

A Review on Transdermal Drug Delivery System, Which is a Current Trends and Future Perspectives on the Treatment on Migraine

Manichandra Das¹, Jyotirmoy Bondyopadhyay²

¹Assistant Professor of Pharmaceutics, Hooghly B. C. Roy Institute (D. Pharm College), WBSCTVESD, West Bengal, India
Corresponding author Email ID: [dasmanichandra6\[at\]gmail.com](mailto:dasmanichandra6[at]gmail.com)

²Assistant Professor of Pharmacology, Hooghly B. C. Roy Institute (D. Pharm College), WBSCTVESD, West Bengal, India
Email ID: [jbondyopadhyay\[at\]gmail.com](mailto:jbondyopadhyay[at]gmail.com)

Abstract: *Migraine is very well - known disease which causes many serious complications in case of human beings. Most of the people does not know about the difference in normal headache and migraine outbreak. There are various drug delivery systems to treat migraine like Oral, Parenteral, Nasal drug delivery systems etc, which have many drawbacks also. In case of TDDS (Transdermal drug delivery systems), transdermal patches have various advantages including avoidance of first - pass metabolism, controlled and sustained drug delivery through skin. Various drugs like Triptans are very useful for the treatment of migraine. Iontophoresis, Microneedle technique etc are the techniques for treating migraine through the skin. Skin is very efficient route for treating migraine which has good patient compliance also. Now - a - days, various research is continuing for prepare more effective transdermal patches, which will be useful for treating various diseases.*

Keywords: TDDS, Skin, Migraine, Headache, Triptan

1. Introduction

The most prevalent illness in the world, migraine affects over 39 million people in the US and one billion people worldwide. Inability to work or function normally is a problem for more than 90% of migraineurs because of the excruciating head pain and other neurological symptoms like nausea, vomiting, and increased sensitivity to light and sound. According to numerous international studies using the International Headache Society's analytical standards, migraine is a well - known but rarely diagnosed neurological condition that affects roughly 6% of men and 15%–18% of women in the general population [1]. According to research, migraine is the third most prevalent ailment worldwide and the eighth most common devastating disorder [2]. Unfortunately, we have limited understanding of the pathogenesis of this illness [3]. 90% of those who suffer from migraines agree that it is a more serious disease than most people think, and that many people don't know the difference between a migraine and a headache. Patients with migraines were also asked to discuss their approaches to the sickness, which revealed their perception that their circumstance is not fully understood. Suicide appears to occur more frequently in migraineurs than in the general population [4]. One of the main symptoms of a migraine is a moderate to severe headache that is accompanied by other symptoms of acute illness and neuro - autonomic disease, such as graphic or other types of complexion, digestive balance, deprived absorption after the small bowel, sickness, vomiting, dizziness that worsens with movement, photophobia, and Sinophobia. The most frequently cited reason for not seeking a treatment was that it was just a regular headache, however a small percentage of migraineurs have expressed concern that doctors would not be able to adequately treat them or that they would have an extremely unpleasant encounter with them.

The third most common primary disorder in the globe and the seventh most severe and debilitating illness in the community are both migraines. However, we only have a fragmentary understanding of the pathophysiology of the disease [3]. Over 90% of migraine sufferers agree with the assertions that migraine is a more acute sickness than most people realise, and that many others are unaware of the differences between migraine disorder and a regular headache. A migraine is a type of headache disorder that primarily affects the head. It can range in severity from mild to severe and is frequently accompanied by other symptoms like vomiting, nausea, illness, dizziness that gets worse with movement, photophobia, sonophobia, severe disability, or other types of nature.

Human civilizations have used chemicals as cosmetic and therapeutic agents on the skin for thousands of years. However, it was not until the twentieth century that the skin came to be used as a drug delivery route [5]. The transdermal patch or skin patch, which delivers a particular amount of medication to the systemic circulation, is another name for a transdermal drug delivery device. It is an adhesive patch with medication. When medicinal chemicals are administered through the human skin for systemic effects, consideration must be given to the skin's morphological, biophysical, and physicochemical characteristics [6]. Scopolamine transdermal patch is the first transdermal patch that the FDA approved in 1981. Scopolamine is delivered transdermally to prevent motion sickness (TransdermScop, ALZA Corp.), and nitroglycerin is delivered transdermally to prevent angina pectoris related to coronary artery disease (Transderm Nitro). Transdermal drug delivery products give therapeutic benefit to patients.

In order to improve the therapeutic efficiency of the

treatment and lessen its negative effects, transdermal patches transfer the medication via the skin in a controlled and predetermined manner. It delivers the drug via skin portal to systemic circulation at a predetermined rate over a prolonged period with a specific amount of dose. Several biological, physiological, pharmacological, and biophysical aspects affect how well a transdermal patch works. The stratum corneum's thickness, integrity, and composition all play a role in this. Diffusivity can be determined by looking at the molecule's size and structure. It depends on the permeability of the membrane in the transdermal drug delivery system, state of skin hydration pH and other physiochemical drug properties.

