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A REVIEW: COMPONENTS USED IN TRANSDERMAL DRUG DELIVERY SYSTEM

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Abstract: Transdermal medication delivery allows for regulated drug release into the patient's bloodstream, resulting in less systemic side effects and, in certain cases, increased effectiveness over other treatment types. The transdermal route of drug administration has the benefit of being relatively painless. The benefits of using the skin as a drug entry gateway include ease of access, large surface area, systemic access through underlying circulatory and lymphatic networks, and noninvasive drug distribution. The key goal of a transdermal patch system is to distribute medications into systemic circulation via the skin at a fixed pace with limited difference and within patients.

Index Terms **- Transdermal drug delivery, Transdermal patches, Controlled release.**

INTRODUCTION

TDDS:-

Transdermal therapeutic systems are characterized as self-contained, separate dosage forms that, when introduced to intact skin, distribute the drug to the systemic circulation at a controlled rate and keep the drug concentration within the therapeutic window for a long time. In order to administer therapeutic agents across the human skin for systemic effects, the precise morphological, biophysical and physicochemical properties of the human skin must be considered. The use of transdermal distribution allows for a more discreet method of administration. Transdermal treatment has an advantage over injectable and oral pathways because it improves patient compliance and avoids first-pass metabolism. Transdermal delivery not only allows for controlled and consistent drug administration, but it also allows for the constant administration of medications with brief biological half-lives and prevents pulsed entry into systemic circulation, which may result in unwanted side effects.

OBJECTIVES:-

1. To have a continuous injection of a drug for a lengthy span.
2. To ensure an equal clinical result, a lower daily dosage of the medication may be elicited through transdermal drug feedback than is required, e.g. the drug is administered orally.
3. To gain noninvasive, painless, and easy self-administration.
4. Because of their physical presence, characteristics, and distinguishing marks, they are clearly and quickly recognized in emergencies (e.g. unresponsive, intoxicated, or comatose patient).
5. To stop hepatic first pass metabolism.
6. Improved bioavailability due to increased ease of administration of drugs that would otherwise need regular dosing.
7. Maintain plasma concentrations of potent drugs with more consistent plasma levels therefore reduce side effects.
8. The ability to simply remove the patch from the skin to stop the medication from being administered.
9. To improve treatment effectiveness, reduce inter-patient and intra-patient heterogeneity.

IDEAL PROPERTIES OF DRUG:

Sr. No.	Parameter	Properties
1	Dose	Less than 20 mg
2	Half life in hrs	Should be 10 or less
3	Molecular weight in Daltons	Should be less than 500
4	Partition coefficient	Log P (octanol-water) between 1 and 3
5	Skin permeability coefficient	Should be less than 0.5 x 10^{-3} cm/hr
6	Skin reaction	Should be non-irritating
7	Oral bioavailability	Should be low
8	Therapeutic index	Should be low
9	pH of saturated aqueous solubility	5-9

APPROACHES

Chemical approach

This includes:

a) Preparation of lipophilic analogs
b) Lipid removal of stratum corneum
c) Co-administration of skin permeation enhancers

Biochemical approach

This includes:

a) Synthesis of bio-convertible pro-drugs
b) Co-administration of skin metabolism inhibitors

Physical approach

This includes:

a) Stripping of stratum corneum
b) Hydration of stratum corneum

COMPONENTS

Polymers

Types of polymer: -

1) Natural polymers: Cellulose derivative, Gelatin, Waxes, Proteins, Gum, Shellac, Natural rubber, Starch.
2) Synthetic Elastomers: Hydrin rubber, Silicone rubber, Nitrile, Acrylonitrile, Neoprene.
3) Synthetic polymers: Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyamiode, Polyurea, Epoxy.

Ideal properties of a polymer to be used in a transdermal system:

- The polymer's molecular weight and chemical functionality should be such that the particular substance diffuses and is released correctly through it.
- The polymer should be long-lasting and non-toxic.
- The polymer should be simple to produce.
- The polymer should be reasonably priced.
- It should contain a large quantity of the active ingredient.

Plasticizers

- Plasticizers are used in film forming systems to give the film has more stability and increase the tensile strength of the finished product.
- Plasticizers should be compatible with the polymers and have a low permeability to the skin.
- Glycerine, polyethylene glycol, sorbitol, dibutyl phthalate, propylene glycol, triethyl citrate, and other plasticizers are commonly used.

