



FORMULATION AND EVALUATION OF TRANSDERMAL PATCH FOR PAIN MANEGEMENT

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1. ABSTRACT

Pharmacotherapy is a major component of the multimodal comprehensive treatment of pain. The degree and kind of the patient's pain, together with their age and any other medical conditions, all influence how well an analgesic works, including how much is prescribed and how it is administered. This study aims to provide doctors, nurses, pharmacists, and other healthcare professionals who work with patients who are in pain with the most recent information on analgesics applied topically and transdermally. Analgesics applied topically or transdermally function via many pathways. Transdermal opioid administration causes the absorption of opioids into subcutaneous tissue vessels, which then transport the opioids on receptors (opioids) throughout the peripheral and central nervous systems via the blood. When administered topically, non-steroid anti-inflammation medications produce analgesic effect primarily by supplying local anti-inflammatory effects and high concentration in joints assembly. Drugs applied topically, such as creams containing antidepressants (doxepin, amitriptyline), capsaicin in cream, EMLA cream, lidocaine and capsaicin in patches, and capsaicin in cream, primarily operate nearby in tissue over receptors, ion channel. There are certain benefits to applying topical and transdermal analgesics as opposed to systemic medication. Since topical analgesics alleviate local pain with little to no systemic side effects, they have a far better adverse effect profile. In addition to the benefits listed above, the transdermal method offers a prolonged analgesic period and may be more suitable, especially beneficial for patients who cannot ingest

medications by oral route. Topical or transdermal opioids carry a lower risk of addiction compared to those administered orally or intravenously.

keywords: pharmacotherapy, multimodal comprehensive treatment, pain management, analgesics, topical application, transdermal administration, opioid absorption, subcutaneous tissue vessels, opioid receptors, central nervous system, peripheral nervous system, non-steroidal anti-inflammatory drugs (NSAIDs), local anti-inflammatory effects, joint structures, antidepressants, capsaicin, EMLA cream, lidocaine, ion channels, systemic side effects.

2. INTRODUCTION

Transdermal drug delivery, often known as patches, is a non-invasive method of administering pharmaceuticals to the skin surface. It could serve as a substitute for oral administration and hypodermic injection. This drug delivery system delivers analgesics to the skin at a predefined rate, resulting in either systemic or local effects.

Transdermal patches are not a new idea. In 1979, scopolamine was licensed in the US for systemically distributed and treat motion sickness by a three-day patch. Transdermal medications gained popularity after the breakthrough of nicotine patches a decade ago [1].

Transdermal patches offer several advantages over oral and hypodermic injections. It improves biocompatibility in first-pass hepatic metabolism. Advantages of patch-based drug administration include more flexibility, painless application, and a one-week treatment duration.

