



Current Trends in Transdermal Patches

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ABSTRACT

Transdermal drug delivery systems have evolved as a successful alternative to systemic drug delivery. Despite their relatively higher costs, transdermal delivery systems have proved advantageous for delivery of selected drugs, such as estrogens, testosterone, clonidine and nitro-glycerine. Transdermal delivery provides a leading edge over injectable and oral routes by increasing patient compliance and avoiding first pass metabolism respectively. The technique is generally non-invasive well accepted by patients and can be used to provide local delivery over several days. Recently there has been an increasing awareness that the benefits of intravenous drug infusion can be closely duplicated, without its potential hazards, by continuous transdermal drug administration through skin. For both local and systemic effects skin is the major site of application. However, to penetrate the drug through skin, stratum corneum is the main barrier.

1 INTRODUCTION

During the past few years, interest in the development of novel drug delivery systems for existing drug molecules has been renewed. The development of a novel delivery system for existing drug molecules not only improves the drug's performance in terms of efficacy and safety but also improves patient compliance and overall therapeutic benefit to a significant extent. When properly designed and developed for a particular drug, novel delivery system can overcome specific hurdles associated with conventional methods of delivery, e.g., drugs that undergo partial or complete degradation before reaching the site of action could be effectively delivered with improved bioavailability by using the novel concepts of timed or pulsatile release.

Oral route is the popular route of drug delivery. Although it has some disadvantages including first pass metabolism, drug degradation in gastrointestinal tract due to enzymes, PH etc. To cross these problems, a novel drug delivery system was developed. In this transdermal delivery system medicated adhesive patches are prepared which deliver therapeutically effective amount of drug across the skin when it placed on skin. Medicated adhesive patches or transdermal patches are of different sizes, having more than one ingredient. Once they apply on unbroken skin they deliver active ingredients into systemic circulation passing via skin barriers. A patch containing high dose of drug inside which is retained on the skin for prolonged period of time, which get enters into blood flow via diffusion process. Drug can penetrate through skin via three pathways-through hair follicles, through sebaceous glands, through sweat duct. Transdermal drug delivery systems are used in various skin disorders, also in the management of angina pectoris, pains, smoking cessation & neurological disorders such as Parkinson's disease.[1,2] The transdermal route has become one of the most successful and innovative drug delivery system for research in pharmaceutical sciences. Transdermal drug delivery provides a leading edge over injectable and oral routes by increasing patient compliance and avoiding first pass metabolism respectively

2 PREPARATION OF TRANSDERMAL PATCHES:

Transdermal drug delivery patches can be prepared by various methods

Mercury Substrate Method:

In this method required amount of drug is dissolved in predetermined amount of polymer solution along with plasticizer. The above solution is to be stirred for some time to produce a homogenous dispersion and it is kept aside until air bubbles removed completely and then poured in to a glass ring which is placed over the mercury surface in a glass petri dish. The rate of evaporation of the solvent is controlled by placing an inverted funnel over the petri dish. The dried films are to be stored in a desiccator 16-20

Circular Teflon Mould Method:

Solutions containing polymers in various ratios are used in an organic solvent. Calculated amount of drug is dissolved in half the quantity of same organic solvent. Plasticizer added into drug polymer solution. The total contents are to be stirred and then poured into a circular Teflon mould. And rate of solvent vaporization controlled with placing inverted glass funnel on Teflon mould. The solvent is allowed to evaporate for 24 hrs. The dried

films are to be stored in a desiccator

By Using EVAC Membranes Method:

In order to prepare the target transdermal therapeutic system, 1% carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membranes can be used as rate control membranes. If the drug is not soluble in water, propylene glycol is used for the preparation of gel. Drug is dissolved in propylene glycol; carbopol resin will be added to the above solution and neutralized by using 5% w/w sodium hydroxide solution. The drug (in gel form) is placed on a sheet of backing layer covering the specified area. A rate controlling membrane will be placed over the gel and the edges will be sealed by heat to obtain a leak proof device

For preparation of same, chloroform is choice of solvent, in chloroform. The drug is dissolved in chloroform and adhesive material will be added to the drug solution and dissolved. A custom made aluminium former is lined with aluminium foil and the ends blanked off with tightly fitting cork block

Advantage:

- Increase bioavailability.
- Reduce dosing frequency.
- It is painless and non-invasive drug delivery system.
- Avoid hepatic first pass metabolism.
- Increase patient compliance mainly in paediatric and geriatric patients.
- Self-administration medicament.

