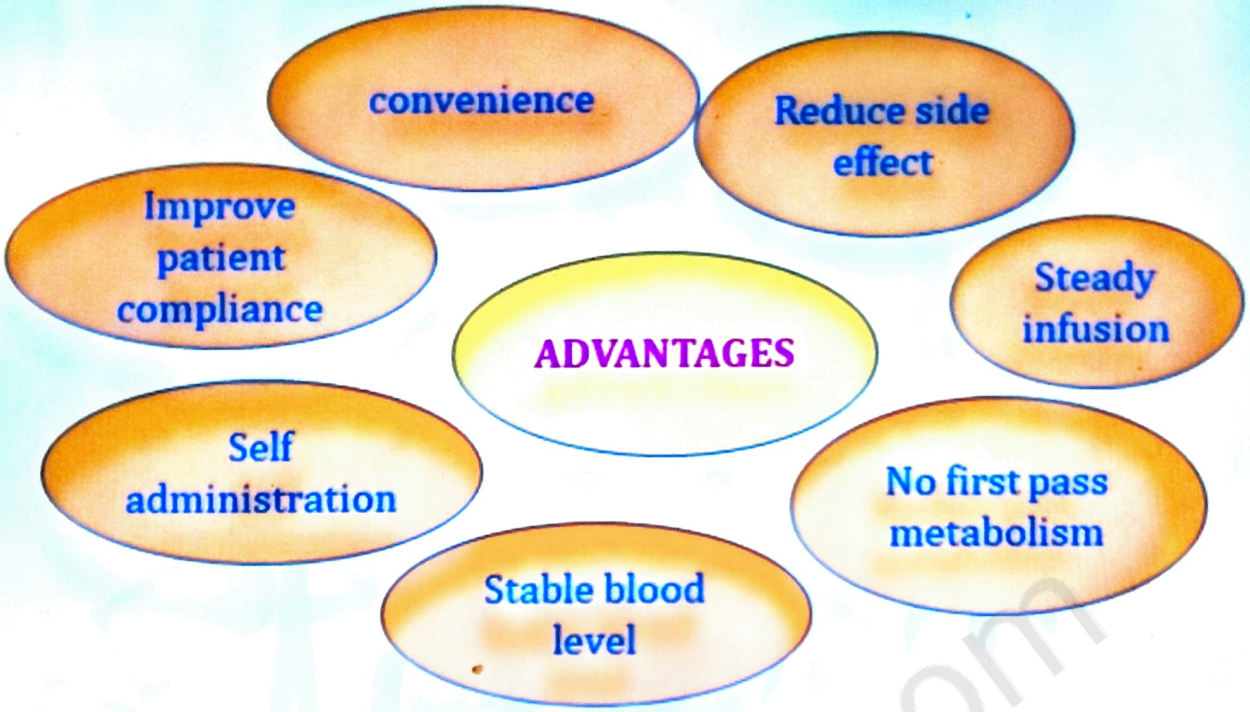
- When drug reaches the **dermal layer,** it becomes available for **systemic absorption** via the dermal microcirculation.
- Transdermal delivery provides a leading edge over injectable and oral routes by increasing patient compliance and **avoiding first pass metabolism respectively.**