Backing membrane

- It shields the patch from the outside world.
- Drugs and penetration enhancers do not pass through the backing layer.
- It holds the whole mechanism together and defends the drug reservoir from the atmosphere.
- Polyesters, aluminized polyethylene terephthalate, and siliconized polyethylene terephthalate are the most popular backing materials.

Adhesive

- A Pressure Sensitive Adhesive (PSA) is a substance that helps keep the transdermal framework and the skin surface in close contact. It should stick with only finger pressure, be vigorously and permanently tachy, and have a good gripping power.
- It should also be able to be removed from a smooth surface without leaving a stain, such as polyacrylamates or polyacrylates, silicone based adhesive.
- The adhesive chosen is determined by a number of considerations, including the patch shape and medication composition.
- PSA must be physicochemically and biologically compatible, with no effect on drug release.
- The PSA may be placed on the device's face or in the rear, with the PSA stretching outwards.

Penetration enhancers

These are compounds which promote the skin permeability by altering the skin as barrier to the flux of a desired penetrate. Ideal properties of penetration enhancers:-

- Enhancing activity that is regulated and reversible.
- Compatibility with drugs and other pharmaceutical excipients in terms of both chemical and physical properties.
- Should not result in the depletion of body fluids, electrolytes, or other endogenous products.
- Non-toxic, non-irritating, and non-allergic.
- Pharmacological inertness Ability to work precisely over a predetermined period of time
- Odorless, colorless, cost-effective, and cosmetically appropriate.

Class	Examples	Mechanism	Transport Pathway
Surfactants	Na-lauryl sulfate Polyoxyethylene-9-laurylether, Bile salts: Na-deoxycholate, Na-glycocholate Na-taurocholate	Transcellular Paracellular	Phospholipid acyl chain perturbation Reduction mucus viscosity, Peptidase inhibition
Fatty acids	Oleic acid, Short fatty acids	Transcellular Paracellular	Phospholipid acyl chain perturbation
Cyclodextrins	α-, β- and γ cyclodextrins, Methylated β-cyclodextrin	Transcelular Paracellular	Inclusion of membrane compounds
Chelating agents	EDTA, Polyacrylates	Transcellular Paracellular	Complexation of Ca2+ opening of tight junctions
Positively charged polymer	Chitosan salts, Trimethyl chitosan	Paracellular	Ionic interactions with negatively charged groups of glycocalix

Release controlling membrane

- An inert membrane encloses an active agent that diffuses through the membrane at a finite, controllable rate in reservoir-type transdermal drug delivery systems.
- The release rate governing membrane may be nonporous, allowing the drug to diffuse directly through the material, or fluid-filled microspores, allowing the drug to diffuse through the fluid and fill the pores.
- The solubility of the drug in the membrane and the thickness of the membrane determine the rate of passage of drug molecules across nonporous membranes. As a result, the material used for the membrane must be consistent with the drug. The composition and thickness of the membrane can be changed to alter the dosage rate per unit area.

Release liner

- A waterproof liner covers the patch during storage, and is discarded and discharged just before the patch is applied to the skin. As a result, it is considered part of the main packing material rather than a dosage method for administering the drug.
- During storage, the linear eliminates the loss of drug that has migrated through the adhesive substrate, as well as contamination. But, since the linear is in direct contact with the delivery system, it must meet stringent criteria for chemical inertness, drug permeation, penetration enhancer, and water resistance.
- A release liner usually consists of a non-occlusive or occlusive base layer and a release coating layer consisting of silicon or Teflon. Polyester foil and metalized laminates are among the other components used in the TDDS release liner.

