



Transdermal Drug Delivery System: An Emphasis on Transdermal Patches

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Abstract

Transdermal drug delivery system was presented to overcome the difficulties of drug delivery especially oral route. A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. It promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of delivery system such as oral, topical, i.v., i.m., etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The main disadvantage to transdermal delivery systems stems from the fact that the skin is a very effective barrier, as a result, only medications whose molecules are small can easily penetrate the skin, so it can be delivered by this method. This review article describes the overall introduction of transdermal patches including type of transdermal patches, method of preparation of transdermal patches and factor affecting etc.

Keywords: Transdermal drug delivery system; Hydrin rubber; Silicon rubber; Polyvinylalcohol; Transdermal patch; Polyvinylchloride; Di-N-butylphthalate; Triethylcitrate

Introduction

Transdermal drug delivery system is the non-invasive delivery of medications from the surface of the skin. Skin is the largest and most accessible organ of human body through its layers to the circulatory systems [1]. The transdermal drug delivery system (TDDS) is a widely accepted mode of drug delivery, and transdermal patches are devised to treat

various diseases [2].

The transdermal patch is a medicated adhesive pad that is design to release the active ingredient at a constant rate over a period of several hours to days after application to the skin. It is also called skin path. A skin patch uses a special membrane to contain which the patch can pass through the skin & into the blood stream [3].

Advantages

1. Avoidance of hepatic first pass metabolism.
2. Poor oral bioavailability.
3. Long duration of action.
4. It enhances patient compliance.
5. Minimizes harmful side effects of drug caused from over dose.
6. Stable & control blood level.
7. Selective targeting to infectious cells that compose to normal cells.
8. Reduce toxicity.

Disadvantages

1. Expensive.
2. Difficult to maintain stability of dosage forms.
3. Possibility of local irritation at the site of application.
4. Technical skill required.
5. Rapid clearance.

Types of Transdermal Patches

1. Single layer drug in adhesive
2. Multilayer drug in adhesive
3. Drug reservoir in adhesive
4. Drug matrix in adhesive
5. Vapor patches

Single Layer Drug in Adhesive

The adhesive layer of this system also contains the drug. In this type of patch, the adhesive layer not only serves to adhere the various layers together, along with the entire system to the skin, but it also responsible for the releasing of the drug. The adhesive layer is surrounded by a temporary liner & a backing [3].

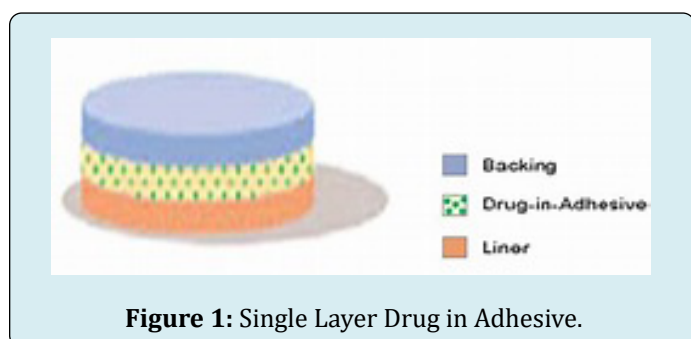


Figure 1: Single Layer Drug in Adhesive.

Multilayer Drug in Adhesive

The multilayer drug in adhesive patch is similar to the single layer system in that both adhesive layers are also responsible for the releasing of the drug. The multilayer

system is different however that it adds another layer of drug in adhesive, usually separated by a membrane [2].

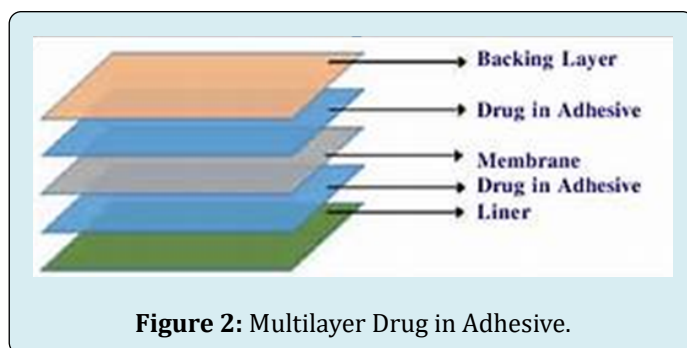


Figure 2: Multilayer Drug in Adhesive.

