TRANSDEMAL DRUG DELIVARY SYSTEM

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- ✓ PERMEATION THROUGH SKIN
- ✓ FACTORS AFFECTING PERMEATION
- ✓ PERMEATION ENHANCERS
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- ✓ FORMULATION APRROACH

INTRODUCTION:

Transdermal drug delivery system is one of the system lying under the category of controlled drug delivery which the aim is to deliver the drug through the skin in the predetermined the controlled route. Transdermal Delivery provides a leading age over the injectable and oral route by increasing patient compliance avoiding first pass metabolism A tropically Administrator dosage form in the form of patches which deliver drug from systemic effect at a predetermined and Controlled rate

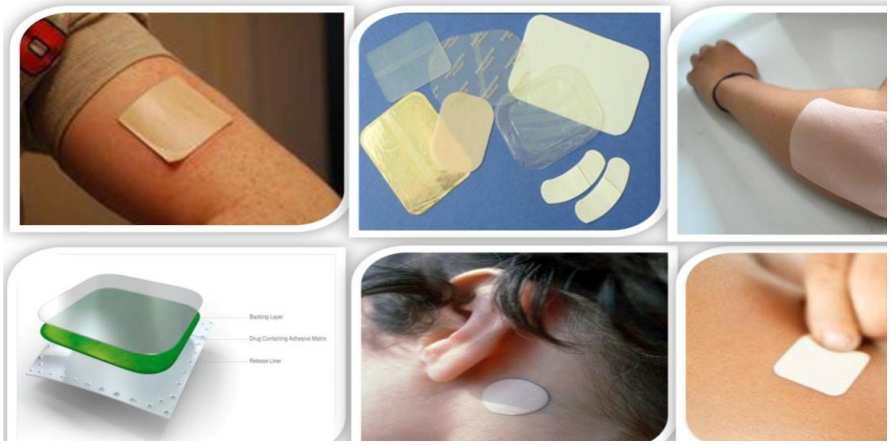


Figure 1 : transdermal patches

ADVANTAGES OF TDDS :

1. Avoid gastrointestinal incompatibility
2. Avoid first pass metabolism
3. Extended duration of activity
4. Enhance therapeutic efficacy

DISADVANTAGES OF TDDS :

1. Drug molecule must be potent
2. Drug with easy elimination
3. Only small lipophilic drug can be deliver
4. Only high melting point drug can be given

