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Novel Techniques in Transdermal Drug Delivery System

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ABSTRACT:

The skin provides a convenient and easily accessible location for medicine administration. In light of this, the topic of transdermal drug delivery has attracted a lot of attention and funding in the past and is still doing so now because novel and effective methods of delivering drugs through the skin are constantly being developed. For the transdermal drug delivery system to be safe, effective, and high-quality, the adhesive is essential. The topical distribution of therapeutic agents presents numerous benefits in comparison to traditional oral and invasive drug delivery techniques. Transdermal drug administration has a number of significant benefits, including limiting hepatic first pass metabolism, improving therapeutic efficacy, and preserving a constant medication plasma level.An overview of TDDS, its benefits over traditional dosage forms, drug delivery routes through human skin, penetration enhancers, different components of transdermal patches, types of transdermal patches, preparation techniques, and its physicochemical methods of evulation are given in this review article.

KEYWORDS: Transdermal Drug Delivery System, Transdermal Patches.

INTRODUCTION:

a new method of applying drugs to the skin to transfer them into the systemic circulation at a set rate. The transdermal drug delivery system, commonly referred to as "Patches," is a dosage form intended to distribute medication via the skin of the patient.[1,2] Transdermal patches are adhesive patches that are medicated. When applied to the skin, they penetrate the skin layer and release the medication into the bloodstream. They have had a major impact on a number of medicinal agents, particularly those used to treat pain and other illnesses. Since they do not involve the gastrointestinal tract, there is no loss from first pass metabolism and medication delivery that is unaffected by pH, enzymes, or gut flora.[3-6]

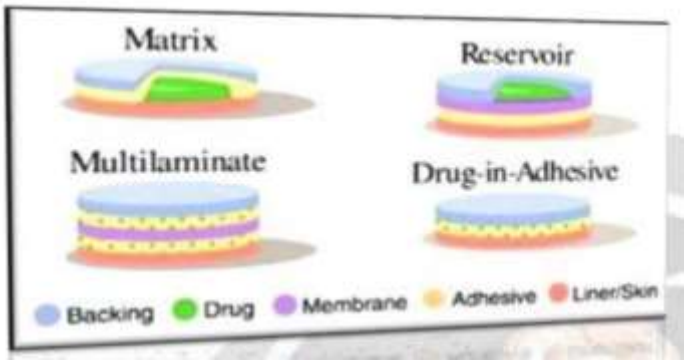
Because the patch is simple to apply, this method of drug delivery improves patient compliance while avoiding the risks and discomforts associated with parental therapy. When a medication is administered orally, its bioavailability increases along with variations in absorption.[7] As the most fruitful novel research area in drug delivery, transdermal delivery has faced competition from oral delivery. This is so that medication concentration in the body can be achieved and maintained within the therapeutic range during oral treatment. This is accomplished by administering a fixed dose at regular intervals, which increases the likelihood of side effects and causes the drug concentration in the body to follow a peak through profile.

To guarantee that drug levels don't go below the minimum effective concentration or above the maximum concentration, TDDS keeps the drug concentration within the therapeutic window for extended periods of time. However, there are some drawbacks as well. For example, some patients may get dermatitis at the application site due to one or more of the TDDS components; as a result, the treatment is stopped, and only strong medications can be used in transdermal

TYPES OF TRANSDERMAL PATCHES :

Transdermal patches were categorized into four main type[10-13]

Fig. -1 Types of transdermal patches



1. Matrix type

2. Reservoir type

3. Membrane matrix hybrid

4. Micro reservoir type

5. Drug in adhesive

- Single layer drug in adhesive
- Multilayer drug in adhesive

1. Matrix Type:

When applied to the skin, this patch is extremely thin and barely noticeable. The film controls the medication's release from the patch in this kind of device. homogeneously distributed in hydrophilic or lipophilic polymer in this kind of medication reservoir. then formed into a disc with a predetermined thickness and surface area. The produced film is taken out of the ring and placed onto the occlusive base plate within a drug-impermeable backing compartment. Next, a polymer adhesive is sprayed all the way around the film. The backing layer and adhesive layer were combined into one layer.[13]