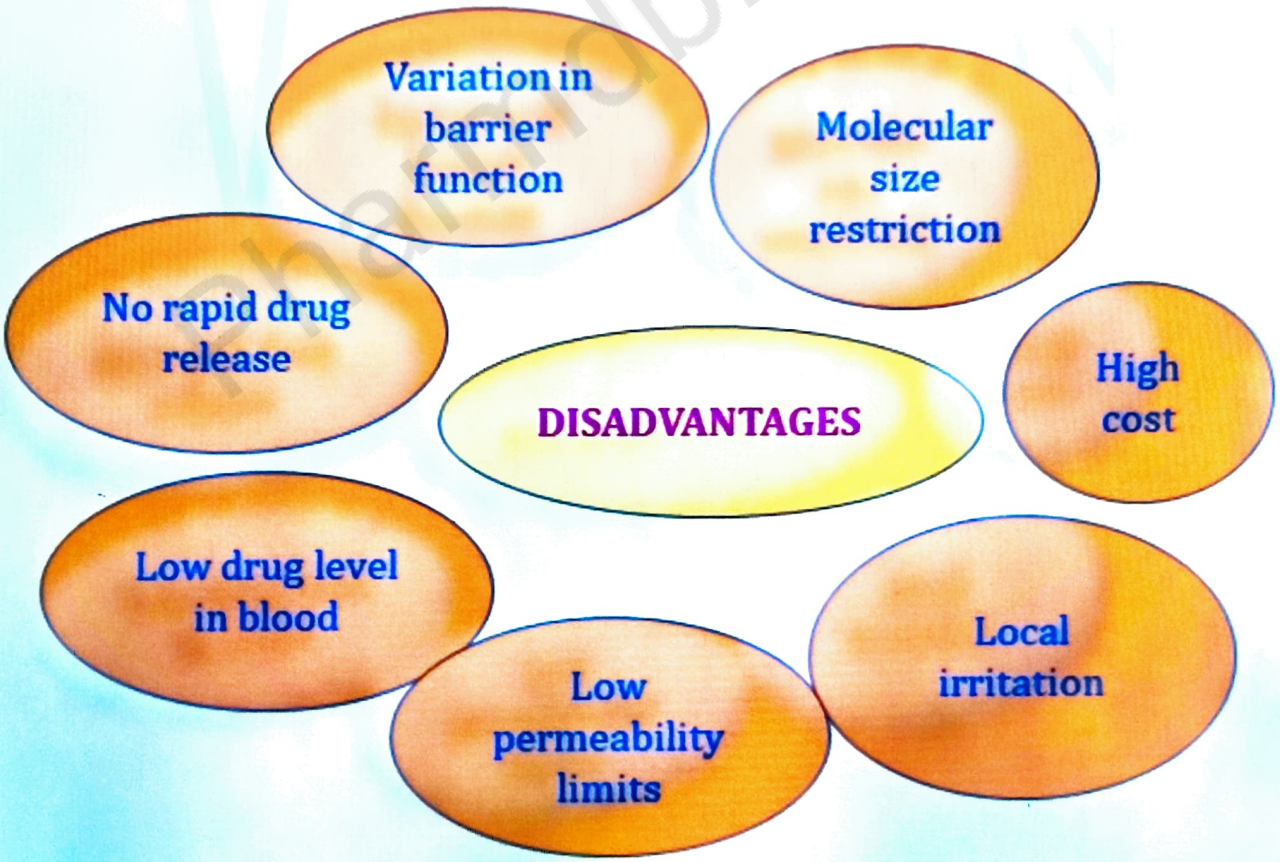


- Transdermal delivery not only provides **controlled, constant administration of the drug,** but also allows continuous input of drugs with **short biological half-lives and eliminates pulsed entry into systemic circulation,** which often causes undesirable side effects.



❖ Advantages and Disadvantages



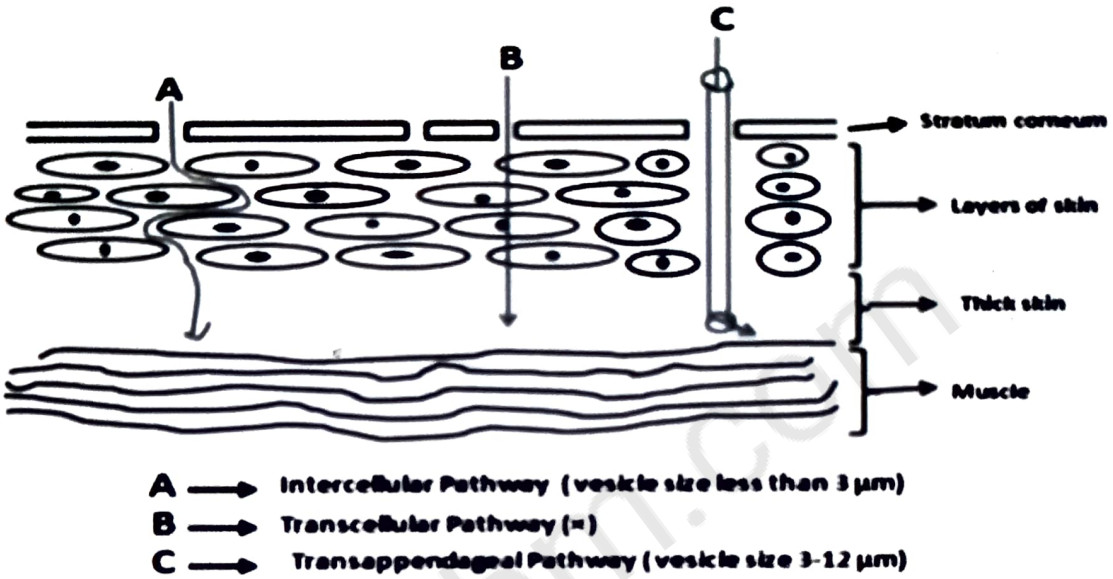


❑ PERMEATION THROUGH SKIN:

The permeation through the skin occurs by the following routes-

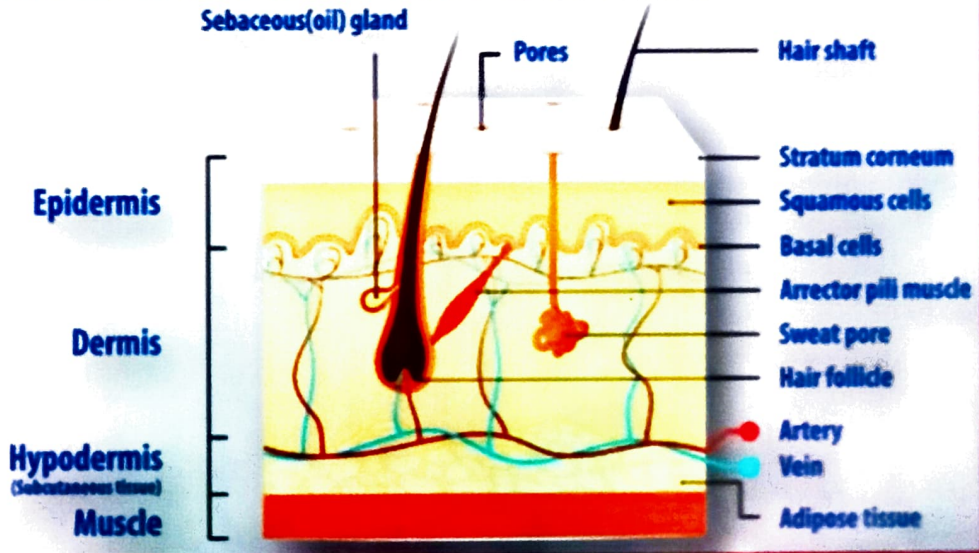
- Transepidermal absorption.
- Transfollicular (shunt pathway absorption).
- A Clearance by local circulation.