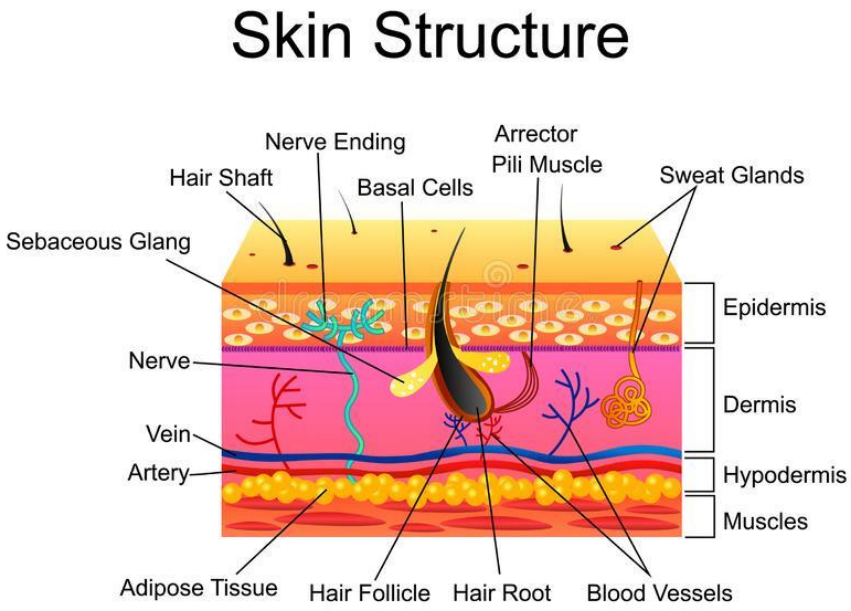


Figure 2 : structure of skin

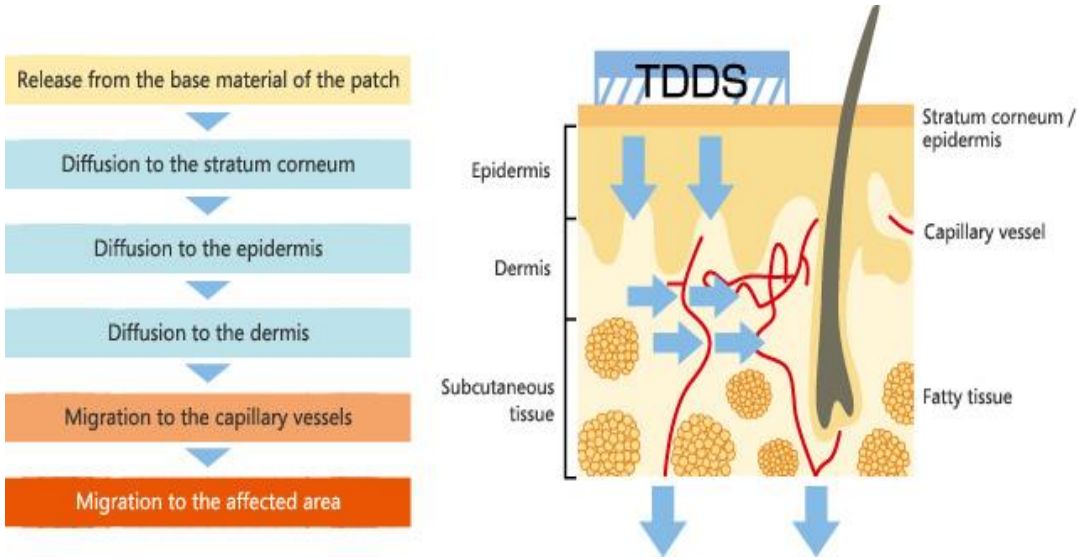


Figure 3 : Mechanism of Transdermal patches

PERMEATION ENHANCER:

A substance enhancer are those substance which promotes the absorption of drug through the skin temporarily by transiently enhancing the skin permeability. They are employed to transfer the delivery of drug which are ionised. Example:Timolol Malate and impermeable Heparin to maintain drug level to blood to provide high dose of less potentially active drug oxymorphane to deliver high molecular permeation enhancer

ADVANTAGES OF PERMEATION ENHANCER:

- High rate of penetration
- Antiseptic substance
- Penetration of unabsorbed drug through skin
- Improved penetration of transdermal surface preparation

DISADVANTAGES OF PEREMEATION ENHANCER:

- Concentration of different drugs so amount of different dos age cannot be administred
- Limited utility for clinical application
- High risk of side effect

MECHANISM OF PERMEATION ENHANCER:

1. Causing disruptions in a highly organized structure and stratum corneum
2. Interaction with protein present intra cellularly
3. Improved drug partitioning through sternum corneum with the help of co-enhancer

THE PERMEATION THROUGH SKIN OCCURS BY FOLLOWING ROUTES:

