TRANSDERMAL DRUG DELIVERY SYSTEM-AN OVERVIEW

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INTRODUCTION

DEFINITION

Transdermal drug delivery systems are topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate

ADVANTAGES

1. Because this method avoids direct effects on stomach and intestine

2. Continuity of drug administration permitting the use of a drug with short biological half life
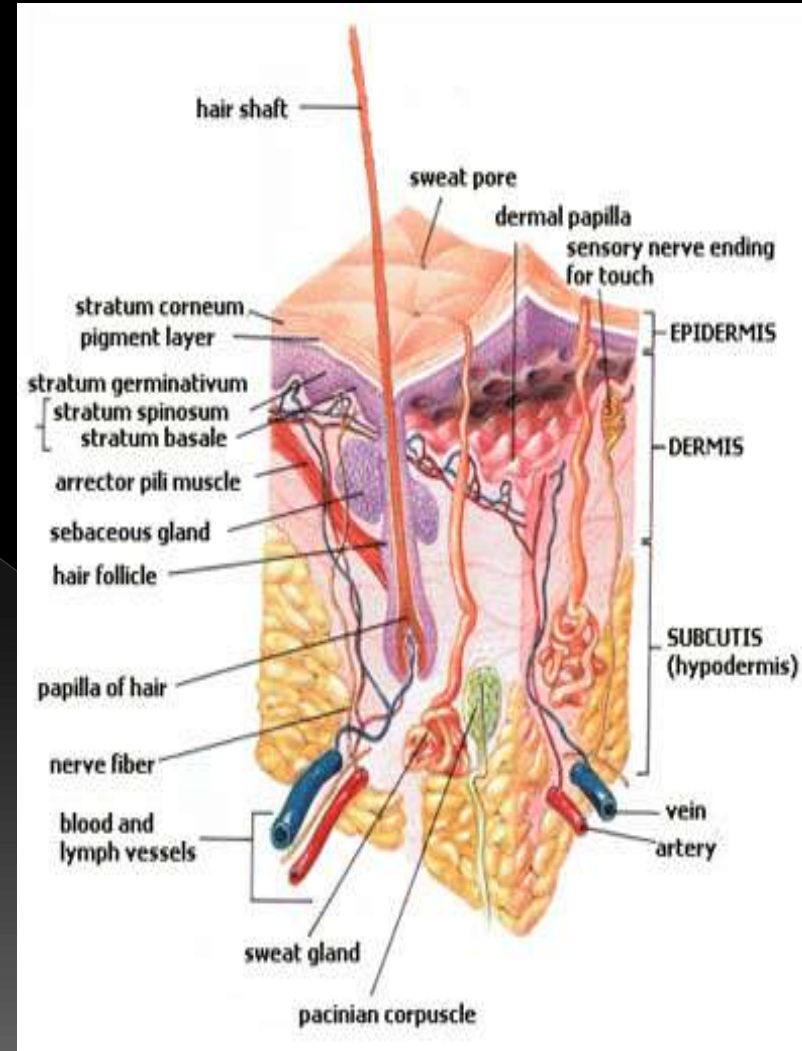
DISADVANTAGES

1. Many drugs with a hydrophilic structure permeate the skin too slowly to be of therapeutic benefit.

SKIN AS A SITE FOR DRUG INFUSION

SKIN CONTAINS FOUR LAYERS

OF TISSUES

1. Non-viable epidermis stratum corneum

2. Viable epidermis

3. Viable dermis

4. Subcutaneous connective tissue.

PATHWAYS OF TRANSDERMAL PERMEATION

Permeation can occur by diffusion via

1. Transcellular permeation, through the stratum corneum.

2. Intercellular permeation, through the stratum corneum.

3. Trans appendageal permeation via the hair follicles,

   sebaceous and sweat

PROPERTIES THAT INFLUENCE TDDS

Biological factors

Skin Condition

Skin Age

Blood Flow

Skin Metabolism

Physicochemical factors

Skin Hydration

Temperature and pH

Diffusion Coefficient

Drug Concentration

KINETICS

Drug involves the following steps

      1. Sorption by stratum corneum.

      2. Penetration of drug through viable epidermis

      3. Uptake of the drug by the capillary network in the dermal papillary layer.

The rate of permeation across the skin is given by

$$\frac{dQ}{dt} = P_s (C_d - C_r) \quad ..\dots\dots\dots\dots\dots\dots.. (1)$$

C_d and C_r =concentration of the skin penetrant

Permeability coefficient is given by the relationship

$$P_s = \frac{K_{Dss}}{h_s}$$

D_{ss} = apparent diffusivity, h_s = overall thickness , K_s = partition coefficient

$$(C_d \gg C_r)$$

$$\frac{dQ}{dt} = P_s C_d$$

C_s .i.e. $C_d \gg C_s$

$$(dQ/dt)_m = P_s C_s$$

From the above equation the maximum rate of skin permeation is equal to skin permeability coefficient P_s and stratum corneum C_s

