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Original Article

Transdermal Drug Delivery Using Anticancer Transdermal Patches

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ABSTRACT

Transdermal drug delivery system is an essential part of novel drug distribution system. The topically administered medications in the form of patches which when applied to the skin deliver the drug .For operative TDDS the drug are easily able to penetrate the skin and easily reach the target site. TDDS avoids the first pass metabolism, less frequency of administration, reduction gastrointestinal side effects. The TDDS review articles provide valuable information regarding the transdermal drug delivery systems and its evaluation process details as a ready reference for the research scientist who is involved in TDDS. Transdermal patch is a transdermal delivery system that can overcome problems in conventional drug administration, such as oral drug administration. Patches can provide controlled drug release and have advantages over oral administration, such as avoiding first-pass metabolism, increasing drug bioavailability, avoiding adverse effects on the gastrointestinal (GI) tract, minimizing patient variability, maintaining a constant drug in plasma, and providing a stable therapeutic effect. The effectiveness of a patch is determined by the drug's ability to release from the patch matrix and penetrate the stratum cornea. The methods used to make the patches are divided into single layer, multi-layer, reservoir system, and matrix system patches. The basic components of a patch are polymer matrix membrane, drug, permeation enhancer, pressure-sensitive adhesives, backing film, release liner, and plasticizer.

Keywords: Cancer, Human Skin, Permeation, transdermal drug delivery, patch, controlled drug release

INTRODUCTION

Cancer is one of the main health is use globally it is defined by unrestricted proliferation and multiplication of aberrant cells. The treatment of cancer depends on the tumor type, stage, and site may involve surgery, radiotherapy, chemotherapy, targeted therapy, immunotherapy or a combination of these approaches. Among them, chemotherapy is commonly employed since anticancer medication may prevent or kill cancer cells that divide quickly. However, conventional chemotherapy given orally or by injection might have systemic side effects. In addition, treatment efficacy and patient compliance can be impacted by factor such as frequent dosing, gastrointestinal issue, inconsistent drug absorption, and hepatic first pass metabolism.

Transdermal drug delivery systems (TDDS), often called patches, offer a unique way to administer medications through the skin. These patches are designed to effectively deliver therapeutic amounts of drug into the bloodstream, allowing for efficient treatment and prevention of various health conditions [1].

A transdermal patch is a medicated adhesive that sticks to the skin, releasing precise doses of medication, which can also aid in healing targeted areas. Compared to oral, intravenous, subcutaneous, or trans mucosal methods, this delivery route provides more consistent drug levels and reduces side effects, overcoming challenges linked with traditional pills or injections. Transdermal systems are ideal for conditions that need long-term, frequent dosing, as they are less invasive, pain-free, and can be used independently by patients, making them both convenient and cost-effective. These systems are tailored to deliver drugs through the epidermis or dermis, effectively managing skin-related conditions by bypassing first-pass metabolism and allowing controlled release over time. [1]

The primary aim is to achieve a steady and predictable drug release rate, reducing patient-to-patient variability. Historically, early transdermal systems used drug-

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

infused patches with natural adhesives to help drugs absorb through the skin. This review highlights recent progress in developing chemical permeation enhancers and carriers, such as gels, emulsions, and vesicular system that improve the effectiveness of transdermal drug delivery. [1]

1. Advantages of TDDs

- It allows for a continuous and stable release of medication over a prolonged period, minimizing the chance of side effects and treatment failures that can occur with intermittent dosing.
- These systems enable patients to administer the medication on their own.
- Transdermal delivery prevents the variations in drug levels that occur with peak and trough cycles, permitting extended and less frequent dosing.
- It provides a quicker and more convenient way to administer medication.
- The rate of absorption can be managed through a layered design.
- Patients are more likely to follow their treatment plans, as they are not required to take multiple doses daily.
- This method allows patients to take control of their medication management independently.[1]

2. Disadvantages of TDDs

- For a drug to be suitable for transdermal delivery, it needs certain physicochemical characteristics to penetrate the stratum cornea. If the required dose is over 10 mg daily, effective transdermal delivery can become difficult.
- At present, only small, lipophilic drugs can be effectively transported through the skin.
- Transdermal administration offers extended drug release, but it can be costly due to the complex formulations involved.
- Drugs with low solubility, limited stability, short half-lives, or sensitivity to oxidation and hydrolysis present challenges, adding to manufacturing costs.
- There are limitations in the amount of medication that transdermal systems can carry.
- Transdermal delivery might result in lower drug levels in the bloodstream due to variations in skin barrier function, which can be influence by factors like skin location and patient age.[1]