1. Trans Epidermal Absorption
2. Tran Follicular (Shunt Pathway Absorption)
3. Clearance By Local Circulation

Transdermal Drug Delivery Systems

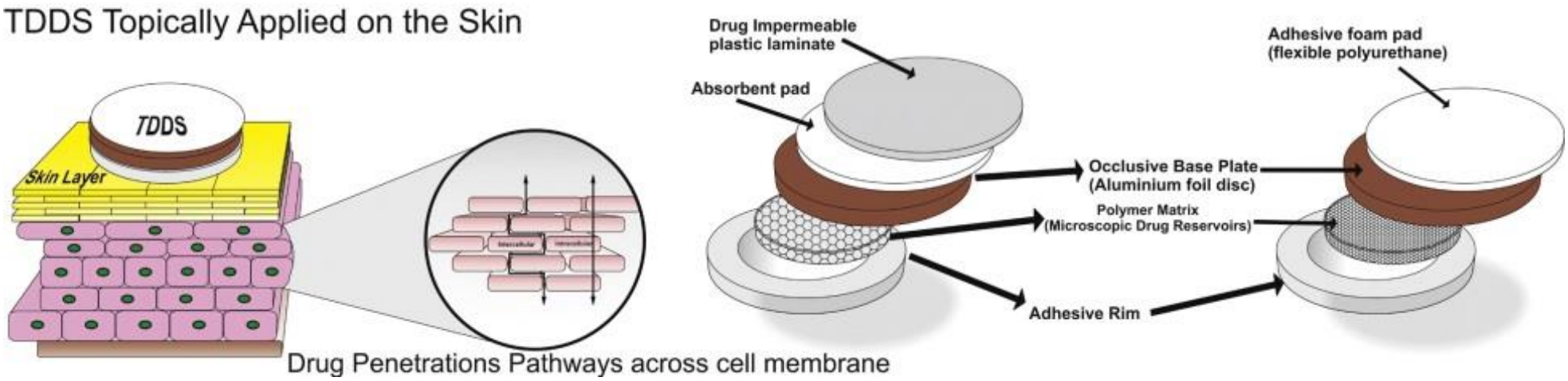


Figure 4 : Tdds Tropically Applied On The Skin

PERMEATION THROUGH SKIN :

