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REVIEW ARTICLE

Transdermal drug delivery system: - a review on transdermal patch

Rajesh Asija[1]*, Avinash Gupta [1], Bhagwan Swaroop Maheshwari[1]

[1] Department of pharmaceutics, Maharishi Arvind institute of pharmacy, Mansarovar, Jaipur-302020, Rajasthan, India

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ABSTRACT

The main advantage of Transdermal drug delivery system is to bypass the first pass metabolism, avertance of the risk and annoyance of intravenous therapy and of the varied conditions of absorption, like pH changes, gastric emptying time and presence of enzyme. The Transdermal drug delivery scheme is generally used where the other systems of drug administration fail or it is mainly used in edema associates congestive heart failure. The transdermal drug delivery has advantage to deliver medicines via skin to systemic circulation at a predetermined rate and maintain therapeutic concentration for prolong period of time. This review describes the assorted formulation aspects, a variety of excipients, evaluation tests, challenges and drugs explored in the pasture of topical drug delivery.

Key words: Transdermal patches, Controlled Drug Delivery System,

INTRODUCTION:

Controlled drug delivery:

Controlled drug delivery technology represents one of the most rapidly advancing areas of science in which chemists and chemical engineers are contributing to human health care. Such delivery systems offers various advantages compared to conventional dosage forms including, improved patient, reduced toxicity, and improved efficacy compliance and convenience. [1]

The different classification of controlled drug delivery systems (CDDS) can be given as follows: [2-3]

1. Rate-preprogrammed drug delivery systems
2. Activation-modulated drug delivery systems
3. Feedback-regulated drug delivery systems
4. Site-targeting drug delivery systems

Out of these classes, first class contains new drug delivery systems as transdermal delivery,ocular inserts, intra uterine delivery and sub dermal implants. The transdermal drug delivery has advantage to deliver medicines via skin to systemic circulation at a predetermined rate and maintain therapeutic concentration for long time.

Transdermal patch or adhesive patch or skin patch used to deliver a controlled dose of a drug through the skin over a period of time. A skin patch uses a special membrane to control the rate at which the liquid drug contained in the reservoir within the patch can pass through the skin and into the blood circulation. Few drugs should be combined with substances, like as alcohol that enhances their ability to penetrate the skin in order to be used in the skin patches. Drugs administered through skin patches include scopolamine (for motion sickness), nicotine (for quitting smoking), estrogen (for menopause and to prevent osteoporosis after menopause), nitroglycerin (for angina) lidocaine to relieve the pain of shingles and many more drugs.

Differents types of transdermal drug delivery systems (TDDS): [8-11]

Transdermal drug delivery systems are vertically classified into two types. The first is called the passive transdermal delivery systems. The second type of the transdermal system is called the Active transdermal delivery system. Both the types of transdermal drug delivery system are horizontally classified into single layer, multilayer, matrix, reservoir, vapor patch etc. The difference between a passive and active transdermal system is that passive transdermal drug delivery system relies completely on the principle of diffusion based on gradients. Active Transdermal drug delivery system is also based on the same principle of diffusion but it consists of different penetration enhancing technologies ranging from electrical current, Iontophoresis, Electroporation, Microporation, Laser Ablation, Mechanical Arrays, Radio Frequency Thermal/Heat, and Ultrasound, etc.