2. Reservoir Type:It has a distinct coating of medication. The drug reservoir layer in this case is a liquid compartment filled with a drug suspension or solution, in which a drug particle is suspended in silicon fluid. It provides pastes that are separated by an adhesive layer, such as suspension, gel, or transparent solutions. Either compression or solvent evaporation is used to prepare the rate-controlling membrane. The backing layer is also a component of this patch.[13]

3. Membrane Matrix Type: It is the modified form of reservoir matrix in which the liquid form of drug reservoir is replaced with solid matrix polymer

4. Micro Reservoir Type:This type of drug suspension forms thousands of unleachable microscopic drug particles by dispersing the drug uniformly through a high shear mechanical force in a lipophilic polymer. The drug is suspended in an aqueous solution of water miscible drug solubilizer poly ethylene glycol (PEG). Cross connecting the polymer chain right away stabilises the dispersion.[13]

5. Drug in Adhesive:

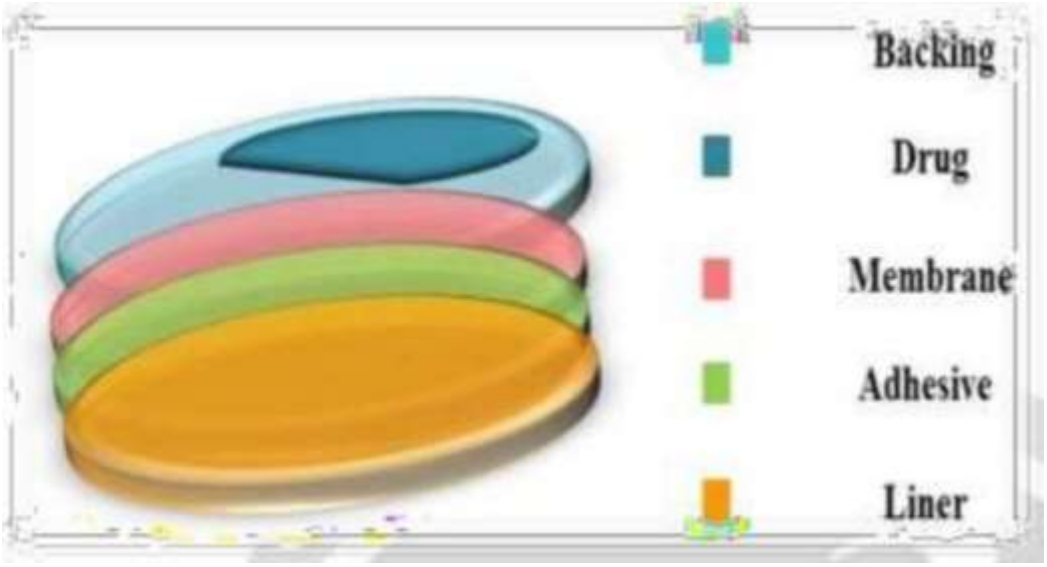
i. Single layer drug in adhesive:

In this type of patch, adhesive layer not only serve to affix the system to the skin, but it is also responsible for drug release from the patch. The adhesive layer is surrounded by backing layer.

ii. Multilayer drug in Adhesive:

The multilayer comprises either the addition of a membrane between two different drugs in adhesive or addition of multiple drug in adhesive layer under in single backing film. This patch is having temporary liner layer and backing layer.