BASIC COMPONENTS

The components of transdermal devices include

1. Polymer matrix or matrices.

2. The drug

3. Permeation enhancers

4. Other excipients

POLYMER MATRIX OR MATRICES

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, Starch etc.

    b) Synthetic Elastomers

        e.g. Polybutadieine, Silicone rubber, etc.

    c) Synthetic Polymers

        e.g. Polyvinyl alcohol, Polyvinyl chloride, etc.

DRUG

Physicochemical properties

1. Molecular weight

2. Drug should have affinity for

   both –lipophilic and hydrophilic phases

3. Low melting point

PERMEATION ENHANCERS

A. SOLVENTS

e.g. Methanol, dimethyl sulfoxide

B. SURFACTANTS

ANOINIC SURFACTANTS

e.g. Dioctyl sulphosuccinate Sodium lauryl sulphate

NONIONIC SURFACTANTS

e.g. Pluronic F127, Pluronic F68, etc

BILESALTS

e.g. Sodium taurocholate, Sodium deoxycholate

C. MISCELLANEOUS CHEMICALS

e.g. Urea, calcium thioglycolate

OTHER EXCIPIENTS

A. ADHESIVES

Both adhesive syste...

(i) Should adhere to the skin aggressively, should be easily removed

(ii)   Should not leave an unwashable residue on the skin

(iii)   Should not irritate or sensitize the skin

B. BACKING MEMBRANE

Desirable features for transdermal patches

Composition relatively invariant in use
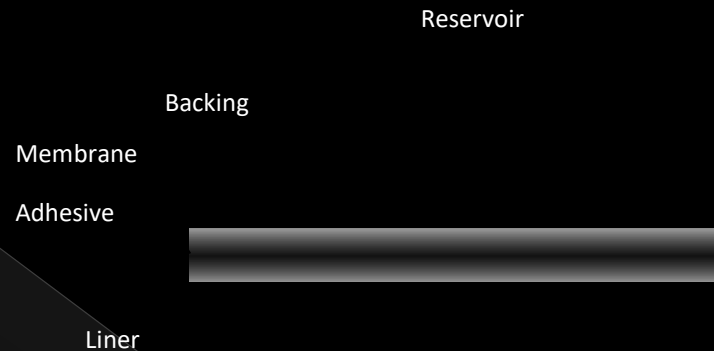
System size reasonable

Defined site for application

Application technique highly reproducible
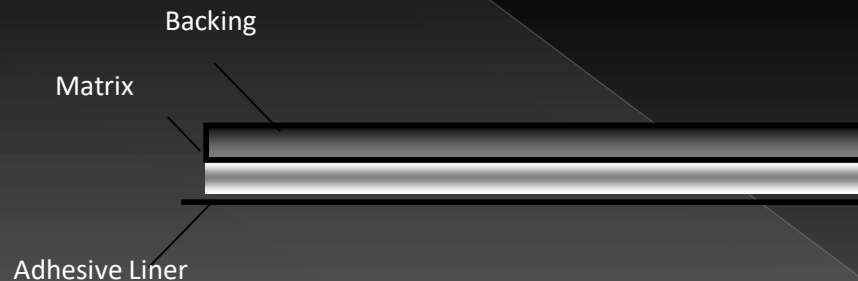
Delivery is (typically) zero order

TDDRUG DELIVERY - SYSTEMS

Two principal types of TD-DDS designs are

1. *Reservoir system*

Reservoir

Backing

Membrane
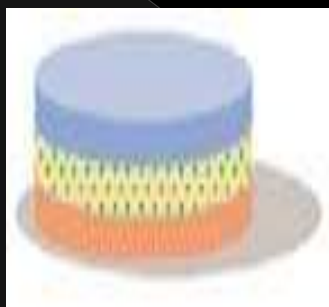
Adhesive

Liner

2. *Monolithic System*

Backing

Matrix

Adhesive Liner

TYPES OF TRANSDERMAL PATCHES

1. Single-layer Drug-in-Adhesive

2. Multi-layer Drug-in-Adhesive

3. Drug Reservoir-in-Adhesive

4. Drug Matrix-in-Adhesive

SINGLE-LAYER DRUG - IN ADHESIVE

Backing

Drug-in-Adhesive

Liner

The intrinsic rate of drug release from this type of drug delivery system is defined

