**Transdermal Drug Delivery Systems; Review Article**

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Abstract

Transdermal drug delivery system is the system in which the delivery of the active ingredients of the drug occurs through the skin. Transdermal drug delivery system can improve the therapeutic efficacy and safety of the drugs because drug delivered through the skin at a predetermined and controlled rate. Skin is an effective medium from which absorption of the drug takes place and enters the circulatory system. Various types of Transdermal patches are used that delivered the specific dose of medication directly into the blood stream. This review article covers a brief outline of the transdermal drug delivery system, advantages over conventional drug delivery system, Layers of the skin, various components of transdermal patch, penetration enhancers, and evaluation of transdermal system and applications of Transdermal patch.

Introduction

Transdermal drug delivery system is defined as the topically administered medications in the form of patches which when applied to the skin deliver the drug, through the skin at a predetermined and controlled rate. Transdermal patches are delivered the drug through the skin in controlled and predetermined manner in order to increase the therapeutic efficacy of drug and reduced side effect of drug. For effective Transdermal drug delivery system, the drugs are easily able to penetrate the skin and easily reach the target site. TDDS increase the patient compliance and reduces the load as compared to oral route. FDA approved the first Transdermal system Transderm-SCOP in 1979 (1).

Transdermal formulation maintain drug concentration within the therapeutic window for prolong period of time ensuring that drug levels neither fall below the minimum effective concentration nor exceed the maximum effective concentration (2).

***Advantages of transdermal drug delivery system***

* Avoidance of first pass metabolism of drugs.
* Transdermal medication delivers a steady infusion of a drug over a prolonged period of time (3).
* The simplified medication regimen leads to improved patient compliance and reduced the side effects, inter and intra-patient variability (4).
* No interference with gastric and intestinal fluids.
* Maintains stable or constant and controlled blood levels for longer period of time.
* Comparable characteristics with intravenous infusion (5).

***Disadvantages of transdermal drug delivery system***

* The possibility of local irritation may develop at the site of application. Many problems like Erythema, itching, and local edema can be caused by the drug, the adhesive, or other excipients in the patch formulation.
* Many drugs with a hydrophilic structure having a low penetration through the skin and slowly to be of therapeutic benefit. Drugs with a lipophilic character, however, are better suited for transdermal delivery.
* The barrier function of the skin changes from one site to another on the same person, from person to person and with age.
* Transdermal drug delivery system cannot achieve high drug levels in blood/plasma.

***Enhancers of transdermal drug delivery system***

Enhancers increase the penetration of permeants by disrupting the structure of skin’s outer layer i.e stratum corneum and increasing penetrant solubility (3). Disruption, either by the means of chemical or physical mean, may affect both the intracellular and extracellular structure. Disruption may be due to protein denaturation, fluidization and randomization of intercellular lipids or intercellular delamination and expansion (6).

***Enhancers of transdermal drug delivery system are:***

* Physical enhancers
* Particulate systems
* Chemical enhancers

***Physical enhancers***

The enhancers of Transdermal drug delivery system are the iontophoresis, electroporation, magnetophoresis, microneedle and ultra sound (also known as phonophoresis or sonophoresis) techniques are examples of physical means of enhancement that have been used for enhancing percutaneous penetration (and absorption) of various types of therapeutic agents.

***Particulate system***

The enhancers of Transdermal drug delivery sytem are liposomes, microemulsion, transfersome, niosomes and nanoparticles are the examples of particulate means of enhancement.

***Chemical enhancers***

The enhancers of Transdermal drug delivery system by means of chemicals are sulphoxides, glycols, alkanols, terpenes, azones etc. Chemicals that promote the penetration of topically applied drugs are commonly referred to as accelerants, absorption promoters, or penetration enhancers. Chemical enhancers act by increasing the drug permeability through the skin by causing reversible damage to the stratum corneum and by increasing the partition coefficient of the drug to promote its release from the vehicle into the skin.

***Transdermal patches***

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied creams and ointments for dermatological disorders (7). A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and directly into the bloodstream. 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 bloodstream. Some drugs must be combined with substances, such as alcohol because alcohol increase their ability to penetrate the skin in order to be used in a skin patch (8).