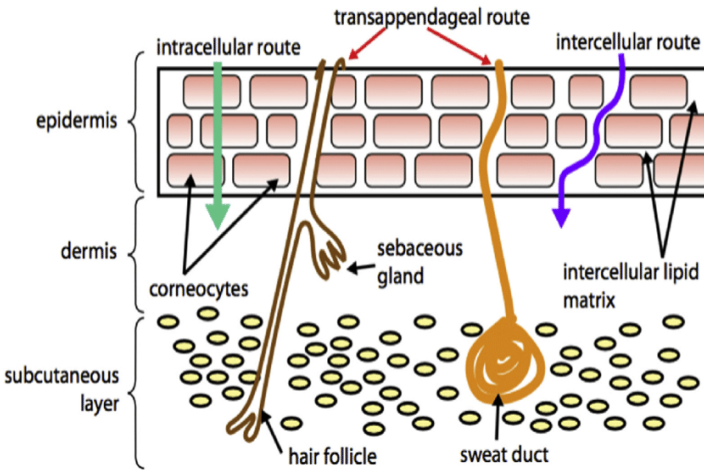
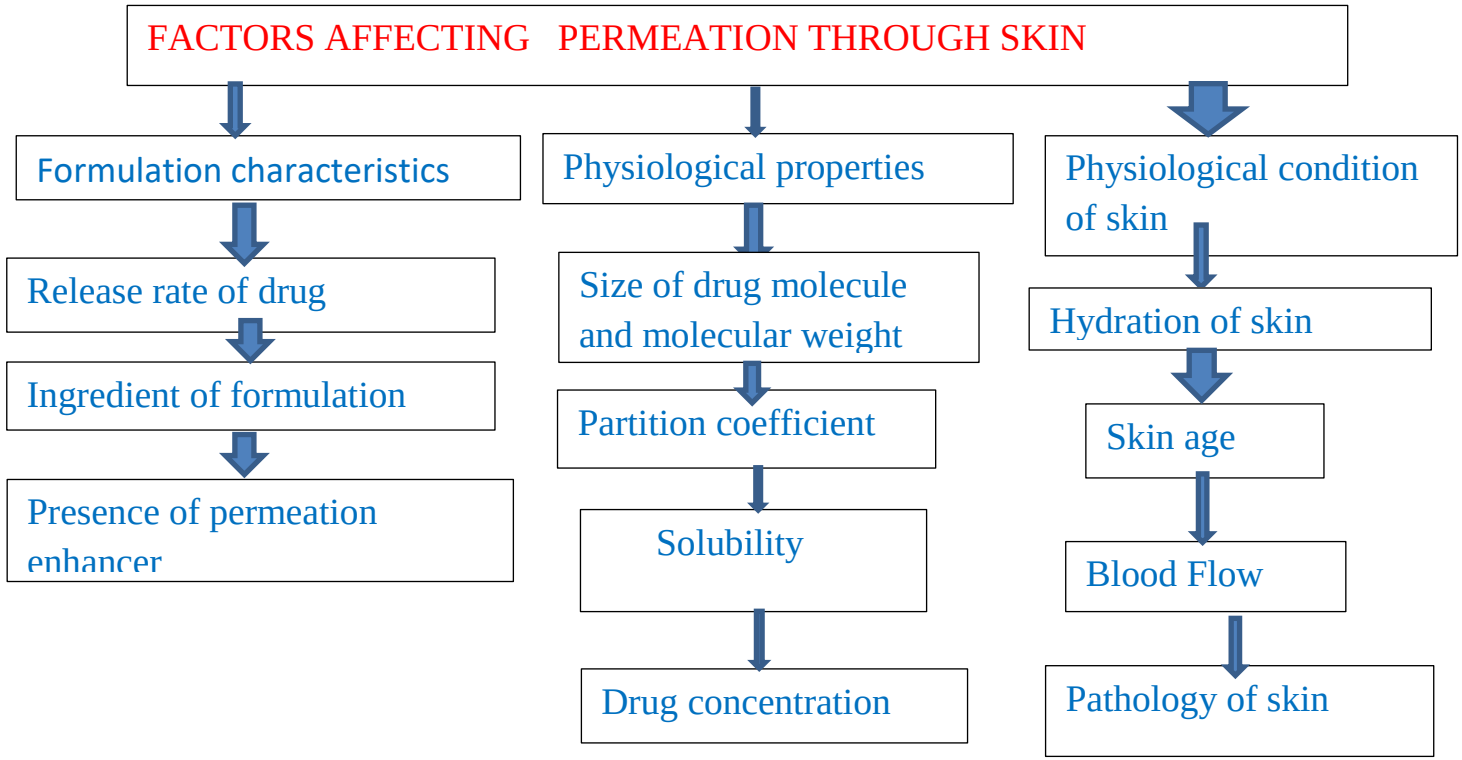


Figure 5: Different Routes Of Penetration



DESIRABLE PROPERTIES FOR IDEAL PENETRATION ENHANCER :

- Non toxic ,non irritating and non allergic
- Rapid working
- Predictable and reproducible duration of action
- No pharmacological activity within the body
- Work unidirectionally
- When removed for the skin barrier properties should return both rapidly and fully
- Compatible with both excipients and drugs
- Cosmetically acceptable

USES OF PENETRATION ENHANCERS :

1. To increase the delivery of ionisable drugs. Example : timolol maleate etc
2. To deliver the impermeable drugs. Example: heparin etc
3. To maintain level of drug into blood stream
4. To improve the efficacy of less potent drugs with higher dose . example : oxymorphane
5. To deliver the drugs having high molecular weight like peptide and hormones
6. To decrease lag time of transdermal drug delivery system
7. Penetration enhancers tend to work well with co-solvents such as PG or ethanol
8. Synergistic effects are found between enhancers such as Azone, oleic acid (and other fatty acids) and terpenes with PG
9. Most penetration enhancers have a complex concentration dependent effect

MERITS OF PENETRATION ENHANCERS:

1. Most drugs penetrate at rates sufficiently high for therapeutics efficiency by using penetration enhancers
2. It is useful for unabsorbable drugs to facilitate there absorption through skin
3. It can improve transdermal absorption of topical prepration
4. No adverse effect on skin
5. Do not affect zero order skin permeation profile of skin