Pathways of permeation through skin



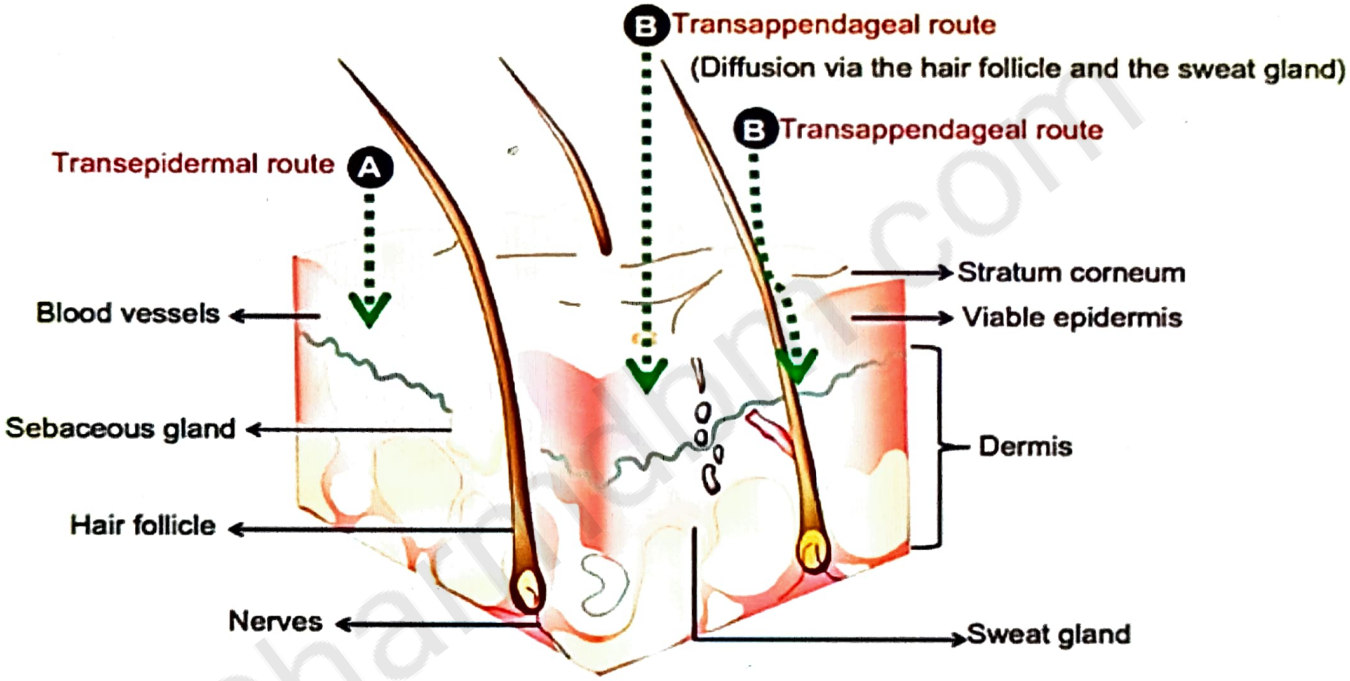
❖ Transepidermal Absorption

- **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 drug** concentrate in and diffuse with relative ease.
- Permeation through the dermis is through the **interlocking channels** of the ground substance.



❖ Transfollicular Absorption

- The **skin appendages (sebaceous and eccrine glands)** are considered as **shunts** for by passing 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.



❖ 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 molecule 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 a lipophilic molecules tend to permeate through the skin faster than mo hydrophilic molecules.
- Drugs with **high melting points have relatively low aqueous solubil** at normal temperature and pressure.