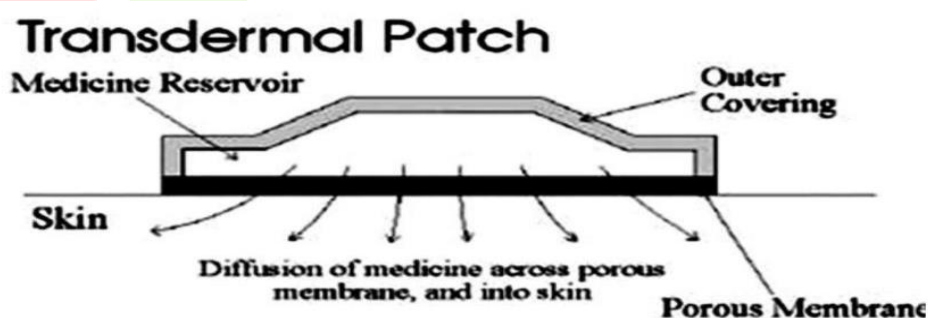


Fig. 1 diffusion of drug across porous membrane of skin

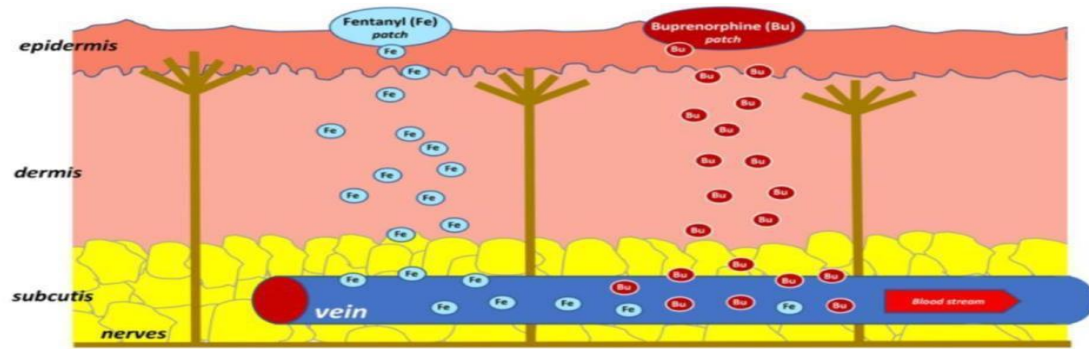


Fig.2 drug component observed by skin

2.1. Transdermal patch type

- a) **One-layer medication within an adhesive.:** This type has the drug contained in the adhesive layer. In addition to holding the several layers together, the adhesive layer is in charge of delivering the medication onto the skin.
 - b) **Multi-layer medication within an adhesive:** This kind resembles a solo film version as well, but it has two layers: one for immediate drug release and the other for controlled release in addition to the adhesive layer.
 - c) **Vapour Patch:** Frequently used to release essential oils for decongestant purposes. Here is a numerous other kinds of vapor patch available in the market intended to lessen the symptoms associated with cigarette smoking and enhance the quality of sleep.
 - d) **Reservoir system:** Only rate-regulating film, that can be a nonporous or microporous, allows the medication to be released. The drug may be available as gel in the reservoir compartment, solution, or disseminated across a solid polymer matrix. [11]
- e) **Matrix system**
1. Drug-in-adhesive system
 2. Dispersion matrix system
- f) **Micro-reservoir system:** This kind of system in drug delivery combines matrix dispersion system with a reservoir. This unstable thermodynamically dispersion rapidly stabilises the polymer by cross-link in in-situ as soon as possible employing linking agents

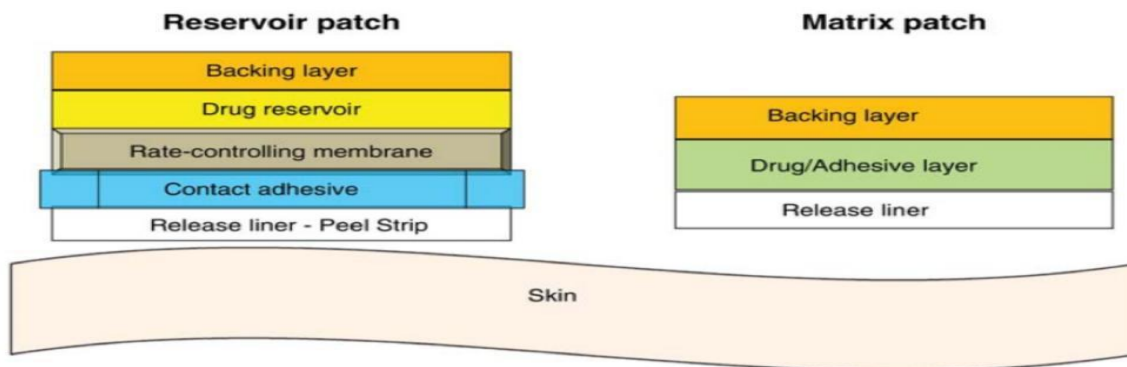


Fig. 3 different type of transdermal patch

- **Procedure for preparing transdermal patches:**

- Methods for preparing transdermal patches:
- Asymmetric TPX membrane approach
- Circular Teflon mold technique
- EVAC membrane procedure
- Mercury substrate method
- Solvent casting technique
- Aluminum-backed adhesive film process
- Solvent evaporation procedure

2.2. Evaluation Parameter for transdermal patches:

(A) Physical Evaluation (22)

- Uniformity of Drug content
- Folding endurance
- Thickness of Patches
- Moisture Lost (23)
- Moisture Gain
- Tensile strength
- Drug carrier Interaction (24)

(B) In vitro method

- In vitro study of Transdermal Patch through Franz diffusion cell.
- Kinetics of drug release

3. Method and procedure

- Spherical teflon mould method
- EVAC film approach
- Solvent casting approach
- Aluminium backed adhesive film method
- Solvent evaporation method

3.1. Circular Teflon method

Organic solvents use polymer solutions in varying ratios. To dissolve the calculated amount of medicine, Utilize fifty percent of the same organic solvent.

In the remaining portion of the organic solvent enhancers are dissolved and introduced at varying concentrations. Di-N butyl phthalate is used in the drug polymer solution as a plasticizer. Before transferring the mixture to a circular Teflon mould 12 hours of stirring is done. The moulds are placed on a flat surface and cover with an inverted funnel with an air speed of 0.5 m/s to control solvent vaporisation in a laminar flow. Evaporation of solvent occurs after 24 hours and to prevent ageing effects, dry films should be stored at 250.5°C with silica gel in a desiccator for a further 24 hours before evaluation., Films must be evaluated within one week of preparation. [10].

3.2. EVAC membrane method

To make a patch that delivers medicine through the skin, you can use a 1% carbopol gel along with polyethylene (PE) and ethylene vinyl acetate copolymer (EVAC) membranes to control how fast the medicine gets released. Propylene glycol helps dissolve medicines that don't dissolve in water. You mix the medicine with propylene glycol, then add carbopol resin and neutralize it with a 5% sodium hydroxide solution. The medicine, now in gel form, is put on a layer that covers a specific area of skin. To make sure it doesn't leak, you cover the gel with a membrane that controls the release rate and seal the edges with heat.