Skin Structure

Indeed, the skin is the body's largest organ, acting as a crucial protective barrier safeguarding the body from a range of external factors and potential threats. Its large surface area, approximately 1.7 square meters in an average person, allows it to effectively shield the body from microorganisms, ultraviolet (UV) radiation, chemicals, allergens, and water loss. This protective function is vital for maintaining overall health and well-being. Additionally, the skin also plays a role in regulating body temperature, sensation, and the synthesis of vitamin D through exposure to sunlight. Taking care of the skin is essential to support its functions and maintain good health. [2]

The skin is commonly categorized into three primary layers:

(a) The outermost layer, known as the epidermis, (b) The middle layer, referred to as the dermis, (c) The innermost layer, called the hypodermis.

Here's a brief overview of each layer:

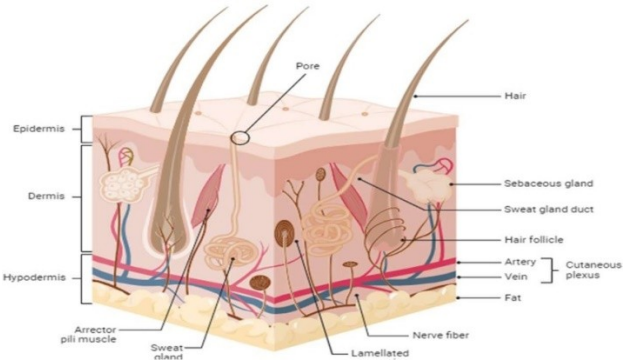

Figure 1: Different Layers of Skin

1. Epidermis

The Structure of the skin-

Epidermis constitutes the skin's outermost layer. It provides a waterproof barrier and contains no blood vessels. The cells in the epidermis include keratinocytes, which produce the protein keratin and help make the skin tough and protective. The epidermis includes melanocytes, responsible for skin color, and Langerhans cells, integral components of the immune system. [2]

The epidermis has several sub- layers, including:

Stratum cornea

Stratum granulosum

Stratum spinosum

Stratum basale

It's different thickness in different parts of our body, about 0.8 mm thick on our palms and the soles of our feet. The epidermis is made up of layers of skin cells. Most of these cells are called keratinocytes. They make up about 95% of the cells in the epidermis. The epidermis houses various cell types, including melanocytes, Langerhans cells, and Merkel cells.

On top of the epidermis, there's a super thin layer called the stratum corneum. It's the very surface of our skin and touches everything around us. This layer is special because it keeps our body safe. Its thickness and how much water it has are important. The stratum corneum is made mainly of tough proteins (70% keratin) and some fats (20% lipid). Water in this layer is connected to these proteins.

2. Dermis

The dermis is located beneath the epidermis which is 3 to 5 mm and is thicker than the epidermis. The dermis is responsible for providing nutrients to the epidermis and housing the skin's appendages and sensory receptors [2].

It comprises diverse structures, such as:

Blood vessels

Hair follicles

Sweat glands

Sebaceous glands

Nerve endings

Tiny blood vessels called capillaries are really close to the skin surface, about 0.2 mm away. These capillaries act like drains, pulling away most of the stuff that tries to get through the skin. This is essential because it keeps the concentration of substances that enter the skin very low. This difference in concentration between the inside and outside of the skin helps push things through it.

When it comes to delivering medicines through the skin, this layer is like a gel made mostly of water. For most medicines that dissolve in water, this layer doesn't offer much resistance, making it easier for the medicines to pass through. “However, if a medicine is oily (like some lotions or creams), this layer can create more of a challenge for it to get through”

3. Subcutaneous (Hypodermis) tissue

The subcutaneous tissue, also known as the hypodermis, constitutes the deepest layer of the skin, consisting of adipocytes (fat cells) and connective tissue. This layer serves as an insulator, helping to regulate body temperature and serves as a protective cushion, shielding the body's organs and bones from impacts. When medicines are applied to the skin, like creams or patches, they have to go through these three layers to get into our bloodstream. For some medicines, they need to go even deeper, reaching our body's circulation but for most skin treatments, they just need to get through the outermost layer, the stratum corneum, and stay in the skin layers to work effectively.[2]

Routes of Drug Penetration through Skin

This route is for substances that dissolve in fats (lipophilic or non-polar solutes). They travel through the continuous fatty layer of the skin. Drug penetration across the skin can occur through two routes: the Trans epidermal pathway, which involves penetration through the epidermis, and the transappendegeal pathway, which involves penetration through appendages such as hair follicles and sweat glands [2, 3, 4].