Drug Reservoir in Adhesive

The reservoir transdermal system design includes liquid compartment containing a drug solution (or) suspension. Which is separated from the release liner by a semi permeable membrane & adhesive? The adhesive component of the product can be act as a continuous layer b/w the membrane & release liner (or) as a concentric configuration around the membrane [4].

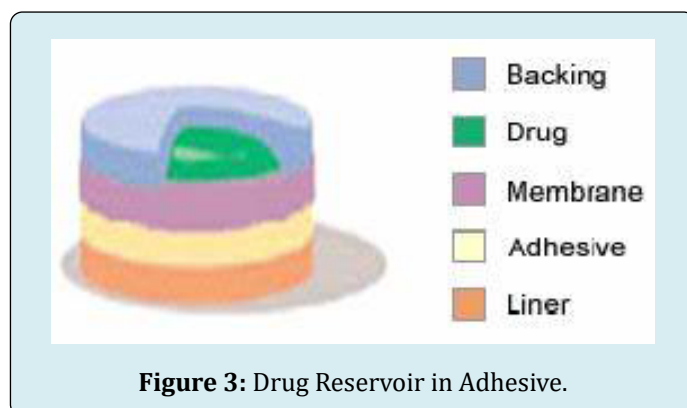


Figure 3: Drug Reservoir in Adhesive.

Drug Matrix in Adhesive

The matrix system design is characterized by the inclusion of a semi solid matrix containing a drug solution (or) suspension which is in direct contact with the release liner. The compartment responsible for skin adhesive is incorporated in an overlay & forms a concentric configuration around the semi-solid matrix [5].

Vapor Patches

In this type of patch, the adhesive layer not only servers to adhesive the various layers together but also to release vapor. The vapor patches are new on the market & they release essential oils for up to 6hrs. The vapor patches release essential oils & are used in case of decongestion mainly [2,3].

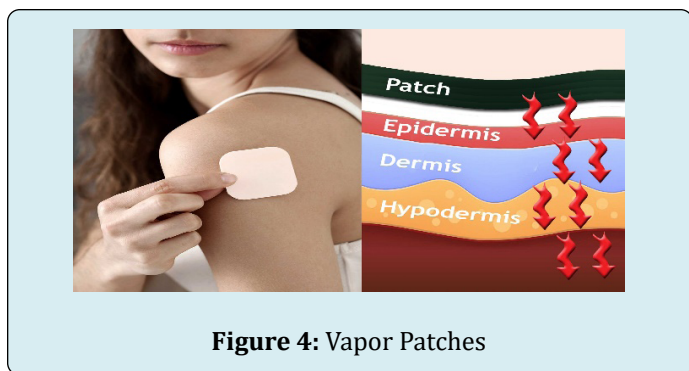


Figure 4: Vapor Patches

Methods of Preparation of TDSS

Polymer Membrane Permeation-Controlled TDSS

In this system, the drug reservoir is embedded between an impervious backing layer & a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous (or) non porous. In the drug reservoir compartment, the drug can be in the form of solution, suspension, gel (or) dispersed in solid matrix. On the outer surface of the polymeric membrane a thin layer of drug compatible, hypoallergenic adhesive polymer can be applied [2,3].

Example: Transderm scop (scopolamine) for 3 days protection of motion sickness & Transderm Nitro (Nitroglycerine) for once-a-day medication of angina pectoris.