❖ Physicochemical properties of the drug delivery system

➢ **The affinity of the vehicle for the 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 th 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-

$$J = D\,(dc)/(dx)$$

D = diffusion coefficient

C = conc 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 principle

- ✓ **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., polybutadieine, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrenebutadieine 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 includes water, pyrolidones, 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:

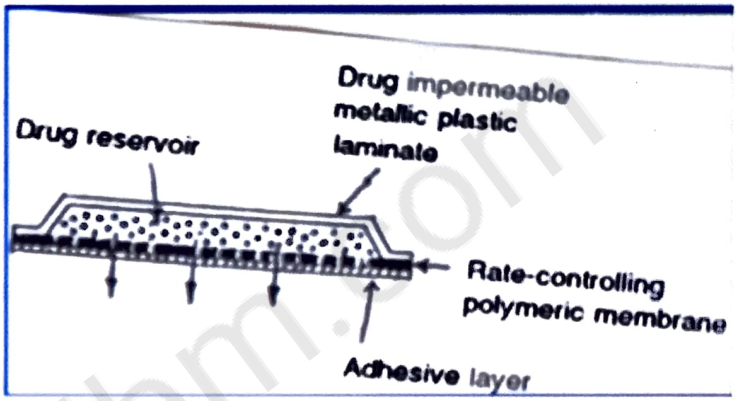
- During storage the patch is covered by a protective liner that is **removed and discarded before the application** of the patch to the skin.
- The release liner is composed of a base layer which may be non-occlusive (e.g. paper fabric) or occlusive (e.g. polyethylene, polyvinylchloride).
- The liner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

❑ FORMULATION APPROACHES OF TDDS:

❖ Polymer membrane permeation controlled TDD 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 a **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.
- Example of this type of patch are **Estraderm**(twice a week in treatment of postmenopausal syndrome) and **Duragesic** (management of chronic pain for 72 hrs)
- The intrinsic rate of drug release from this type of drug delivery system is defined by



{dq/dt}=Cr/1/Pm+1/Pa.

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 micro porous rate – controlling membrane,

Pm approximately represents the sum of permeability co-efficient across the pores and polymeric material.

Pa and Pm may be separately defined as Pa

❖ Polymer matrix diffusion controlled TDD 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.
- Examples: Nitro-glycerine releasing transdermal therapeutic system at a daily dose of 0.5g/cm2 for angina pectoris.

Rate of drug release in this system is given by the equation

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

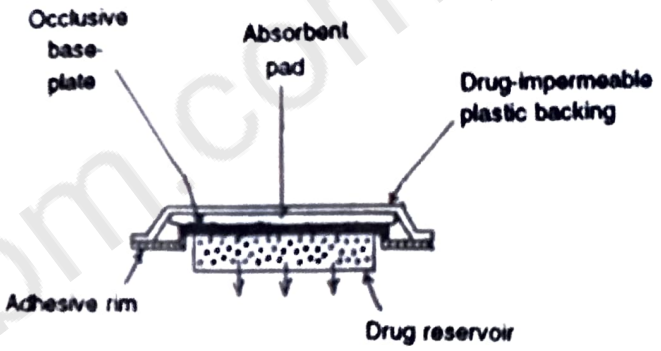
Where,

A = Initial drug loading dose dispersed in polymer matrix

Cp = Solubility of drug in Polymer

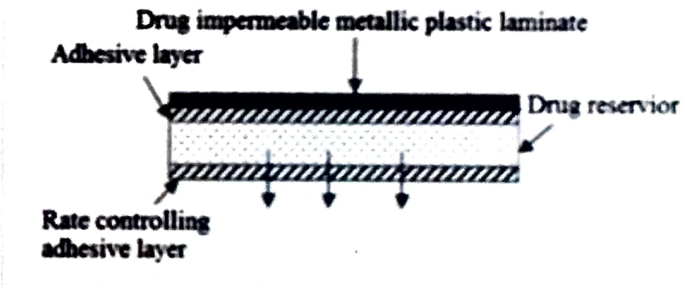
Dp = Diffusivity of drug in Polymer

since Cp is equal to Cr.



❖ 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 the then
- **sandwiched between the banking**
- **laminate and rate –controlling**
- **adhesive polymer** membrane.

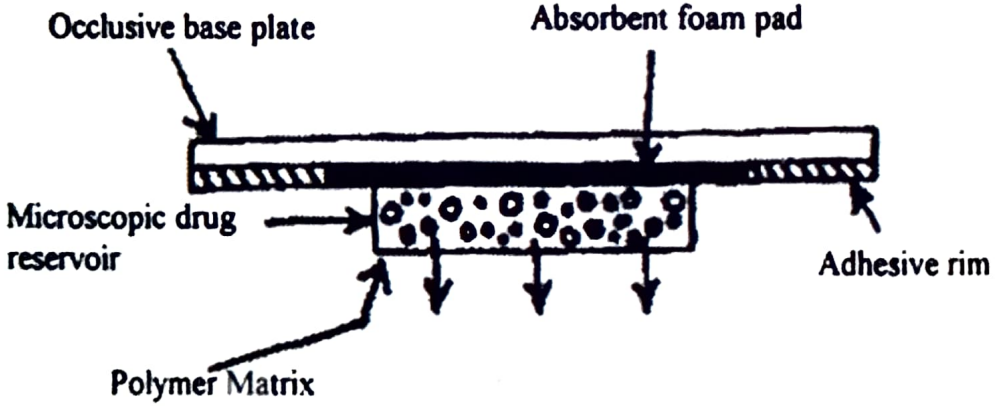


- The rate of drug release from this system is given by,

$$dq/dt = Cr.Ka/r.Da/ha$$ Ka/r = Partition co-efficient for interfacial partitioning of drug from reservoir layer to adhesive layer.