Trans epidermal Pathway: In this pathway, drugs permeate through the skin's outermost layer, known as the stratum corneum. This layer is a structurally complex, multi-layered, and multi-cellular barrier.

Intra-cellular Route: Some drugs can go through specific skin cells called coenocytes, which are specialized skin cells. This route is for substances that dissolve in water (hydrophilic or polar solutes).

Inter-cellular Route: Other drugs can move through the spaces between these skin cells

Tran’s appendegeal Pathway: This pathway involves drugs passing through sweat glands and hair follicles into the skin.

Sweat Glands and Hair Follicles: These are like tiny tunnels or openings in the skin that some substances can travel through.

So, when drugs need to get into our body through the skin, they can either go through the outer layer of skin cells or use these tiny tunnels created by sweat glands

and hair follicles. Each pathway has specific characteristics, allowing different types of substances to enter the body.

Penetration Enhancers

Penetration enhancers, also referred to as permeation enhancers or skin penetration enhancers, are substances employed to enhance the permeability of active compounds, such as drugs, through the skin. They function by temporarily modifying the structure and properties of the stratum corneum, the skin's outermost layer. This alteration allows for better penetration of the active ingredients into the bloodstream or deeper layers of the skin, enhancing the effectiveness of topical medications. [2, 3, 4]

Table 1: Classification of Penetration Enhancers and Techniques [2, 3]

Types of penetration enhancers	Examples
1.chemical enhancers	1. azones 2. cyclodextrins 3. pyrrolidones 4. amine and amides: urea 5. fattyacids: lauric acid, capric acid and myristic acid 6.oxizolidinones(4- decycloxazolidine-2-one) 7. surface active agents: sls, benzalkonium chloride
2. Drug Vehicle Based	1. Ion pairs and complex coacervates chemical potential adjustment.
3. Natural Penetration enhancers	1. Terpenes: Menthol, Linalool, Limonene, Carvacrol. 2. Essential oil: Basil oil, Ylang- Ylang, Neem oil, Eucalyptus, Chenopodium.
4. Physical Enhancers	1. Radiofrequency 2. Sonophoresis 3. Needleless injection 4. Magnetophoresis 5. Electroporation 6. Phonophoresis
5.Biochemical Approach	1. Synthesis of bio-convertible prodrugs Co-administration of skin metabolite Inhibitors

BASIC PRINCIPLE OF TRANSDERMAL PERMEATION

The transdermal permeation theory is to deliver a drug into the bloodstream via the skin instead of injecting it or taking it in the form of tablets. The drug is typically applied to the skin via a transdermal patch, which releases the drug slowly over a long period of time. The drug first has to permeate through the stratum corneum, the tough outer skin that keeps things out. Then it moves through the epidermis and dermis, where it reaches blood vessels and enters the bloodstream. To work effectively, the drug should be small, lipid-soluble, and stable in skin environments. This kind of treatment is ideal for drugs that must be delivered slowly over a long period of time, such as painkillers, nicotine, or hormone replacement therapy. Transdermal permeation bypasses the digestive system, bypasses the breakdown of the drug in the stomach or liver, and provides a safe, convenient, and painless method of taking medication [6, 7].

Transdermal Patch

A transdermal patch, also known as a skin adhesive patch, is a device designed to administer a precise dosage of medication by placing it on the skin. This allows the drug to be delivered through the skin and into the bloodstream. The specialized membrane regulates the passage of liquid medication from the patch reservoir through the skin and into the bloodstream. Numerous patients encounter challenges swallowing tablets or receiving injections, and patches remain effective for more extended durations compared to tablets, so frequent dosing is reduced. Patches are utilized in various therapeutic areas, such as pain management, heart disease treatment, smoking cessation, motion sickness management, and hormone replacement therapy.