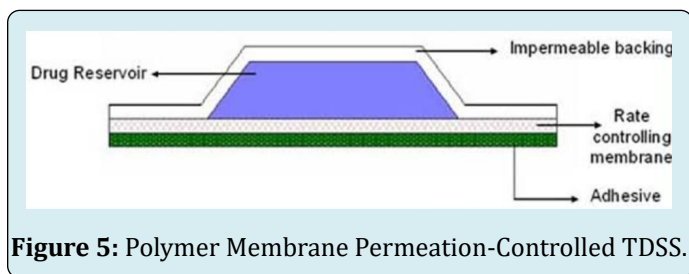


Figure 5: Polymer Membrane Permeation-Controlled TDSS.

Adhesive Diffusion Controlled TDSS

The drug reservoir is formed by dispersing the drug in an adhesive polymer & then spreading the medicated polymer adhesive by solvent casting or by melting the adhesive onto an impervious backing layer. The drug reservoir layer is then covered by a non-medicated adhesive polymer of constant thickness to produce an adhesive diffusion controlling drug delivery system.

Example: Deponite (nitroglycerine) for once a day medicated of angina pectoris.

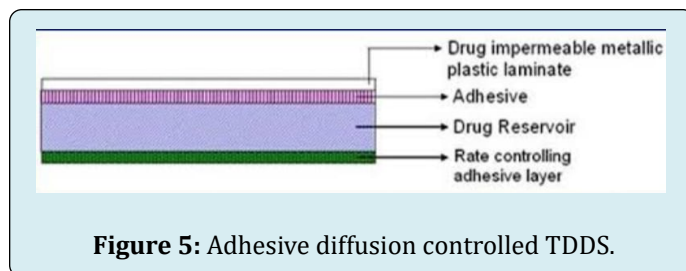


Figure 5: Adhesive diffusion controlled TDSS.

Matrix Diffusion Controlled TDSS

The drug is dispersed homogeneously in a hydrophilic [or] lipophilic matrix. The drug containing polymer disk then is fixed onto an occlusive base plate in a compartment fabricated from a drug impermeable backing layer. Instead of applying the adhesive on the face of the drug reservoir, it is spread along the circumference to form a strip of adhesive rim. Example: Nitro Dur [nitroglycerine] used for once a day medicated for angina pectoris [5].

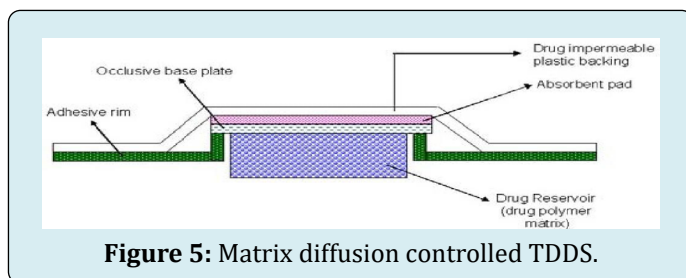


Figure 5: Matrix diffusion controlled TDSS.

Micro Reservoir Controlled TDSS

The drug delivery system is a combination of reservoir & matrix dispersion system the drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer & then dispersing the solution homogeneously in a lipophilic polymer to form thousands of & unreachable, microscopic spheres of the drug reservoir. A transdermal system therapeutic system thus formed as a medicated disc positioned at the center & surrounded by an adhesive rim [6].

Example: Nitro-dur system [nitroglycerine] for once a -day treatment of angina pectoris

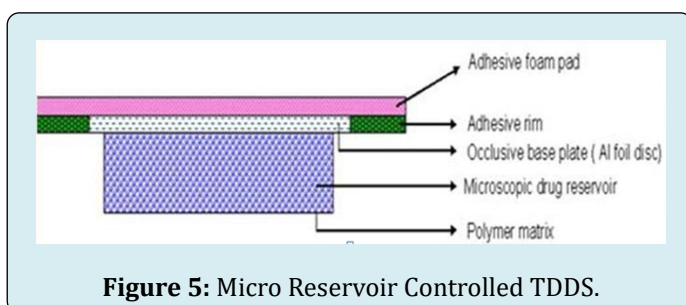


Figure 5: Micro Reservoir Controlled TDSS.