❖ Microreservoir dissolution controlled TDD 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 solubilser e.g. polyethylene glycol
- Than **homogeneously dispersing the drug suspension with controlled aqueous soluble lipophillic polymer** by high shear mechanical force to form thousands of un-leachable microscopic drug reservoir.



UNIT-3

GASTRO RETENTIVE DRUG DELIVERY SYSTEM

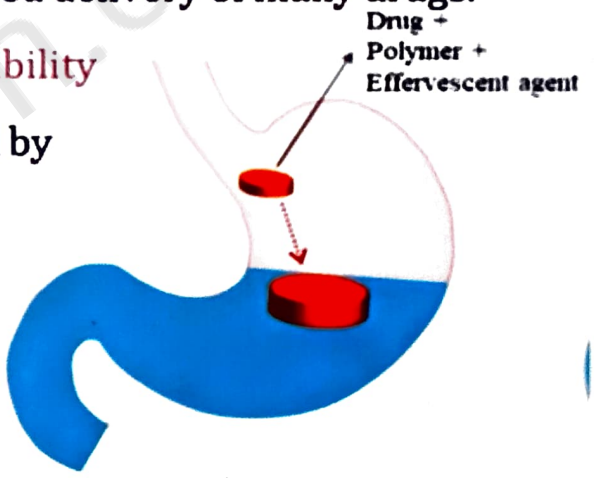
Points to be covered in this topic

- ❑ 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 the 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 undergoes 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 through GIT. E.g. Isosorbide dinitrate, Nifidipine.

❑ 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** and the drug is released slowly at a desired rate from the system,
- Results in an **increase** in the **gastric residence time**
- A better control of **fluctuations in the plasma drug concentrations.**
- Minimal gastric content needed to allow the proper achievement of the buoyancy retention
- **A minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal.**

- 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.

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

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

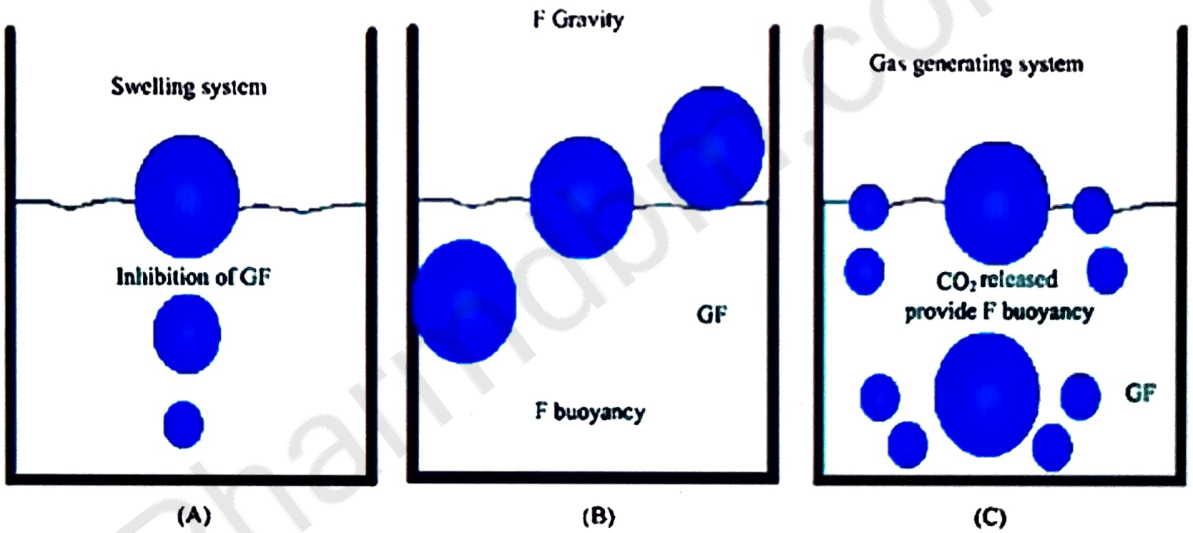
RW = total vertical force,

Df = fluid density,

Ds = object density,

V = volume and

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.

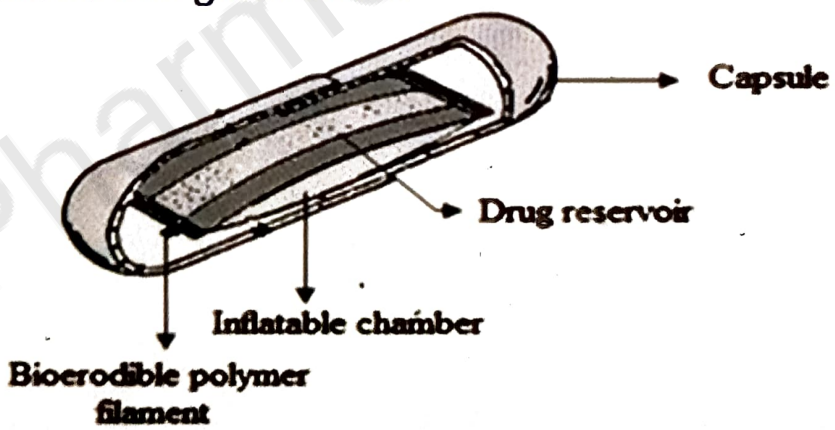
  b) Effervescent system.