***Corresponding author:** Dr. Rajesh Asija || **E-mail:** bhagwanmalu88@gmail.com*

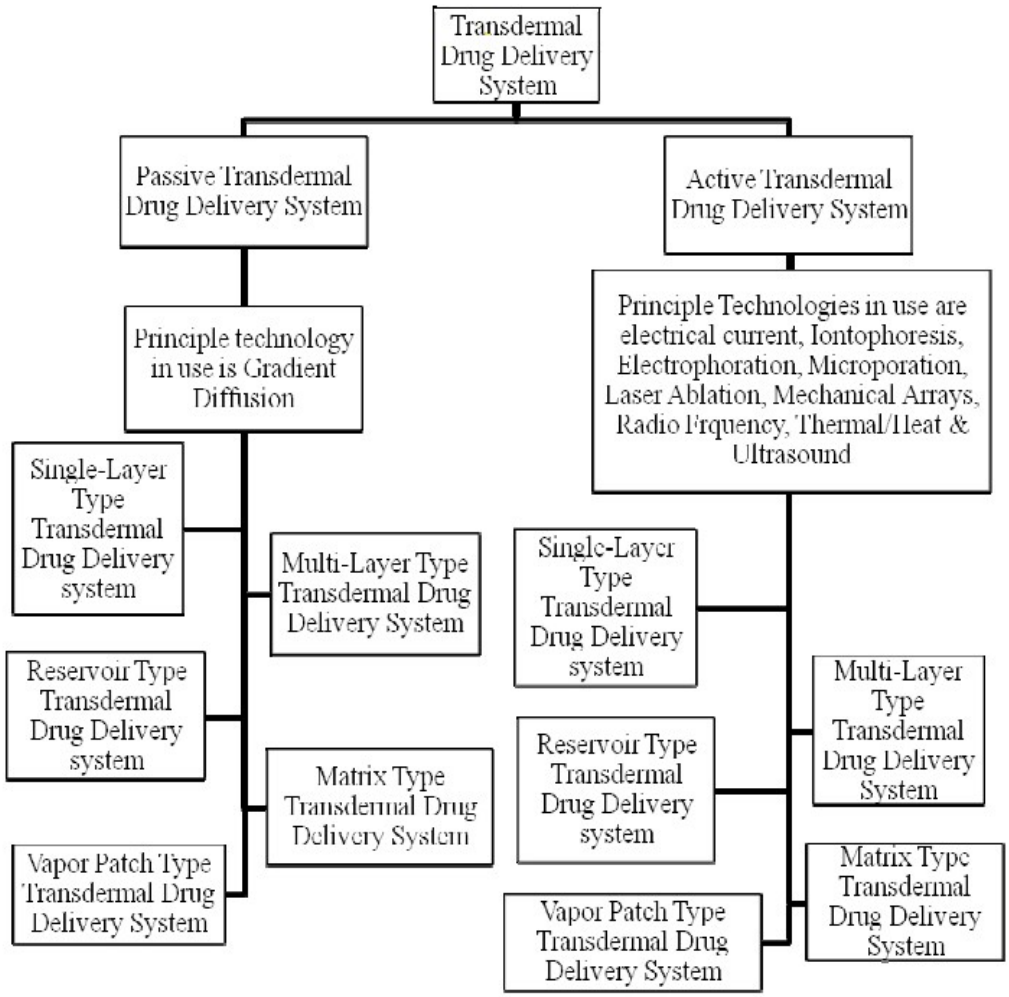

Figure 1: A of classification of TDDS

Ideal requirements of drug molecule for transdermal drug delivery systems: [12-16]

Selection of proper drug candidate should be done as every drug candidate cannot be suitable for this system.

Table 1: Ideal properties of drug candidate

Parameter	Properties
Dose	Should be low
Half life in hr	10 or less
Molecular weight	< 400
Partition coefficient	Log P (octanol-water) between –1.0 and 4
Skin permeability coefficient	> 0.5 x10-3cm/hr
Skin reaction	Non irritating and non sensitizer
Oral bioavailability	Low
Therapeutic index	Low

Various contents of transdermal drug delivery systems:

A. Polymer matrix or matrices.
B. The drug
C. Permeation enhancers
D. Other excipients

A.Polymer Matrix:

The Polymers tackle the release of the drugs from the device. Possible useful polymers for transdermal devices are,

❖ **Natural Polymers:**

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

❖ **Synthetic Elastomers:**

e.g. Nitrile Polybutadieine, Acrylonitrile rubber, Polysiloxane, Silicone-rubber, Hydrin, , , Styrenebutadieine rubber, Neoprene, Butyl rubber etc.

❖ **Synthetic Polymers:**

e.g.Polyacrylate, Polyurea, Polyvinylalcohol, PVC, Polyethylene, Polypropylene, Polyamide, Polyvinylpyrrolidone, Epoxy etc

A. The drug:

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

B. Penetration Enhancers:

There are many substances that improves skin permeability by altering the skin as a barrier to the flux of a desired penetrant.

❖ **Solvents:**

These compounds increase penetration possibly by swallowing the polar pathway and/or by fluidizing lipids. Examples include water alcohols – methanol and ethanol; alkyl methyl sulfoxides –, alkyl homologs of methyl sulfoxide, dimethyl acetamide dimethyl sulfoxide and dimethyl formamide ; pyrrolidones – 2 pyrrolidone, Nmethyl 2-purrolidone; laurocapram (Azone), miscellaneous solvents – silicone fluids, glycerol, , isopropyl palmitate.

❖ **Surfactants:**

These compounds are proposed to enhance polar pathway transport, specially of water soluble drugs. The capacity of a surfactant to alter penetration is a function of the polar head group and the hydrocarbon chain length.

1. Anionic Surfactants: [18-20]

e.g Sodium lauryl sulphate. Dioctyl sulphosuccinate, , Decodecylmethyl sulphoxide etc.

2. Nonionic Surfactants:

e.g. Pluronic F68, Pluronic F127 etc. Bile Salts: e.g., ,Sodium tauroglycocholate Sodium deoxycholate Sodium ms taurocholate.

3. Binary system:

These systems apparently open up the heterogeneous multilaminate pathway as well as the continuos regular pathways. e.g. 1, 4-butane diol- linoleic acid and. Propylene glycol-oleic acid

4. Miscellaneous chemicals:

These include urea, a hydrating and keratolytic agent; N, Ndimethyl- m-toluamide; calcium thioglycolate; anticholinergic drugs. few potential permeation enhancers

have recently been described but the available data on their effectivity sparse. These include, di-o-methyl-ß-cyclodextrin. eucalyptol and soyabean casein.