DEMERITS OF PENETRATION ENHANCERS

1. The effective concentration varies from drug to drug
2. The uses of different penetration enhancer with various concentration are restricted completely
3. Physiochemical properties of enhancer are also affecting the side effects in the body

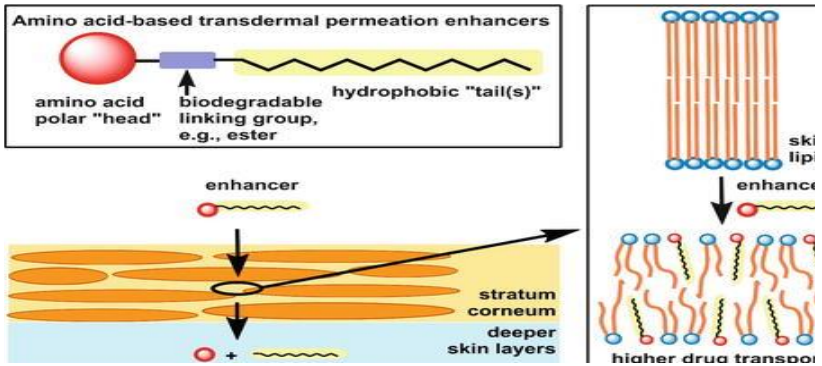


Figure 6 : Penetration Enhancer

DRUG SELECTION CRITERIA:

- Drug is less than 10 mg/day
- Molecular weight is equal to < 1000 Dalton
- Aqueous Solubility :>1mg/ml
- Oil solubility : >1mg/ml

BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEM :

1. DRUG:

- Dose:low <20 mg/day
- Half life:10 hr or less
- Molecular weight: <4000 Dalton
- Partition coefficient: log a
- PH:between 5.0 to 9.0

2. POLYMER MATRIX:

- These are foundation of transdermal system
- The selection of the polymer design are of prime important
- Consideration of polymer selection in transdermal delivery system

3. RELEASE LINEAR:

- The patch is covered by protective line during storage until it is used
- The release linear is composed of a base linear with may be non occlusion

4. BACKING LAMINATE:

While designing the backing layer following points Must be consideration:

- Must be flexible
- Skin permeability of drug
- Should be compatible with transdermal system
- Should be chemically resistant

FORMULATION APPROACH:

- ✓ POLYMER MEMBRANE PERMEATION CONTROLLED TDDS
- ✓ MATRIX DIFFUSION CONTROLLED TDDS
- ✓ MICRIO RESERVIOUR CONTROLLED TDDS
- ✓ ADHESIVE CONTROLLED TDDS

Figure 7 : Marketed Product Nicoderm

FORMULATION APPROACH :