- The Non-effervescent FDDS is based on 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 afloating 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.



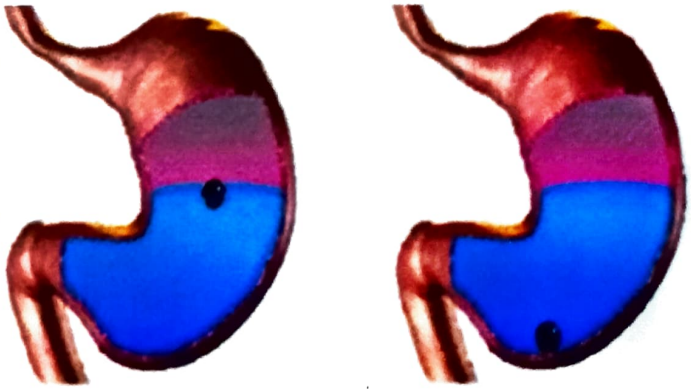
❖ Bioadhesive Systems

- 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** produce an adhesive interaction based on **hydration-mediated**, **bonding mediated** or **receptor mediated adhesion** with a biological membrane or mucus lining of GI mucosa.
- The binding of polymers to the mucin-epithelial surface can be subdivided into three broad categories-
  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 its peristaltic movements.
- The only major drawbacks with such systems is that it is technically **difficult to manufacture** such formulations with **high amount of drug** (>50%) and to achieve a density of about 2.5 g/cm^3.
- This approach involves formulation of dosage forms **with the 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 gm/cm3 seems necessary for significant prolongation of gastric residence time.



Intragastric floating system (density > 1 g.cm^{-3})

High-density system (density > 1 g.cm^{-3})

❑ 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 those are specifically absorbed form 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 shows a longer duration for administration (16 hours) in the 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

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:

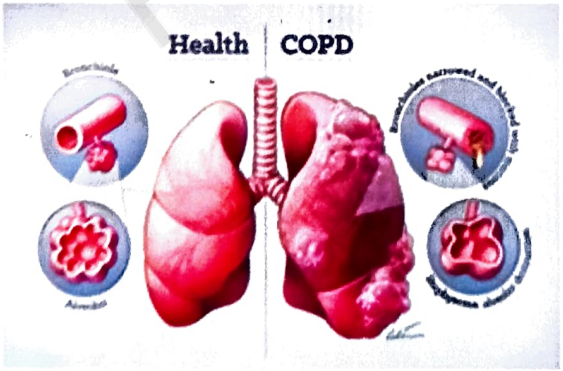
- Nasal route of drug delivery has been considered as a potential administration route to **achieve faster and higher level of drug absorption**.
- It is permeable to more compounds than the gastrointestinal tract due to **lack of enzymatic activity**.
- It is a useful delivery method for drugs that 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 provided 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 **orally not absorbed** can be delivered by nasal drug delivery.

❑ INTRODUCTION OF PULMONARY ROUTES OF DRUG DELIVERY:

- PDD systems are known to be able to simply deliver the drug to the required site in the body directly 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 system** for symptomatic relief in 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.
- The ability to **nebulize viscous drug formulations** for pulmonary delivery, thereby overcoming drug solubility issues.
- **Increased drug delivery efficacy** due to size-stable aerosol droplets.
- **Liposomal drug formulations remain stable**, when nebulized.
- Ability to **nebulizer protein-containing solutions**.
- Inhaled drug delivery puts drug where it is needed.

❑ FORMULATION OF INHALERS:

❖ Dry power inhalers:

- The 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 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.**

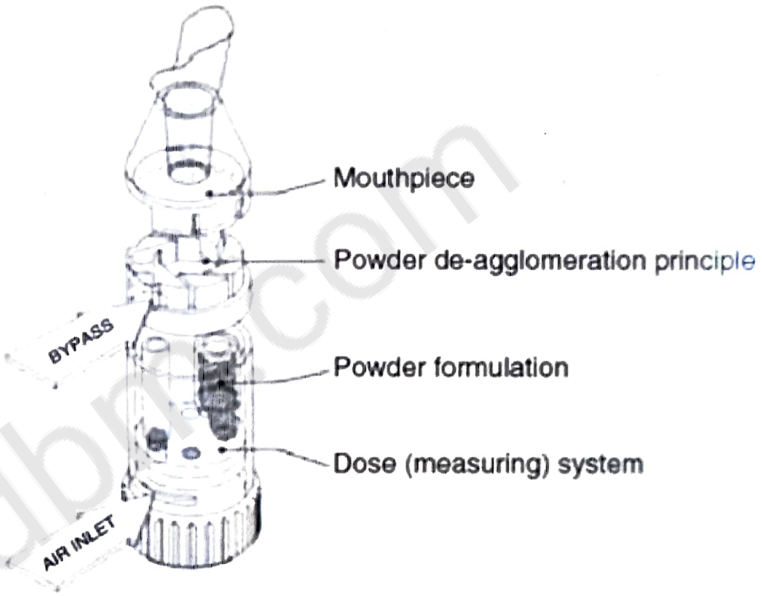
b. Formulation of API with or without carriers.