$$dQ/dT = \frac{--------}{1/Pm}$$
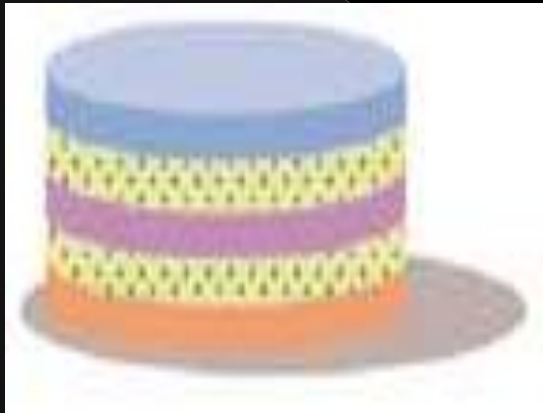
$$Pm = \frac{K_{m/r} \cdot Dm}{hm}$$

$$Pa = \frac{K_{a/m} \cdot Da}{ha}$$

$K_{m/r}$ and $K_{a/m}$ = partition coefficients

MULTI-LAYER DRUG-IN-ADHESIVE
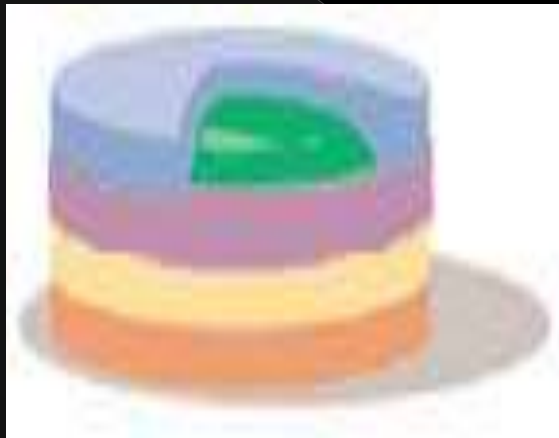

	Backing
	Drug-in-Adhesive
	Membrane
	Drug-in-Adhesive
	Liner

The rate of drug release in this system is defined by:

$$dQ / dt = \frac{K_{a/r} \cdot D_a}{ha} \, C_r$$

$K_{a/r}$ = partition coefficient

DRUG RESERVOIR-IN-ADHESIVE

Backing

Drug

Membrane

Adhesive

Liner

$$dQ/dt = \frac{K_{a/r} \cdot Da}{ha(t)} A(ha)$$

In the above equation, the thickness of the adhesive layer for drug molecules to diffuse through increases with time ha (t)

DRUG MATRIX-IN-ADHESIVE

■	Backing
□	Adhesive
■	Drug
■	Liner

The rate of drug release from this type of system is defined as

$$\frac{dQ}{dt} = \frac{AC_p D_p}{2t}^{1/2}$$

A = initial drug loading dose and
C_p and D_p = solubility and diffusivity of the
drug respectively
C_p = essentially equal to C_R ,
C_R = drug concentration in the reservoir compartment

EVALUATION STUDIES

1.PHYSICOCHEMICAL EVALUATION

2. IN VITRO DRUG RELEASE STUDIES

3. EX VIVO SKIN PERMEATION

STUDIES

PHYSICOCHEMICAL EVALUATION

1. **THICKNESS AND WEIGHT VARIATION**

   The thickness of the patches was assessed at 6different points using

   screw gauze. For each formulation, three randomly selected patches were used

2. **FLATNESS**
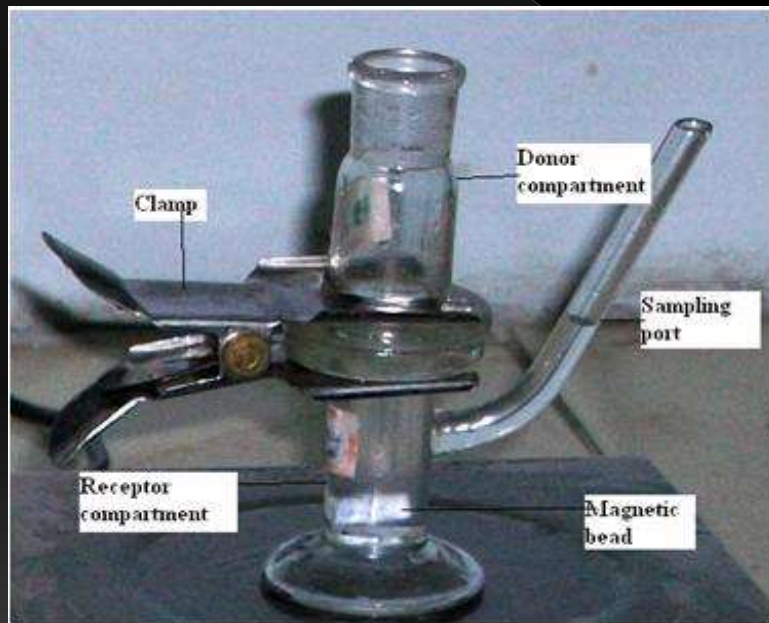
   0 %constriction equivalent to 100% flatness (20).