Basic components:-

1. Polymer

The Polymer controls the release of the drug from the device. [8, 9]

a) **Natural Polymers**: Cellulose derivatives, Zen, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.

b) **Synthetic Elastomers**: Poly butadiene, Hydrin rubber, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene butadiene rubber, Neoprene etc.

c) **Synthetic Polymers**: Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Poly acrylate, Polyamide, Poly urea, Epoxy etc.

2. Drug

For successfully developing a transdermal drug delivery system, the drug should be chosen with great care. The following are some of the desirable properties of a drug for transdermal delivery.

- Physicochemical properties

1. The drug should have a molecular weight less than approximately 1000 daltons.
2. The drug should have affinity for both – lipophilic and hydrophilic phases. Extreme partitioning characteristics are not conducive to successful drug delivery via the skin.
3. The drug should have low melting point. Along with these properties the drug should be potent, having short half- life and be nonirritating.

3. Permeation Enhancers

These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant. These may conveniently be classified under the following main headings [9].

A) Solvent

These compounds increase penetration possibly by swallowing the polar pathway and/or by fluidizing lipids.

Examples

Water alcohols: methanol and ethanol

Alkyl methyl sulfides: dimethyl sulfide

Alkyl homolog: methyl sulfide dimethyl acetamide

Pyrrolidones: 2 pyrrolidone,

Mechanism of permeation enhancer

- These are the chemical compounds that increase permeability of stratum corneum so as to attain higher therapeutic level of drug.
- Permeation enhancers interact with structural components of stratum corneum that is proteins and lipids.
- They alter protein and lipid packaging of stratum corneum thus chemically modifying barrier function leading to increased permeability.

Natural permeation enhancer eugenol:

- It is having less toxicity profile.
- Irritation is not produced.

b) Surfactants

These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs. The ability of a surfactant to alter penetration is a function of the polar head group and the hydrocarbon chain length.

- Anionic Surfactants: e.g. Dactyl sulphosuccinate, Sodium lauryl sulphate
- Nonionic Surfactants: e.g. Pluronic F127, Pluronic F68, etc.
- Bile Salts: e.g. Sodium taurocholate, Sodium deoxycholate, Sodium tauroglycocholate.

c) Miscellaneous chemicals

These include urea, a hydrating and catalytic agent; N, N-dimethyl-m-toluidine; calcium thioglycolate; anticholinergic agents. Some potential permeation enhancers have recently been described but the available data on their effectiveness sparse. These include eucalyptol, di-o-methyl-ß-cyclodextrin and soyabean casein.

4. Other excipients

a) Adhesives:

The fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face of the device or in the back of the device and extending peripherally. Both adhesive systems should fulfill the following criteria:

- Should adhere to the skin aggressively, should be easily removed. Should not leave an unwashable residue on the skin.

- Should not irritate or sensitize the skin. The face adhesive system should also fulfill the following criteria.
- Physical and chemical compatibility with the drug, excipients and enhancers of the device of which it is a part.
- Permeation of drug should not be affected.
- The delivery of simple or blended permeation enhancers should not be affected.

b) Backing membrane:

Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, and accept printing. It is impermeable substance that protects the product during use on the skin e.g. metallic plastic laminate, plastic backing with absorbent pad and occlusive base plate (aluminium foil), adhesive foam pad (flexible polyurethane) with occlusive base plate (aluminium foil disc) etc.

Desirable features for transdermal patches

- Composition relatively invariant in use.
- System size reasonable.
- Defined site for application.
- Application technique highly reproducible.
- Delivery is (typically) zero order.
- Delivery is efficient.

Types of transdermal patches

Single layer drug-in-adhesive patches

A reservoir is employed as a singular polymer layer with adhesive properties to disperse the drug. Below this single layer, an impermeable backing laminate is applied. The medication, situated within and adhering to the polymer layer, is released from the backing laminate layer, which serves as support for the drug reservoir. An illustration of a single-layer drug-in-adhesive transdermal patch is daytarana, which contains methylphenidate [10, 11].

Multilayer drug-in-adhesive patches

Drug release is controlled over a period of time consist of a drug reservoir layer and adhesive layer. It contains a temporary protective layer and backing laminate in multilayer systems. Multi-layer patches can be prolonged for up to seven days are used to deliver pain medication, smoking cessation treatments, and hormone therapy.