- ✓ The part 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**.

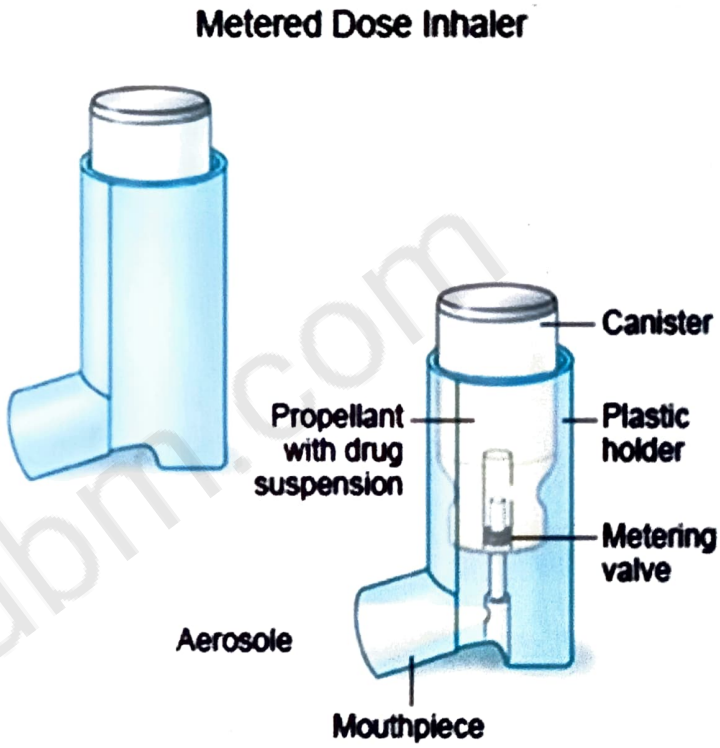
- ○ **Currently there are two types:**
  - ➢ Unit dose devices:
  - ➢ Multi dose Devices:



❖ Pressurized Metered Dose Inhalers:

- 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 may be formulated as **either solutions or suspensions of drug** in the liquefied propellant.
- Compared with suspension formulations, solution MDIs offer the **benefits of homogenous 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.

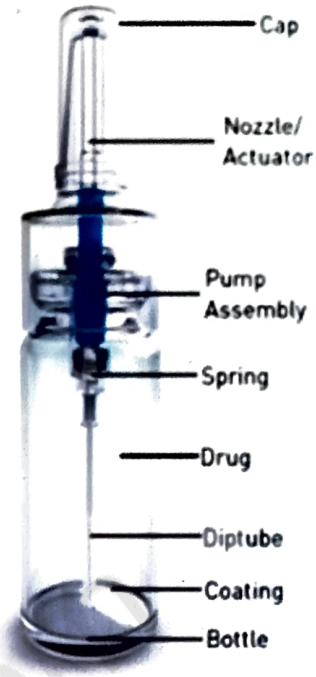


❑ NASAL SPRAYS

- 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.

- The three main types available for local effect are: **antihistamines, corticosteroids,** and **topical decongestants**
- Metered- dose pump sprays include the **container, the pump** with **the valve** and **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:

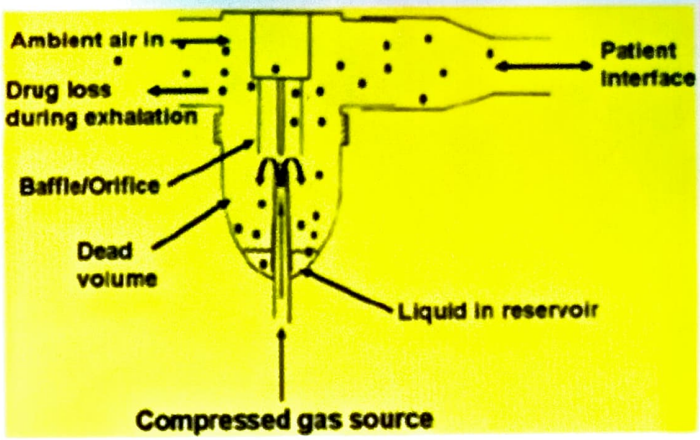
- A device **converts liquids into aerosols** that can be inhaled into the lower respiratory tract.
- Nebulizers are used in aerosol drug delivery produce a **poly-disperse aerosol** where the drug delivered in the **particles size range 1–5 µm** in diameter.
- Most Nebulizers use **compressed air for atomization**, but some use ultrasonic energy.
- There are following three main types of nebulizers commercially available.