   % Constriction = l1-l2/ l2 X 100

3. **FOLDING ENDURANCE**

4. **DRUG CONTENT DETERMINATION**

IN VITRO DRUG RELEASE STUDIES

Franz diffusion cell

The temperature was maintained at 37 $\pm$ 0.5ºC

pH 7.4 solution

The data was fitted to different kinetic models to explain the release mechanism and pattern using the following equations.

Zero order equation $Q = Q_o - kt$

First order equation $Q = Q_o e^{-kt}$

Higuchi equation $Q = kt^{1/2}$

Q = cumulative amount of drug released,

Q = initial amount of drug,

k = release constant and t is time.

EX VIVO SKIN PERMEATION STUDIES

The whole assembly was kept in a water bath at $37 \pm 0.5^{\circ}C$. Samples (3 ml)

STABILITY STUDIES

The ability of vesicles to retain the drug

(Drug Retention Behavior) was assessed by keeping the proniosomal gel at three different temperature conditions, i.e., Refrigeration

Temperature (4-80C), Room Temperature (25±20C) and oven (45±20C).

the formulations was analyzed for drug content spectrophotometrically.

DRUGS IN TRANSDERMAL SYSTEM

S.NO	GENERIC NAME	BRAND NAME
1.	Spiranolactone	Aldactone
2.	Theophylline	Aminophylline
3.	Isotretinoin	Accutane, Claravis (Generic Only)
4.	Amphetamine salts	Adder all
5.	Amoxicillin	Amoxil
6.	Hyoscyamine	Anaspaz, Levis,
7.	Meclizine	Antivert
8.	Baclofen	Baclofen
9.	Dicyclomine	Bentyl, Byclomine
10.	Verapamil	Calan, Covera

ADVANCE DEVELOPMENT IN TDDS
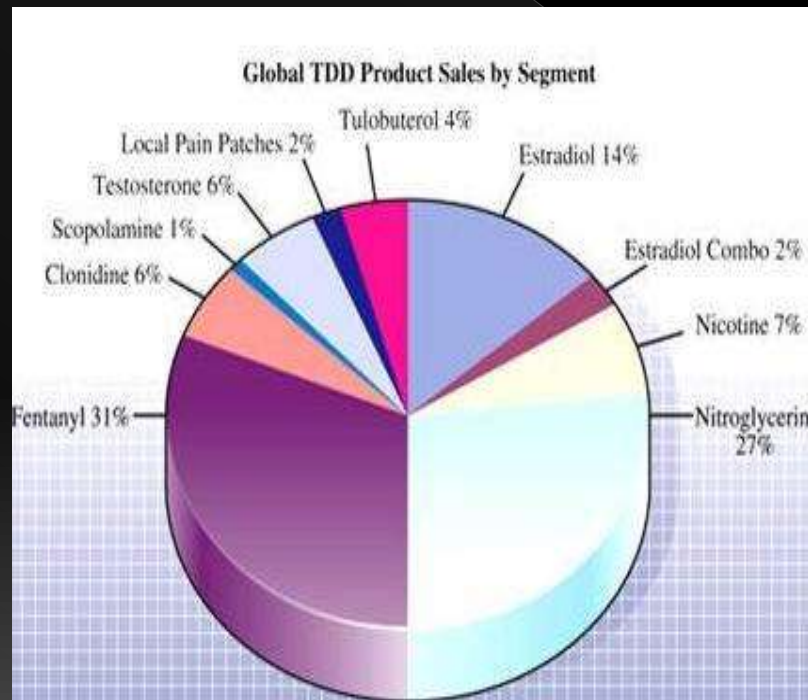
A rich area of research over the past 10 to 15 years has been focused on developing transdermal technologies that utilize mechanical energy to increase the drug flux across the skin by either altering the skin barrier (primarily the stratum corneum) or increasing the energy of the drug molecules. These so-called "active" transdermal technologies include iontophoresis

Global TDD Product Sales by Segment

Tulobuterol 4%
Local Pain Patches 2%
Testosterone 6%
Scopolamine 1%
Clonidine 6%
Fentanyl 31%
Estradiol 14%
Estradiol Combo 2%
Nicotine 7%
Nitroglycerin 27%

CONCLUSION

Thus TDDS provides numerous therapeutic and

commercial advantages. A large number of

companies are involved in the TDDS development

of which is proved by increased number of

products in the market.

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ANY QUERIES???????