BASIC COMPONENTS OF TDDS



1. Active Pharmaceutical Ingredient (API)

2. Polymer Matrix or Drug Reservoir

3. Permission enhancer

4. Pressure Sensitive Adhesive

5. Backing Laminated

6. Release liner

7. Other excipients such as plasticizer and solvents

1. Active Pharmaceutical Ingredient (API): Selection of API should be based upon the following properties API should not induced cutaneous irritation and also should not affected to the non-target tissues. [15]

2. Polymer Matrix or Drug Reservoir: Various polymeric material classes are utilised to achieve a rate-regulating membrane. Based on the following characteristics, the polymer matrix or drug reservoir should be chosen. The medication and polymer shouldn't come into contact chemically or physically. The polymer ought to be affordable and simple to transform into the intended result. The polymer needs to be non-toxic, stable, and unable to break down while the medication and other excipients are present. Natural polymers include starch protein, methyl cellulose, gum acacia, and gelatin. Synthetic polymers include polyester, polyvinyl chloride, polyethylene, and polyamide.[15]

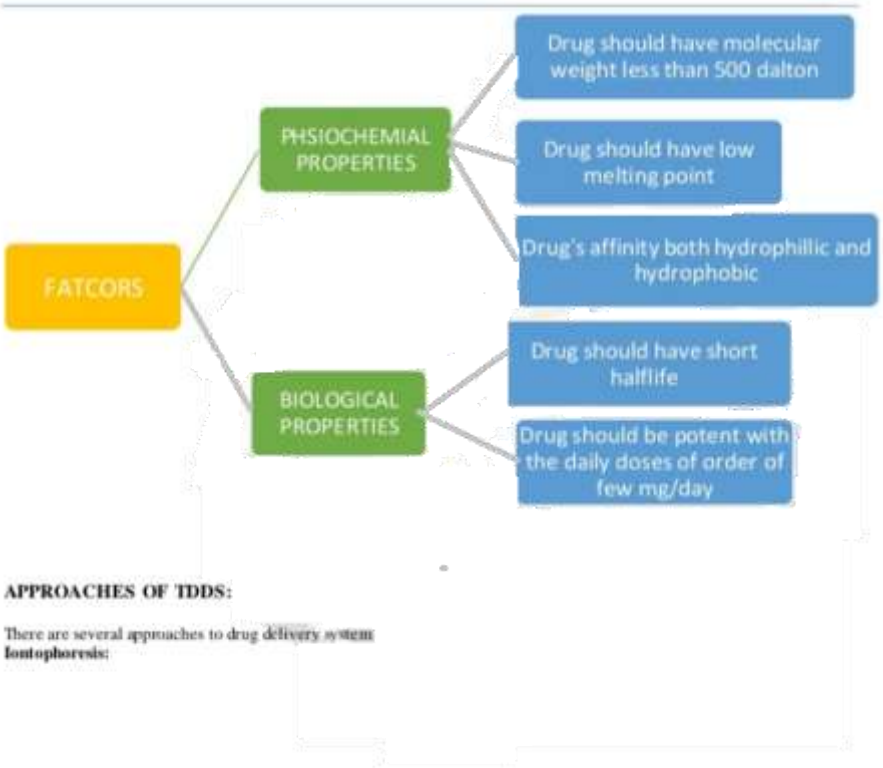
3. Permission enhancer: These are substances added to the formulation to increase the permeability of the drug through skin. They can modify the structure of skin or enhance drug solubility

. 4. Pressure Sensitive Adhesive: The selection are based on patch design and drug formulation which helps to maintaining a closed contact with patch and skin surface. It is also based upon following criteria adhere with not more than applied finger pressure. It should be easily removal from smooth surface without leaving a residue.

5. Backing Laminated: Backing membrane are flexible. This layer provide the drug reservoir and provide mechanical support. It is also prevent loss of drug and protect the skin from any kind of irritation.