***Conditions in which transdermal patches are used when:***

1. When the patient has intolerable side effects including constipation and dysphagia .
2. Where the pain control might be improved by reliable administration.
3. It can be used in combination with other enhancement strategies to produce synergistic effects.

***Types of transdermal patches***

**a) Single layer drug in adhesive**

In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and this type of layer is responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

**b) Multi -layer drug in adhesive**

This type is also similar to the single layer but it contains a immediate drug release layer which is different from other layer which will be a controlled release along with the adhesive layer.

**c) Vapor patch**

In this type of patch the role of adhesive layer not only serves to adhere the various layers together but also serves market, commonly used for releasing of essential oils in decongestion.

**d) Reservoir system**

In this system the drug reservoir is embedded between the two layers; an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix. (9)

***Applications of transdermal patches***

* + Transdermal patch of nicotine, which releases nicotine in controlled doses to help with cessation of tobacco smoking.
  + Nitroglycerine patches are also sometimes prescribed for the treatment of Angina.
  + Clonidine, the antihypertensive drug and ketoprofen, the non-steroidal anti-inflamatory drug are also available in the form of transdermal patches.
  + Transdermal form of the MAOI selegiline,became the first transdermal delivery agent for an antidepressant.
  + Transdermal delivery agent for the Attention Deficit Hyperactivity Disorder (ADHD). (5)

***Transdermal gels***

The use of transdermal gels has expanded both in cosmetics and in pharmaceutical preparations (10). Transdermal application of gels at pathological sites offer great advantage in a faster release of drug directly to the site of action, independent of water solubility of drug as compared to creams and ointments .The U.S.P. defines Gels as a semisolid system consisting of dispersion made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by liquid. Gels consists of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains. A gel is colloid that is typically 99% weight liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from small amount of a gelating substances present (11). Topical drug administration a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes.

***Gel forming substances***

Polymers are used to give the structural network, which is essential for the preparation of gels. Gel forming polymers are classified as follows:

**1. Natural polymers**

* Proteins – Collagen, Gelatin
* Polysaccharides – Agar, Alginate acid,Sodium or Potassium carageenan,Tragacanth, Pectin, Guar Gum, Cassiatora, Xanthan, Gellum Gum.

**2. Semisynthetic polymers cellulose derivatives**

Carboxymethyl cellulose, Methylcellulose, Hydroxypropyl cellulose, Hydroxy propyl (methyl cellulose) and Hydroxyethyl cellulose.

**3. Synthetic polymers**

* Carbomer – Carbopol 940, Carbopol 934
* Poloxamer
* Polyacrylamide
* Polyvinyl alcohol
* Polyethylene and its co-polymers

**4. Inorganic substances**

* Aluminium hydroxide
* Bentonite

**5. Surfactants**

* Cebrostearyl alcohol
* Brij (5)

***Advantages***

The topical administration of drug is important because of various advantages:

* They can avoid gastrointestinal drug absorption difficulties .
* They can substitute for oral administration of medication when that route is unsuitable.
* To avoid the first pass effect .
* They are non-invasive and have patient compliance.
* They are less greasy and can be easily removed from the skin.
* Cost effective.
* Reduction of doses as compare to oral dosage forms.
* Localized effect with minimum side effects.
* Improving drug bioavailability, reducing dose frequency.
* Stabilizing drug delivery profiles. (14,15,16)

***Methods of Preparation***

1. Dispersion Method
2. Cold Method
3. Chemical Reaction
4. Temperature effect
5. flocculation with salts and non-solvents .

***Evaluation***

* pH
* Drug content
* Viscosity
* Spreadability
* Extrudability study
* Skin irritation studies
* In vitro release
* In vivo study
* Stability
* Consistency

***Conclusion***

Transdermal drug delivery system is useful for topical and local action of the drug, Due to large advantages. various permeation enhancers which would significantly increase the number of drugs suitable for TDDS .Transdermal drug delivery through the gel is suitable candidate for drug which show hepatic first pass effect and unstable in GI conditions .

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