Plasticizer

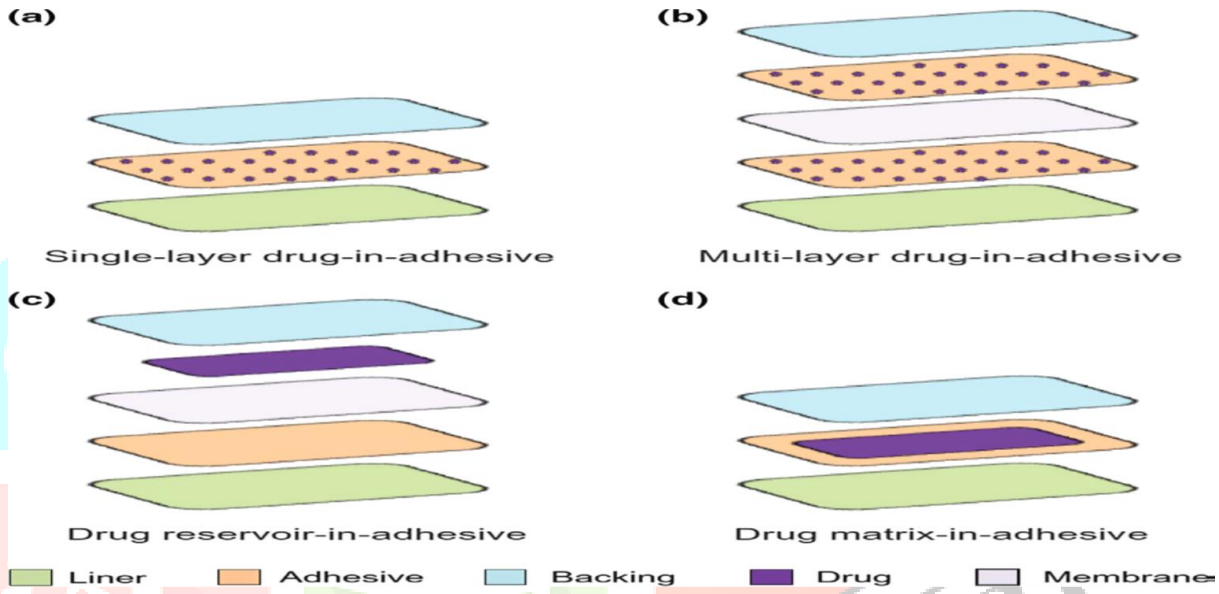
Plasticizers are used in film shaping processes to give the film more stability and increase the tensile strength of the finished product. Plasticizers should be compliant with the polymers and have minimum skin permeability. Glycerin, polyethylene glycol, sorbitol, dibutyl phthalate, propylene glycol, triethyl citrate, are most commonly used plasticizers.
If the tightness of intermolecular forces loosens with the inclusion of plasticizer, the flexibility of polymer macromolecules or macromolecular segments increases.

- Glycols :- Propylene glycols, polyethylene glycols
- Alcohols :- Ethanol, butanol, isopropanol, benzyl alcohol, lanolin alcohols, fatty alcohol
- Other solvents :- Ethyl acetate, oleic acid, isopropyl myristate

Solvent

To dissolve or spread the polymer, adhesive, or drug used in the preparation of the transdermal system, various solvents are used. Chloroform, methanol, acetone, isopropanol, and dichloromethane are among the most commonly used solvents.

Types of Transdermal Patch :-



Ideal properties of transdermal patch

S.No.	Properties	Range
1.	Shelf life	Should be up to 2.5 years
2.	Patch size	Should be less than 40 cm^2
3.	Dose frequency	Once a daily - once a week
4.	Appearance	Should be clear or white color
5.	Packaging properties	Should be easily removable of release liner
6.	Skin reaction	Should be non-irritating
7.	Release Properties	Should have consistent pharmacokinetic and pharmacodynamic profiles over time
8.	Packaging properties	Should be easily removable of release liner

Examples of Transdermal Patch:-

S. No.	Product	Active Drug	Type of Patch	Purpose
1	Estraderm	Estradiol	Membrane	Postmenstrual syndrome
2	Duragesic	Fentanyl	Reservoir	Pain relief patch
3	Transdermscop	Scopolamine	Matrix	Motion sickness
4	Deponit	Nitroglycrine	Drug in adhesive	Angina pectoris
5	Lidoderm	Lidocaine	Drug in adhesive	Anaesthetic
6	Testoderm TTS	Testosterone	Reservoir	Hypogonadism in males
7	Fematrix	Estrogen	Matrix	Postmenstrual syndrome
8	Nitrodur	Nitroglycrine	Matrix	Angina pectoris

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