Evaluation Methods

Evaluation methods are classified into

1. Physicochemical evaluation
2. *In-Vitro* evaluation
3. *In-Vivo* evaluation

Physicochemical Evaluation

Interaction Studies: The drug & the excipients must be compatible with one another to produce a product that is stable. The interaction b/w drug & excipients affects the bioavailability & stability of drug. Interaction studies are taken out by thermal analysis, IR, UV & chromatographic techniques.

Thickness of The Patch: The thickness of the drug prepared patch is measured by using a digital micrometer at different point of the patch & determines the average thickness & standard deviation for the same to ensure the thickness of the prepared patch [6].

Weight Uniformity: A specific area of patch is to be cut in different parts of the patch & weigh in digital balance. The prepared patches to be dried at 80°C for 4hrs before testing.

Percentage Moisture Content: The prepared patches are to be weighed individually & to be kept in a desiccator containing fused CaCl_2 at room temperature.

$\% \text{moisture content} = \frac{\text{Initial weight} - \text{final weight}}{\text{final weight}} \times 100$

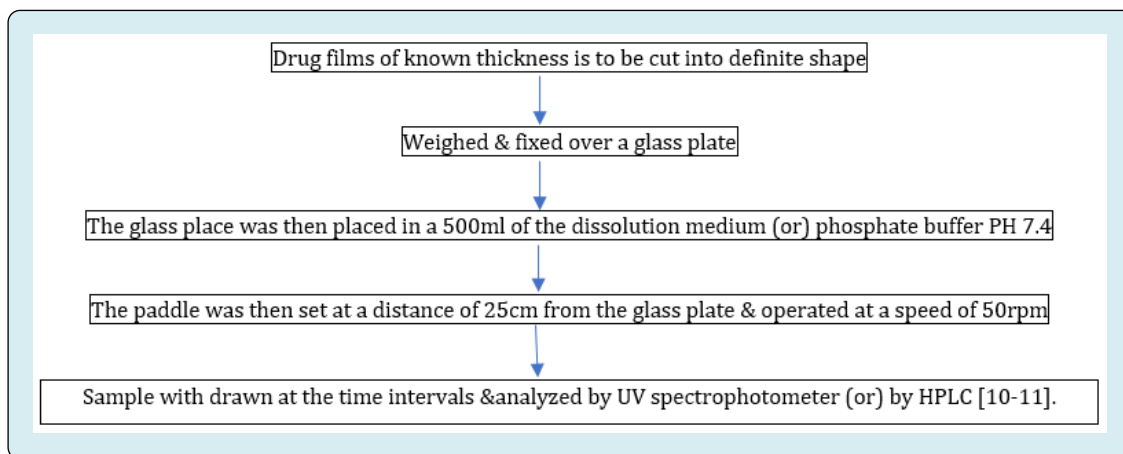
Percentage Moisture Uptake: The prepared patches are to be weighed individually & kept in a desiccator containing saturated solution of KCL in order to maintain 84% RH [8,9].

$\% \text{moisture uptake} = \frac{\text{final weight} - \text{initial weight}}{\text{initial weight}} \times 100$

Content Uniformity: 10 patches are selected & content is determined for individual patches. 9 out of 10 patches have content b/w 85% to 115% of the specific value. Then transdermal patches pass the test of content uniformity.

In-Vitro evaluation

***In-Vitro* drug release studies:** Paddle over disc method can be employed for the assignment of the release of the drug from the prepared patches.



In-Vivo Evaluation

In-Vivo evaluation of TDDS can be carried out by using animal models & human volunteers.

Animal model: Most common animal species used for evaluating TDDS are mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit & guinea pig etc.

Human volunteers: It involves collection of pharmacokinetic & pharmacodynamic data. Clinical trials have been conducted to assess the efficacy, risk, side effects etc.

Phase-1: Trails for safety

Phase-2: Effectiveness in patients

Phase-3: Safety & effectiveness of large no. of patients

Phase-4: Post marketing surveillance [10,11].

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