Lipophilicity of the drug, degree of partitioning of the drug and associated components are also essential. Presently this method of drug delivery has the most potential than other

routes of administration because it avoids problems like gastric irritation, metabolic variation and due to the presence of food certain food drug interactions may happen. Those who are unconscious can also benefit from this delivery mechanism. It has some restrictions on the use of low dosage medications, slow penetration rates, and a lack of dosage flexibility. Its main advantage is that it avoids first - pass metabolism. [7]

Mechanism of Action of Transdermal Drug Delivery (TDDS):

At first, drug penetrates through the stratum corneum layer of the skin. Then passes through the deeper epidermis and dermis layers without drug accumulation in the dermal layer. After reaches the drug in dermal layer, it goes to systemic circulation via dermal microcirculation.

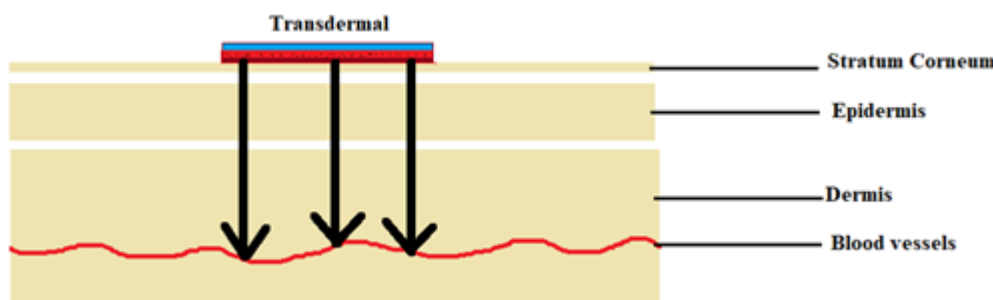


Figure 1: Mechanism of action of TDDS [6]

Advantages of TDDS in case migraine treatment:

The transdermal method provides an expansive and diverse surface in addition to being simple to apply. TDDS (Transdermal drug delivery systems), transdermal patches have various advantages and also including avoidance of first - pass metabolism, controlled and sustained drug delivery through skin. There are limitations for this type of delivery since molecules with molecular weight greater than 1kDa are unable to cross the stratum corneum. First - line treatments for moderate to severe migraines, triptans are available as oral pills, nasal sprays, and injections.

The restrictions imposed by each of these administration methods vary. The most popular method of treating migraines, oral medications, are slowly absorbed by the body, causing delayed symptom relief. Although nasal sprays may provide speedier relief, the nasal route has a small surface area, and the rapid mucociliary clearance and drainage into the oesophagus may lead to greatly varied absorption. Although the medication is sprayed into the nose, a sizable portion is eaten and then absorbed by the body, which can cause gastroparesis, a prevalent symptom among migraineurs. The pulmonary route provides a sizable and highly vascularized mucosal surface for drug absorption, but access with the inhalers that are currently on the market is limited and can be further complicated by patient self - administration variability.

The most efficient delivery method is injection. However, this approach has problems, such as pain, stigma attached to giving shots in public, and needle anxiety. According to research, migraine treatment is a race against time. A patient is more likely to benefit fully from a medicine if it is

administered quickly. Although migraine is not life - threatening, it is severely debilitating and reduces the quality of life of those who suffer from this disease. [8]

General medication for various types of migraine attack (acute, moderate, emergency and vomiting condition):

Table 1: Medications for various types of migraine attack [9]

• In case of Vomiting/Nausea:	Metoclopramide or Domperidone
• Drugs used for severe migraine attack:	Analgesics, ASA, Diclofenac
• Drugs used for moderate migraine attack:	Sumatriptan, Zolmitriptan, Frovatriptan
• Emergency drugs for migraine attack:	Metoclopramide, Lysine acetylsalicylate

Mechanism of Action of Drug:

Triptans used for migraine relief. Triptans are a class of medications that are selective serotonin receptor agonists, meaning they work by stimulating serotonin (5 - HT), a neurotransmitter (NT) found in the brain. Triptans are often used in treating migraine because they reduce inflammation, constrict blood vessels and block pain pathways in the brain. [8]

Techniques for Drug Delivery:

Iontophoresis: Drug is applied to the skin beneath the active electrode in iontophoretic delivery systems, and a current of around 0.5 mA is transmitted between the two electrodes to

efficiently repel the drug away from the active electrode and into the skin.

An iontophoretic device is worn on the skin and may consist of an anode electrode (+) in a reservoir containing positively charged drug in solution, a cathode electrode (-) in a

reservoir containing a negatively charged salt solution, an electronic device to control a mild electrical current, and a power supply (FIG.2). Once applied, the electrical current carries the positively charged drug molecules from the patch into the skin and across the stratum corneum, where it is rapidly absorbed and distributed systemically. [10]