C. Other Excipients[21]

a) Adhesives:

The fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face of the device or in the back of the device and extending peripherally. these adhesive systems must satisfy the following criteria:

- should combine to skin fastly, should be easily removed.
- Should not leave the unwashable residue remaining on the skin.
- Should not annoyed or sensitized the skin.

The face adhesive system ought to fulfill and satisfy the following criteria. [22-23]

- chemical and Physical compatibility and suitability with the drug, excipients and enhancers of the device of which it is a part.
- Permeation of drug must not be affected and disturbed.
- The delivery of simple or mixer permeation enhancers must not be affected.

Backing membrane:

Backing membranes are flexible and they provide a good bond to the drug reservoir, avert drug from leaving the main dosage form through the peak, and take printing. It is opaque substance that preserve the product during use on skin e.g. plastic metallic laminate, plastic backing with absorbent pad and occlusive footing plate (aluminium foil), adhesive foam pad (flexible polyurethane) with occlusive footing plate.

Rationale and Objective of Study: [4-6]

Some chronic diseases like diabetes, hypertension, tuberculosis, cancer require prolong administration of drugs and frequent dosing to maintain constant drug plasma concentration level and may lead to poor patient compliance. Many orally administered drugs can irritate the GI tract or undergo first pass metabolism and leads to poor bioavailability. This led to development of transdermal drug delivery system (TDDS).

TDDS provides continuous administration of drug through the skin, which maintains constant plasma drug levels and avoids the peaks and troughs seen with oral administration. TDDS offers no first-pass hepatic metabolism and enzymatic degradation in the gastrointestinal tract. Continuous delivery of drug may reduce systemic side effects associated with high plasma drug levels. The multiday dosing that is made possible by the sustained delivery of drugs with short half-life. It includes a non oral route of administration for patients who are unable to take oral medications and the immediate cessation of drug administration with removal of the patch.

Torasemide is sulfonyl urea loop diuretics which has been shown to be effective in the treatment of edema associated with congestive heart failure , renal disease, or hepatic disease. Also used for treatment of hypertension alone. The most frequently reported side effects are gastric disturbances like nausea, anorexia, vomiting, and enhanced appetite after oral treatment. Because these drugs are generally intended to take for a long period, patient compliance is very important. The plasma half life of this drug is very short i.e. about 3.5 hours which makes frequent dosing necessary to maintain the therapeutic blood levels of the drug for a long term treatment. Therefore to avoid conventional multiple oral dosing, controlled release transdermal patch of Torasemide can be prepared.

Objective of the study: [7]

1. Preparation of matrix transdermal patches by using combination of appropriate polymers.

2. To study the effect of varying concentration of polymers and plasticizer on in vitro drug release.

3. Characterization of prepared matrix transdermal patches.

4. The main objective of this transdermal dosage form is to deliver drug into systemic circulation at a predetermined rate with less side effects and skin irritation.

Benefits of transdermal drug delivery system: [24-27]

1. They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal enzymatic activity pH, and drug interactions with drink food, and diffrent orally taken drugs.

1. They can substitute for oral administration of medication when that route is unfit, as with diarrhea and vomiting.

2. They avoid the *g.i. first pass metabolism.*, this is, the first pass of a drug substance through the systemic and portal circulation following gastrointestinal absorption, may be averting the deactivation by liver and digestive enzymes.

3. They are noninvasive, avoiding the inconvenience of parenteral therapy.

4. They provide extended therapy with a only application, enhancing compliance over different dosage forms requiring more frequent dose administration.

5. The activity of a drugs having short half-life is extended through the reservoir of drug in the therapeutic delivery system and its controlled release can be achieved.

6. Drug therapy may be terminated rapidly by removal of the application from the surface of the skin.

7. They are easily and rapidly identified in emergencies (e.g., unresponsive, unconscious, or comatose patient) because of their features physical presence,and recognizing markings.

8. They are used for drugs with narrow therapeutic window. At the same time transdermal drug delivery has some drawbacks that are limiting the benifits of transdermal delivery system.

Hindrence of transdermal drug delivery system: [28-30]

1. Only relatively potent drugs are suitable candidates for transdermal delivery because of the natural limits of drug entry imposed by the skin‟s impermeability.

2. Some patients develop contact dermatitis at the site of application from one or more of the system components.

3. The delivery system cannot be used for drugs requiring high blood levels.

CONCLUSION:

This TDDS form can substantially reduce the dosing frequency and oral side effects of Torasemide as compared to its conventional dosage form. This transdermal patch will surely increase patient compliance due to its benefits over oral dosage forms. This system can be further explored for combination with other suitable drugs.

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