Vapor transdermal patches

These patches consist of a single layer of adhesive polymer designed with a vapor release feature, allowing the release of vapors. Various vapor dermal patches are available for different purposes. One example is Nicoderm CQ®, a nicotine vapor transdermal patch containing essential oils that aid in smoking cessation. Introduced to the European market in 2007, it helps individuals quit smoking by releasing these oils. Another type is altacura vapor patches, which contain essential oils and are used for decongestion purposes. Additionally, there are vapor patches available in the market designed as antidepressant medications or sedatives.

Membrane moderated transdermal reservoir patches

A transdermal patch consists of a drug reservoir, an impermeable backing layer composed of metallic plastic laminate, and a porous polymeric membrane responsible for controlling the release of the drug. This membrane is composed of polymeric materials such as ethylene vinyl acetate copolymer and hypoallergenic adhesive polymer. The drug within the transdermal patch is controlled through the molecular dispersion of the drug in a polymer matrix as part of the preparation process.

Micro reservoir transdermal patches

Micro-reservoir transdermal patches integrate a drug reservoir with matrix dispersion. The reservoir is created by suspending the drug in an aqueous solution of a hydrophilic polymer, followed by uniform dispersion of the drug suspension on a lipophilic polymer. This dispersion process involves high shear mechanical force, leading to the formation of numerous microscopic, non-leachable spheres. Drug release from these patches follows a zero-order kinetic rate, ensuring a consistent drug level in the plasma. To maintain thermodynamic stability, crosslinking polymeric agents are typically included in the drug dispersion.

Matrix system

Drug-in-adhesive system

In this system, the drug reservoir is created by mixing the drug with an adhesive polymer. The medicated adhesive polymer is then spread either by solvent casting or melting. In the case of hot melt application, un-medicated adhesive polymer layers are added on top of the medicated layer. [10]

Matrix-dispersion system

In this system, the drug is evenly distributed within a hydrophilic or lipophilic polymer matrix. This polymer disk containing the drug is affixed onto an occlusive base plate within a compartment formed by a drug-impermeable backing layer. Instead of being applied directly onto the drug reservoir, adhesive is spread around the perimeter to create an adhesive rim.

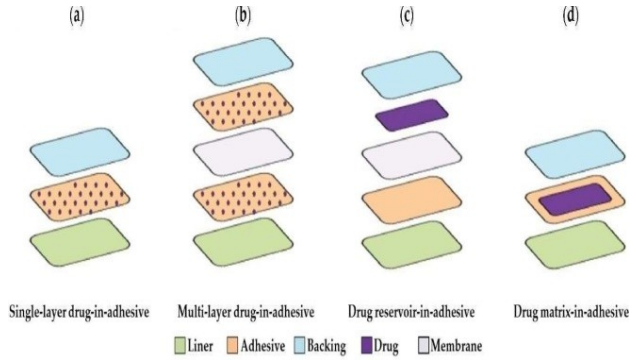

Figure 2: Types of Transdermal Patches

METHODS FOR THE PREPARATION of TRANSDERMAL DRUG DELIVERY SYSTEM

1. Solvent Casting Method

This is a common way to make patches. Here, the drug is mixed into a liquid that also has a polymer, a plasticizer, and other ingredients. This liquid is then poured onto a flat surface, like a piece of glass or a Teflon sheet. After pouring, the liquid evaporates under controlled conditions, leaving behind a thin, flexible film. Once it's dry, the film is cut to the right size and given a backing layer and a liner to help with application. This method creates even patches and helps control how thick the film is and how much drug it contains [11, 12, 13].

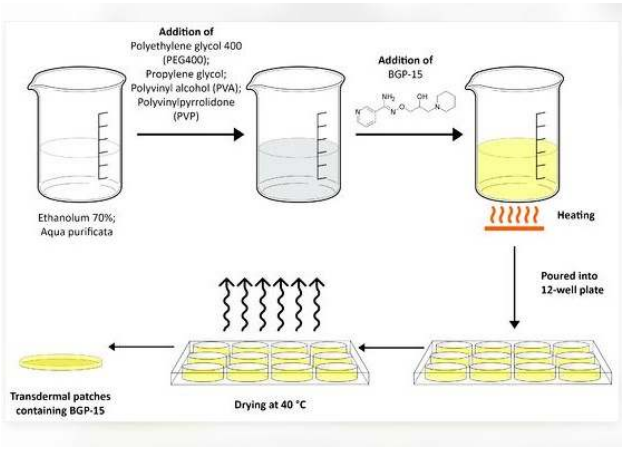

Figure 3: Solvent Casting Method

2. Hot-Melt Extrusion Method

This method doesn't use any liquid solvents and is good for drugs and polymers that can handle high heat. The drug is mixed with polymers and melted together in a machine called a hot-melt extruder. The hot mix is then made into a thin film, cooled down, and cut into patches. It's a great way to blend the drug and polymer without using harmful substances, making it gentle on the environment and good for going production [14].