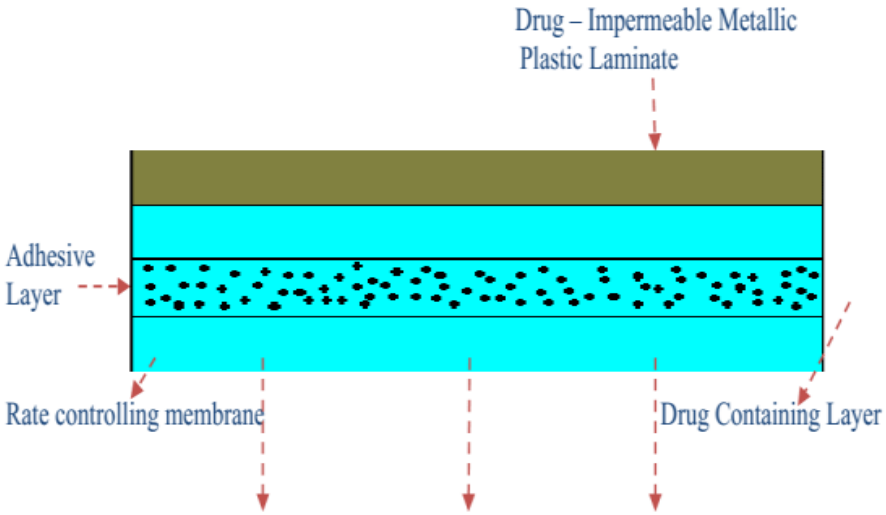


Figure 8: Adhesive Controlled Tdds

1. The drug reservoir formed by dispensing the drug in an adhesive polymer and spreading the medicated polymer adhesive by melting the adhesive onto an impervious backing layer.
2. The drug reservoir layer is then covered by non medicated rate controlling adhesive polymer of constant thickness to produce an adhesive diffusion controlling drug delivery system
3. The drug reservoir layer is then covered by a non medicated rate controlling adhesive controlling drug delivery system

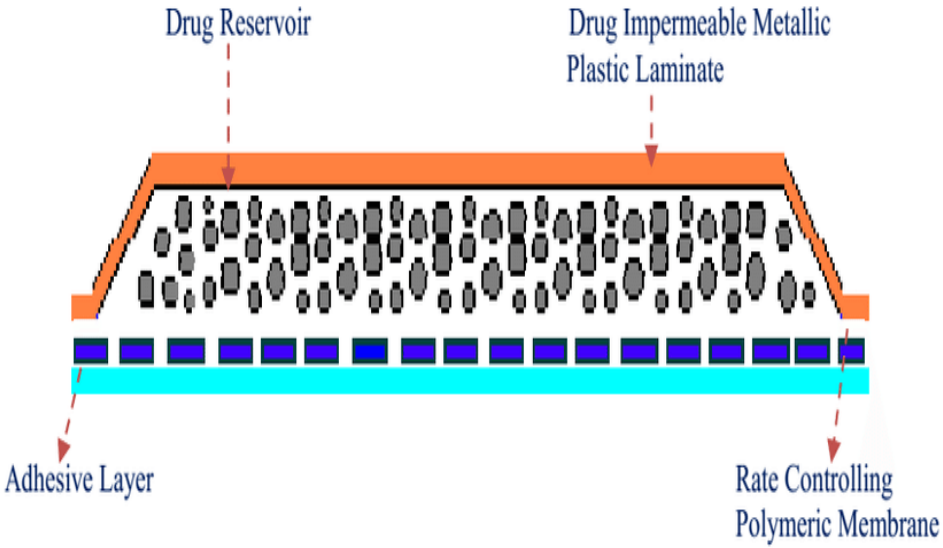


Figure 9: Polymer membrane permeation controlled tdds:

1. In this system the drug reservoir is embedded between on in previous backing layer and a rate controlling membrane
2. The drug release only through the rate controlling which can be micro-porous or non-porous
3. In this reservoir compartment the drug can be in the form of a solution suspension or jel or dispersed in solids polymer matrix on the outer surface of polymeric membrane a thin layer of drug compatible hypoallergenic adhesive polymer can be applied
4. The rate controlling factors of the drug release polymer composition permeability coefficient