Disadvantages:

Transdermal drug delivery systems have few disadvantages.

- Small amount of drug are administered through the skin.
- Skin irritation may occur.
- It cannot achieve high drug levels in blood. Some patients develop contact dermatitis at the site of application on for one or more of the system components, necessitating discontinuation. Higher should not use ionic drug.

3 FACTORS AFFECTING TRANSDERMAL PATCHES:

There are various factors which affect the action of transdermal patches. These are given below:

a. Physicochemical Properties

- i. Partition coefficient
- ii. Molecular size
- iii. Solubility/melting point
- iv. Ionization

b. Physiological & Pathological Conditions of Skin

- i. Reservoir effect of horny layer
- ii. Lipid film
- iii. Skin hydration
- iv. Skin temperature
- v. Regional variation
- vi. Pathological injuries to the skin
- vii. Cutaneous self-metabolism
- viii. Skin barrier properties in the neonate and young infant
- ix. Skin barrier properties in aged skin
- x. Race
- xi. Body site
- xii. Penetration enhancers used

4 THE FUTURE OF TRANSDERMAL PATCHES IN PSYCHIATRY:

Understanding how the use of TDS patches may alter the treatment paradigm for patients is important. The effectiveness of patches in the treatment of illnesses that have a chronic pattern compared with those with an acute presentation is yet to be elucidated. The effects of regional blood flow and permeability of skin, dose rate in economically driven health markets, and the cost of prescribed treatment is almost always debated.

There are cost implications for developing transdermal formulations, such as the patented design and technology. Patches are more expensive compared with the parent oral drug: the primary care cost of rivastigmine (Exelon) 4.6 mg patches is combination treatment with patches and tablets, cumulative effects of long-term TDS use and drug interactions are yet to be fully understood. There are identifiable gaps in the literature on legal and ethical implications of use of transdermal patches in specific scenarios when limited capacity or lack of capacity to consent to treatment and issues around vulnerability can be an issue. Twice as expensive compared with 4.5 mg of rivastigmine capsules [Joint Formulary Committee, 2011].

Biological Properties:

- Drug should be very potent, i.e. it should be effective in few mg/day
- The drug should have short biological half-life. The drug should not be irritant and non-allergic to human skin. The drug should be stable when contact with the skin.
- They should not stimulate an immune reaction to the skin.

- Tolerance to the drug must not develop under near zero order release profile of transdermal delivery.
- Dose is less than 50 mg per day, and ideally less than 10 mg per day.
- The drug should not get irreversibly bound in the subcutaneous tissue.
- The drug should not get extensively metabolized in the skin.

Antischaemics:

a) Isosorbide dinitrate:

Bioavailability, when administered by conventional route varies significantly; the drug has a short half-life 50 minutes \pm 25 minutes. Demanding frequent administration & prescribed dosage regimen is 2.5- 10 mg every 2 to 3 hrs from TDDS route. A flux of 4.01 mg/hr is necessary to achieve the level of clinical efficiency of maintenance therapy.

b) Verapamil hydrochloride:

It is a calcium ion influx inhibitor. It is widely used in the treatment of angina, hypertension, and supraventricular tachyarrhythmia.

Antihypertensive:

a) Clonidine:

Is a centrally acting antihypertensive drug having plasma half-life of 8-12 h and peak concentration occurs in 2-4 h. It effectively reduces blood pressure in patients with mild-to-moderate hypertension. When transdermal therapy was compared with oral delivery of clonidine, efficacy was similar for the two delivery modalities. However, side effects such as drowsiness and dry mouth occurred less frequently in patients treated with transdermal clonidine

b) Timolol maleate:

a beta adrenoceptor blocking agent used in treatment of cardiovascular diseases like myocardial infarction, angina pectoris and hypertension.

5 CONCLUSION

The advance state of research & patent application filed for TDDS clearly indicates the renewed interest of pharmaceutical industry. By knowing different antihypertensive, hypoglycemic, anti-schaemic, opioids drugs revealed that transdermal route can improve the bioavailability and patient compliance by many ways. Only demerit is that all the drugs cannot be given by transdermal due to its physicochemical properties which should be suited for permeation through skin. Researcher exploring the sophisticated techniques of permeation enhancer like use of electron beam radiation in development of transdermal delivery has opened newer approaches.

There is hope that the drugs which have been poor candidates would be developed in to successful transdermal delivery system in upcoming days.

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