3. Direct Compression Method

This method involves mixing the drug with dry ingredients like polymers, fillers, and binders. This dry mix is then pressed by a machine into a thin sheet or film. The sheet is then given a backing and sticky layers to make a complete patch. This method is fast, cost-effective, and doesn't need heat or liquids, which is useful for drugs that can't stand heat or moisture.

4. Membrane Controlled Reservior System

Here, the drug is turned into gel or liquid and stored in a reservoir. The reservoir sits between a backing layer and a membrane that controls the release of the drug. The reservoir is sealed to prevent leaks. This setup ensures a steady release of the drug over time, making it suitable for long-term treatments that need stable blood levels, like hormone or pain relief patches.

5. Matrix Dispersion Method

In this method, the drug is directly mixed with a polymer to form a solid or semi-solid structure called a matrix. This matrix is spread on to a backing layer and allowed to dry. Once the film forms, it's covered with an adhesive and liner. The drug is evenly spread

in the matrix, and when the patch is used, it slowly passes through the skin. This straight forward method doesn't require a special reservoir or membrane [14].

6. Adhesive Dispersion Method

In this approach, the drug is mixed into a pressure-sensitive adhesive that serves as both the drug holder and the sticky part that attaches to the skin. This mixture is spread on a backing layer and dried to create the patch. It's a popular method due to its simplicity and effectiveness in ensuring close contact with the skin for better absorption. It tends to be used for drugs that are needed in low doses [15].

7. Micro reservoir System

This hybrid system combines the benefits of reservoir and matrix patches. It creates tiny droplets of the drug within a gel, embedded into a polymer matrix. This allows for precise control of drug release over a longer period. The droplets are stable and evenly spread across the patch, offering both flexibility and controlled release. This system is perfect for drugs that need extended release and steady blood levels [15].

8. Multi-laminate Film Method

In this technique, multiple film layers are made separately, with each layer doing a different job, like a drug layer, a sticky layer, or a barrier layer. These layers are then joined together to form one patch with controlled drug release. The multilayer design allows for adjusting drug release, protecting the drug from outside exposure, and improving the patch's strength and flexibility.

9. Electro spraying Technique

This method is used to create super-thin films or particles. The drug-polymer mixture is charged and sprayed in a high-voltage electric field onto a surface to form a thin film. Electro spraying forms small structures and increases the surface area, helping the drug release better. Although it's more complex, it's helpful for modern patches that need to act quickly or enhance absorption [15, 16].

10. Supercritical Fluid Method

This innovative approach uses supercritical fluids like supercritical CO_2 to create films that go on the skin. These fluids work as solvents under high pressure and temperature, dissolving the drug and polymers. Then, when the pressure lowers, the fluid disappears, leaving a thin film filled with the drug. This method is environmentally friendly, doesn't leave harmful residues behind, and achieves uniform, stable drug films, making it suitable for sensitive drugs and advanced skin patch systems (Wilma et al., 2023).Recent advancements in transdermal patch technology have significantly improved drug delivery efficiency and patient compliance. Innovations such as electroporation, which uses high-voltage pulses to enhance skin permeability, and nanotechnology, which enables precise drug targeting, are transforming the field. Additionally, good materials and micro fabrication techniques are being integrated into patch designs to optimize drug absorption and minimize variability in therapeutic effects. These advancements address challenges like skin barrier limitations and inconsistent drug absorption, making transdermal patches more effective for modern drug delivery [16].

Evaluation of transdermal patches

All the prepared transdermal patches were evaluated by the following parameters [17].

Physical appearance

All the prepared patches were visually inspected for color, clarity, entrapment of any air bubble, flexibility and smoothness.

Thickness

Thickness of the patch was measured by using digital thickness gauge at 4 different ways and average thickness was determined.

Weight variation

10 patches from each formulation were weighed individually and the average weight was calculated. The individual weight should not deviate significantly from the average weight.