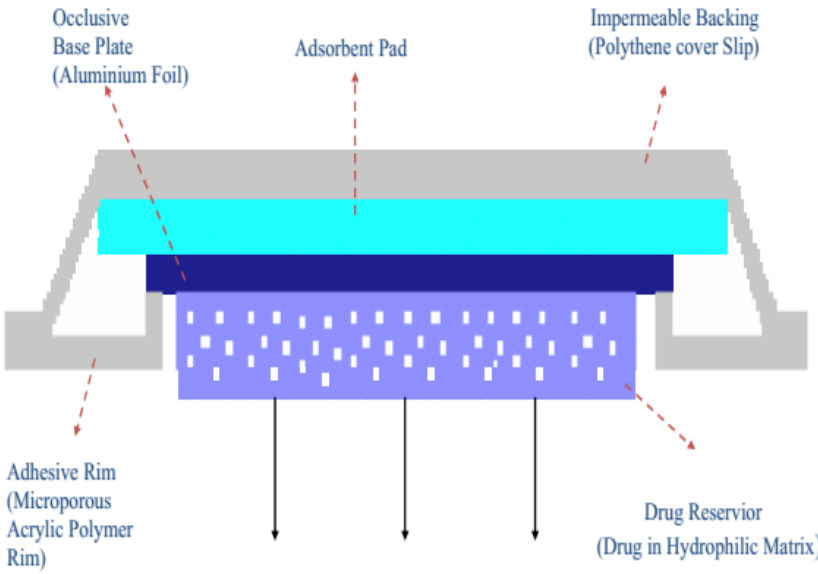


Figure 10: Matrix Diffusion Controlled Tdds

1. The drug is dispersed Homogeneously in Hydrophilic Or Lipophilic polymer matrix.
2. The drug containing polymer then is fixed disk onto an occlusive base plate in compartment fabricated from a drug impermeable backing layer
3. Instead on applying adhesive on the force of the drug reservoir it is spread along the circumference to form a strip of adhesive rim
4. The drug reservoir is prepared by homogenously dispersing drug particles in a hydrophilic or lipophilic polymer matrix

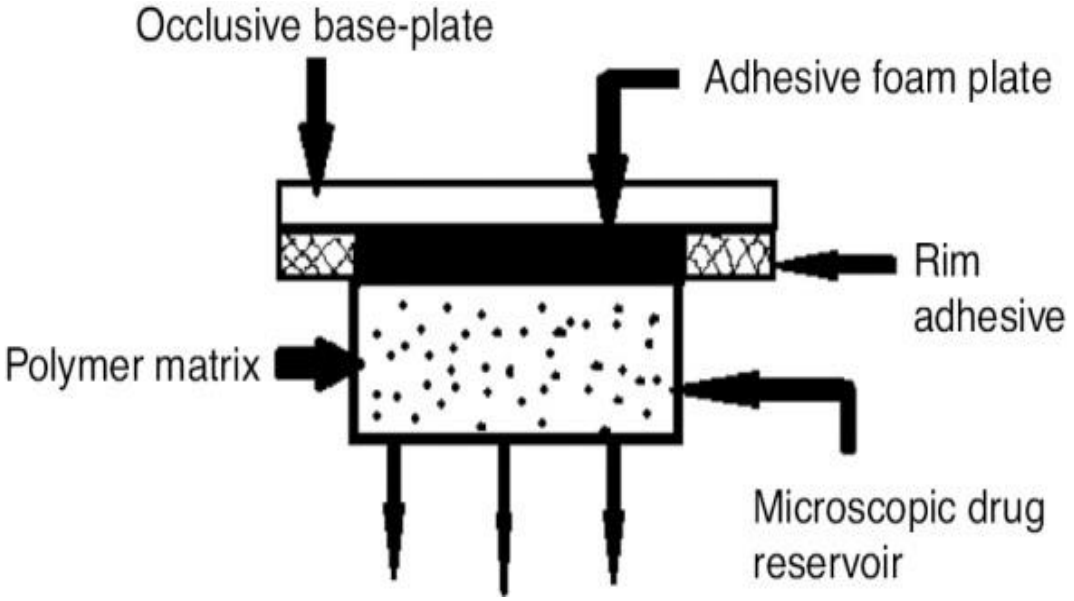


Figure 11: Micro Reserviour Controlled Tdds

1. drug delivery system is combination of reservoir and matrix dispersion system
2. The drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogeneous thousands of unreachable microscopic sphere of drug reservoir
3. The thermodynamically unstable dispersion is stabilized quickly by immediate cross linking the polymer in situ
4. Transdermal patches can be applied over the micropores in the skin so that the drugs are released to the targeted site through the micropores

MARKETED PRODUCT:

Figure 12 : Marketed Product Sandor

Figure 13 : Marketed Product Rupatch

Drug Delivery

- Delivery
  - Transdermal
- Current Products
  - Nurofen
    - 5% w/w ibuprofen
    - Only In UK
  - Salonpas
    - Aspirin patch
    - Marketed in US

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