3.3. Aluminium backed adhesive film method

If the initial dose is more than 10 mg, the skin patch for delivering medicine might not stay stable. Using an aluminum-backed adhesive film can help in this case. Chloroform works well for this because it can dissolve most medicines and adhesives. First, the medicine is dissolved in chloroform, and then other substances are added and dissolved together with the medicine. A special aluminum mold is prepared, lined with foil, and sealed at the ends with tight cork blocks. [16]

3.4. Solvent evaporation method

Materials and Ingredients:

Active Pharmaceutical Ingredient (API): The drug that will be delivered through the transdermal patch.

Polymeric Matrix: A biocompatible and biodegradable polymer that will form the backbone of the patch.

Solvent: A suitable solvent to dissolve the polymer and other excipients.

Plasticizer: To improve the flexibility of the patch.

Permeation Enhancers (Optional): Substances that enhance drug penetration through the skin.

Backing Material: Provides structural support to the patch.

Release Liner: It is removed before application and during storage protects the patch from any damage.

3.5. Procedure:

- a) Choose a polymer or a combination of polymers based on the drug's properties, the desired release profile, and skin compatibility.
- b) Preparation of Drug-Polymer Solution
- c) Dissolve the API and polymer(s) in an appropriate solvent to form a homogeneous solution. Use a magnetic stirrer or other mixing techniques to ensure uniform dispersion.
- d) Addition of Plasticizer (if needed)
- e) If the polymer is rigid, a plasticizer may be added to improve flexibility. Common plasticizers include glycerol, propylene glycol, or polyethylene glycol.
- f) Incorporation of Permeation Enhancers (if desired):
- g) Add permeation enhancers if needed to improve drug absorption through the skin. Examples include azone, menthol, or fatty acids.
- h) Casting or Coating
- i) Pour the drug-polymer solution onto a flat surface, such as a glass mold, to create a thin, uniform film. The thickness of the film will determine the drug release rate.
- j) Solvent Evaporation
- k) Allow the solvent to evaporate, leaving behind a solid film. This can be achieved by air-drying or using controlled temperature conditions.

l) Cutting and Assembly

m) Cut the dried film into the desired shape and size for the transdermal patch. Attach the film to a backing material, ensuring a sealed edge.

n) Application of Release Liner

o) Attach a release liner to cover the adhesive side of the patch, protecting it during storage.

p) Quality Control

q) Perform quality control tests to ensure the patch meets specifications for thickness, drug content, and adhesive properties.

4. Future Aspect

As long as design advancements are made, transdermal analgesic administration is expected to gain more and more traction. Research is underway to make medicines work better and safer. This includes making sure the medication spreads more evenly and lasts longer in the body. Also, they're trying to make using patches easier and more comfortable for the people wearing them.

Improved transdermal technology, which boost drug flux uses mechanical energy through the skin by changing the skin barrier or by raising drug molecule's energy, is a new possible enhancement.

An effective creation of patches using iontophoresis or any other transdermal technology is being researched for diverse treatments. This consists of Sonophoresis that uses electrical pulses of relatively high-voltage to produce temporary aqueous holes in the skin and electroporation.

Thermal energy which use heat and raise energy of drug molecules and make the skin more permeable and disrupt the stratum corneum by low-frequency ultrasonic energy. Use of magnetophoresis, has been studied as a way to improve medication flow through the skin.

5. Conclusion:

The pathophysiology of pain and its management have been the subject of ongoing research and development. Analgesics can be administered orally, sublingually, buccally, intrathecal, transdermally, subcutaneously, intravenously, intramuscularly, rectally, intramedullary, and topically. Despite the fact that parenteral and oral analgesics are the primary means of treating pain in most patients, a growing body of research, supported by well-established clinical trials, suggests that locally administered medications may be at least as effective as oral ones [20]. Because topical medications are intended to alleviate localized pain with little to no systemic effects, they got far better profile for adverse effects when administered via this method. This is particularly applicable to medication classes when systemic absorption is minimal. When

compared to oral and parenteral methods of administering opioid analgesics, transdermal and topical administration is also linked to a decreased risk of addiction.

It is important to keep in mind that certain medications can be applied topically to provide basic pain relief [21]. Analgesics that is topically applied on skin are: NSAIDs, opioids, medications that act locally via receptors and/or ion channels, such as 8% capsaicin, EMLA cream, 5% lidocaine, cannabinoids, nitrates, tricyclics, and α -2 agonists.

Transdermal administration of opioids is a non-invasive and practical technique for pain relief that is particularly recommended for individuals with gastrointestinal tract abnormalities and stable pain syndromes.

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