Drug content

A specified area 2x2 of patch was dissolved in mixture of chloroform and methanol. It was closed and shakes vigorously for 24 hours in a shaker. The resulting solution was filtered and the amount of drug present in the filtrate was determined by using UV spectrophotometer at 242 nm.

Flatness

Longitudinal strips from patches of each formulation were cut one from the center and one from the other side of patch. The length of each strip was measured and the variation in length because off the nonuniformity of flatness was measured. 0% constriction was considered to be 100% flatness. Flatness was calculated using given formulae.

% Constriction =

I1 Initial length of each strip- I2 (Cutted film length) I2 (Cutted film length) x 100

Folding endurance

Folding endurance was determined by repeatedly folding a small strip of patches (approximately 2×2 cm) at the same place till it broke. The number of times patches could be folded at the same place, without breaking gave the value off folding endurance and it was recorded.

Tensile strength

The patches were evaluated for its tensile strength to calculate their mechanical properties. It was determined by using a self-designed assembly by the following formula.

Tensile Strength =

Break Force. B (1+ ΔL/L)

Where,

a = Width of the patch, b = Thickness of the patch, L = Length off the patch,

ΔL = Elongation of patch at break point, Break Force = Weight required to break the patch (Kg)

Moisture content

The patches were accurately weighed and kept in a desiccator containing calcium chloride 24 hrs. Then the concluding weight was noted. It can be calculated by following formula

% Moisture content =

Final weight - Initial weight Initial weight x 100

Moisture uptake

Prepared patches was kept in desiccators at room temperature for 24 h with silica gel and weighed and transferred to other desiccators to expose off 75% RH using a saturated solution off sodium chloride at 25°C. The moisture uptake capacity was calculated according to the given formulae]

% Moisture uptake =

We - SWs x 100

In-vitro permeation study

The release studies from formulated patches were carried out by using Franz diffusion cell in order to determine delivery and permeation of drug from the skin in to the body.

The drug release data off all formulations were fitted to various mathematical models such as zero order as cumulative % off drug released vs. time, first order as leg cumulative % off drug remaining vs. time and Higuchi's model as cumulative % drug released vs. square root off time. To determine the mechanism off drug release from formulations, the data were fitted into Korsmeyer Pappas equation as leg cumulative % off drug released vs. Leg time.

Ex-vivo permeation study

Ex vivo permeation studies are conducted by using Franz diffusion apparatus to forecast the in vivo absorption of the drug. The rat skin was kept between the diffusion cells, with stratum corneum facing the donor compartment. The patch is applied above the stratum cornea (upper side) and a dialysis membrane was kept over the patch. The receiver phase (lower phase) was containing 24 ml of buffer stirred at 500 rpm on a magnetic stirrer.

The amount of the drug transferred was estimated by taking 5ml of the sample at graded time intervals up to 24 hrs. The absorbance was measured at 242 nm spectrophotometric ally. The graph was plotted between Cumulative amounts of drug transferred in $\mu g/cm^2$ against time.

Enhancement factor

The effectiveness of various permeation enhancers was determined by comparing drug flux in the presence and absence off each permeation enhancer, and obtained ratio was known as the enhancement factor (EF).

EF = Drug flux with enhancer Drug flux without enhancer

Skin irritation test

To determine the irritant effect or any chance off edema with the use of transdermal patches, primary skin irritancy test was evaluated according to Raise

test. Transdermal patches were applied in to the dorsal skin off albino rats which was shaved in the previous day off the study. The rats were divided into five groups (six animals in each group). The patch is to be removed after 24 hr. and the skin was observed and classified into 5 grades (0 to 4) on the basis of the severity of skin injury[17]

The scores were given for erythema from 0 to 4 depending in the degree off erythema as follows: 0 = no erythema, 1= slight erythema (barely perceptible-light pink), 2 = moderate erythema (dark pink), 3 = moderate to severe erythema (light red), 4 = severe erythema (extreme redness).

The edema scale was: 0 = nine, 1 = slight, 2 = well defined, 3 = moderate and 4 = severe.]

Stability study (As per ICH guidelines)

Stability studies off formulation were conducted according to ICH guidelines by string at 40 °C and 75% RH for 3 months. The samples were withdrawn at 30, 60 and 90 days and evaluated for physical appearance and drug contents. The ex vivo permeation study was performed after 90 days and compared with fresh batch [17].