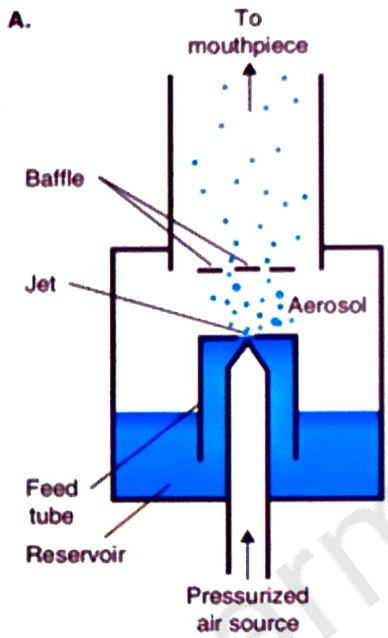
❖ Jet Nebulizer:

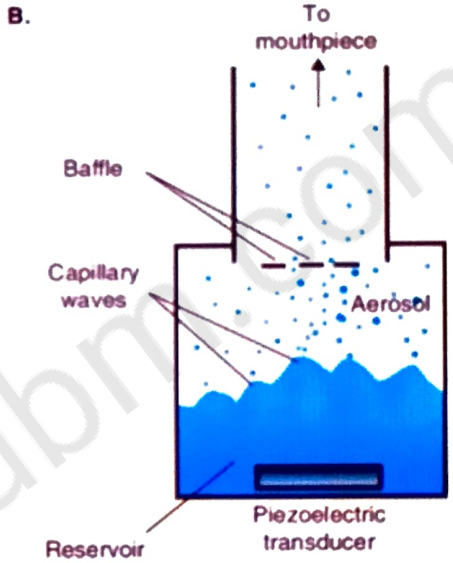
- ✓ This uses **compressed gas** to make an aerosol (tiny particles of medication in the air).
- ✓ Jet nebulizers are applicable for **acute and domiciliary treatment** of various respiratory diseases, pediatric and adult medical practices.
- ✓ These types of nebulizers required **2-10 L\min withdraw medication**

a capillary tube from the reservoir of the nebulizer.

- ✓ It may cause generate a wider range of particles which blasted into one or more baffles (to convert larger particles to smaller particles) out of suspension and return them to nebulizer.





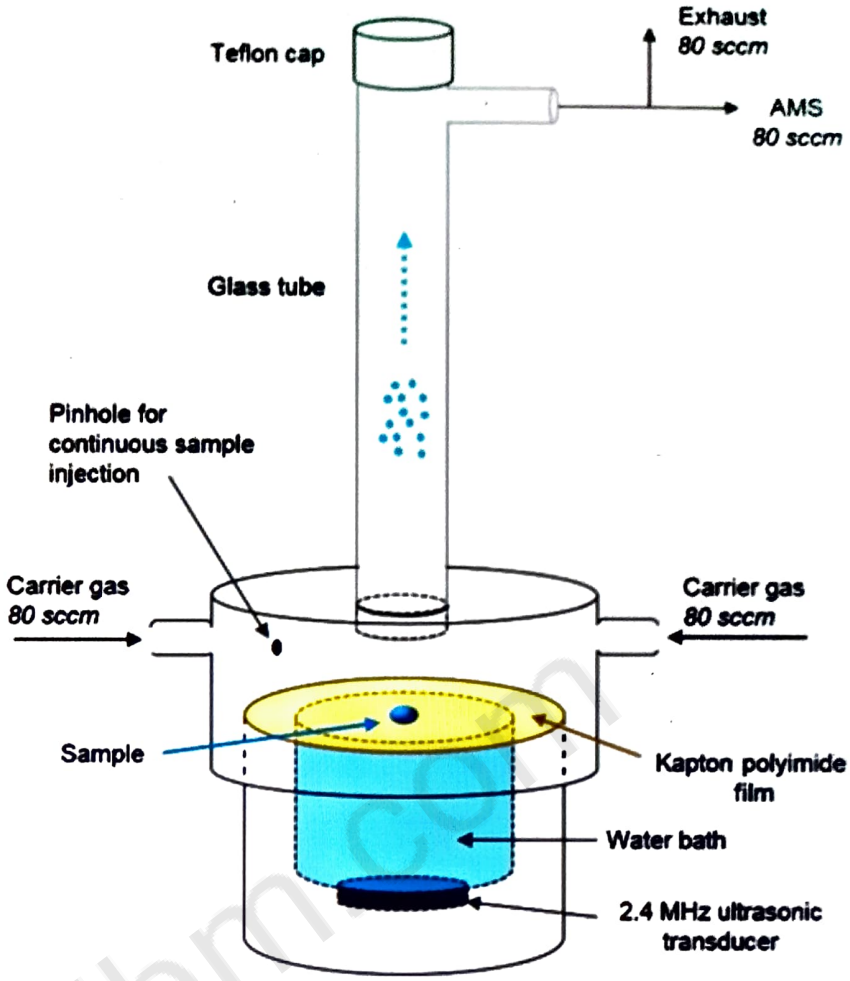


❖ Ultrasonic Nebulizer.

- ✓ 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.
- ✓ We can say that 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 we applied force, 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**