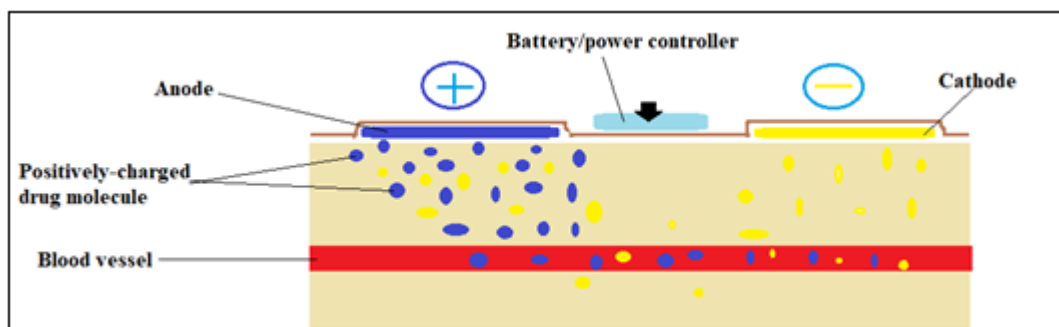


Figure 2: Schematic of iontophoresis. [10]

Microneedle Technique:

When the patch is applied to the skin, microneedles coated with drug physically break the stratum corneum and penetrate the epidermis/dermis, where the dry drug coating is dissolved by the drug is directly injected into the bloodstream through the interstitial fluid of the skin. Clinical results to date demonstrate its potential to provide positive symptom relief to patients with migraine. [10]

2. Literature Review

Ajina. C. T, et al. found that Transdermal patches deliver the drug through the skin in a controlled and predetermined manner in order to increase the therapeutic efficacy of drug. Rizatriptan a 2nd generation triptan that has a favourable tolerability profile and patients have reported greater satisfaction. The drug - containing transdermal patch was created using various polymeric ratios and plasticizer concentrations. The solvent casting procedure was used to create the patch. Ethanol and propylene glycol were employed as the plasticizers and casting solvents, respectively. HPMC, PVP, and EC were the polymers employed. The manufactured patches' physicochemical analysis was examined. The improved formulation's released kinetics follow first order. It can be concluded that it is possible to fabricate a transdermal delivery of Rizatriptan for treatment migraine where the patient acceptance and tolerability profile is high. [11] [15] [16]

C. Balaguer - ferna' ndez et al. found that Sumatriptan transdermal systems with various polymer compositions, including methyl cellulose (MC), polyvinyl pyrrolidone (PVP), and a combination of polyvinyl pyrrolidone (PVP) and polyvinyl alcohol (PVA), have been effectively developed. The systems included an occlusive liner, methacrylate copolymer as an adhesive, 1, 2 - propilenglycol (MC) or sorbitol as a plasticizer (PVP and PVP - PVA). Azone® (5%, w/w) was incorporated into all the systems as a percutaneous enhancer. When dried, transdermal systems are clear, non - adhesive, and thin. The systems created were used to study how sumatriptan succinate permeated through the skin of pig ears. In comparison to the PVP and PVP - PVA formulations, the formulation containing the MC

polymer resulted in a statistically significant increase ($p < 0.05$). The sumatriptan flow values of all three transdermal systems increased when Azone® was added to the system compared to the controls ($p < 0.05$). In addition, the application of iontophoresis to the wet methyl cellulose - Azone® formulation produced a much higher increase of sumatriptan transdermal flux. [12] [14] [18]

Chao Liu et al. found that zolmitriptan could be administered transdermally through drug - in - adhesive type TDDS. With the help of Azone, a sufficient amount of zolmitriptan could be delivered into the blood in a short amount of time, as evidenced by the absolute bioavailability of 63%, MRT0 - t of 5.740.83 h, and Tmax of 1.631.11 h. The ease of use of the drug - in - adhesive patch without any irritation phenomenon would also increase migraineurs' compliance. So, development of an effective transdermal drug delivery system for zolmitriptan may be a feasible strategy for the treatment of migraine.

[13] [17] [20]

3. Conclusion

Transdermal drug delivery system is an important and established route which is easy to apply and very affordable. This route has various advantages than other traditional routes including avoidance of the gastrointestinal tract, controlled and sustained release delivery. In case of the treatment of migraine skin considered as a safest port for administration of drug with continuous drug release. So, it is possible to fabricate a transdermal delivery for migraine with high patient acceptance and tolerability profile. [17] [19]

4. Future Scope

In future days, there should be more study and research on this transdermal drug delivery system for the treatment of various kind of disease and this will be very much helpful for our mankind.

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Author Profile



Miss Manichandra Das is a Good scholar and she holds a good academic record in her studies. She has done her Bachelor degree in Pharmacy at Bengal School of Technology, Chuchura, West Bengal, with very well academic record and after that she got her Master's degree in Pharmacy with the specialisation on Pharmaceutics. Presently she is an academician and she is doing her job very attentively in Hooghly B. C. Roy Institute (D. Pharm) college which is situated in Hooghly, West Bengal.



Mr. Jyotirmoy Bondyopadhyay has done his Graduation and Masters in Pharmacy at Bengal School of Technology which is situated in Chuchura, West Bengal. He has done his master's degree with Specialisation in Pharmacology. At present he is working as an academician in Hooghly B. C. Roy Institute (D. Pharm) college which situated in Hooghly, West Bengal. He already wrote different review and research articles as his previous work.