Drug Use Are-

The medicine needs to be carefully evaluated before constructing a transdermal patch. Some ideal physicochemical and biological qualities of a drug appropriate for transdermal distribution are listed below:

1. A drug should be fewer than 1000 Daltons in molecular mass and must have a low melting point.
2. A drug should exhibit hydrophilic and lipophilic phases of affinity. Extensive partitioning properties make it difficult to administer drugs transdermal.
3. The drug must not be harsh and allergic but should be powerful with a short half-life

Example- 5-Fluorouracil (5-FU): used in treatment of skin cancer and actinic keratosis

Doxorubicin: used in treatment of breast cancer

Methotrexate: used in treatment of breast cancer and other cancer

Paclitaxel: used in treatment of breast, ovarian and lung cancer

Docetaxel: used in treatment of breast, prostate and lung cancer

Future Perspective of Anticancer Transdermal Patches

Potential Prospects for Anticancer Transdermal Patches Transdermal anticancer medication delivery is a developing field of pharmaceutical research. Overcoming the skin barrier, increasing drug delivery, reducing side effects and improving patient ease are the goals of future advancements [18].

1. Micro needle Technology: Dissolving, hollow and coated micro needles may enhance medication penetration through the stratum cornea and facilitate local delivery to accessible tumors.
2. Delivery Using Nanotechnology: Polymeric nanoparticles, liposomes, nanostructured lipid carriers, and solid lipid nanoparticles have the ability to improve the stability, solubility and delivery of drugs to certain skin tissues.
3. Focused drug delivery: Targeted strategies and tumor-responsive carriers may help to limit exposure to healthy tissues and concentrate anticancer agents at desired site.
4. Stimuli-responsive and intelligent patches: More regulated drug release may be made possible by formulations that are sensitive to pH, temperature, enzymes, or other local variables.
5. Combination therapy: While their safety and efficacy need experimental validation, patches carrying two or more compatible therapeutic drugs may offer complementary anticancer actions.
6. Biocompatible and biodegradable polymers: Novel polymer materials have the potential to improve the skin compatibility, environmental sustainability, drug release, and patch flexibility.
7. Individualized drug delivery: Precision manufacturing and 3D printing may make it possible to customize patches for certain application sites and medication requirements.
8. Regulatory development and clinical translation: Future studies must use well designed studies to demonstrate repeatable manufacture, long term stability, appropriate dosing, safety, and clinical effectiveness.

Despite these possibilities, hurdles still exist, such as the limited permeability of numerous anticancer

treatments, possible skin irritation, drug loading limits, and a lack of confidence in systemic delivery. More investigation is required as the majority of cutting-edge anticancer patch technologies are still in the experimental or preclinical stages.

CONCLUSION

Transdermal patches have transformed the delivery of medicine into the body. These patches are easy to use and do not involve injections or swallowing pills unlike taking a pill or getting an injection, the patches work by allowing the medicine to pass directly through the skin, bypassing the stomach. This means the body absorbs the medicine better and there are fewer side effects. They are especially useful for people who need regular medication or have trouble swallowing pills.

A major benefit of these patches is that they release medicine slowly over time, which helps maintain the right level of medicine in the body. This results in fewer doses being necessary. The simple application and removal of the patches make them suitable for elderly, young, and long-term patients alike.

Scientists carefully select drugs for these patches. Ideal drugs are usually small, dissolve in fats, and are very potent. Ongoing research continues to expand the range of medicines that can be delivered this way, using advancements like micro needles and other innovative methods to enhance skin absorption. There are several types of transdermal patches, such as reservoir, matrix, adhesive dispersion, and micro reservoir types. Each type uses a different technique for releasing medicine. The creation of these patches involves various methods like solvent casting and hot-melt extrusion, aiming to make them effective and safe for patients.

While these patches offer many benefits, there are some limitations. They can sometimes cause skin irritation and can only hold a limited amount of medicine. They are also suitable only for certain types of drugs that can pass through the skin easily. However, the advantages often outweigh these downsides, and ongoing innovations are helping to overcome these barriers, leading to a promising future for transdermal patches in medicine.

In conclusion, transdermal patches are an effective and user-friendly method of delivering drugs. They offer sustained release of medicine, reduce side effects, and help ensure patients follow their treatment plans. With continuous research and improvement, these patches have the potential to expand treatment options, refine drug formulations, and ultimately enhance patient care for various medical conditions.

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