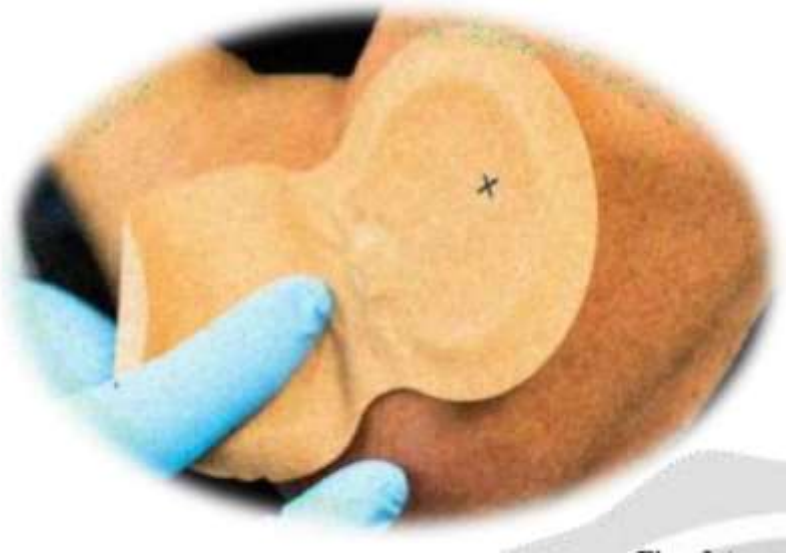
6. Release liner: It is a protective layer that is removed before applying the transdermal system. It prevent the drug reservoir from drying and protect it from contamination. It is composed of abase layer which may be non-occlusive or occlusive and released coating layer made up of silicon or Teflon.

FACTORS AFFECTING TO PERMEATION :



APPROACHES OF TDDS:

There are several approaches to drug delivery system
Iontophoresis:



Iontophoresis :

Iontophorosisworks by applying a few milliamperes of current to a tiny patch of skin via the electrode that is in contact with the formulation, helping to spread the drug over the barrier. [16] Iontophoresis has been shown to enhance skin penetration and accelerate the release of certain drugs with low permeability profiles or poor absorption. using a potential electrochemically. [17] The drug's polarity, valency, and mobility, as well as the kind of electrical cycle being employed, all affect how successful iontophoresis is. [18]

Sonophoresis;Using the desired spectrum of ultrasound frequencies from the ultrasound device can improve the efficacy of transdermal medication delivery. [19, 20] Because it creates an aqueous phase that is stabilised by an interfacial membrane made of molecules of surfactant or co-surfactant that are so small that they form minuscule droplets, low frequency ultrasonography is more successful at promoting drug circulation. The commonly utilised Nanoemulsion particle size ranges from 100 to 1000 nm, despite the fact that an upper limit has been suggested because of its Nano scale dimension.

Nanoemulsions have a similar droplet size range, composition, and appearance to micro emulsions. are different from them in terms of long-term effects and structural characteristics.

Needleless Injection:

Needleless injection is a painless way to deliver medication to the skin. Using this technique, supersonic particles are shot through the stratum corneum with liquid or solid particles. The method's limitations include expensive development costs for both the dosage form and the device, as well as the inability to programme or control drug distribution to take intersubject variability into account. Skin permeability mechanism for needleless injection: As part of the mechanism, a compressed gas, such as nitrogen or helium, is driven through the nozzle. The drug particles that are entrained inside the jet flow are believed to travel quickly enough to pierce the skin.

Abrasion:

To aid in the penetration of topically applied medications, the abrasion techniques directly removes or disrupts the top layers of the skin. Some of these devices are based on dermatologists techniques for superficial skin resurfacing (such as microdermabrasion), which are used to treat acne, scars, hyperpigmentation and other skin imperfection.

Laser Radiation: This procedure includes applying a laser to the skin in a direct and regulated manner. This eliminates the stratum corneum while slightly affecting the epidermis beneath. It has been demonstrated that utilizing this technique to remove the stratum corneum improves

1.Physically Examination of Transdermal patches were visually checked for their

•Colour

•Clarity

•Flexibility

•Homogeneity

• Smoothness

2. Thickness : The thickness of the medicine loaded patches is measured in different points by using digital micrometer and determine the average thickness and standard deviation to ensure thickness of prepared patch[28,29] .

3. Weight Uniformity : The prepared patch are dried at 60 C for 4 hours before testing. A specific area of patch is to be cut in different zones of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from individual weights.[29] .

4. Folding endurance : A strip of specific area is to be cut unevenly and constantly folded at the same place till it breaks. The number of times the film could be folded at the same place without breaking gives the value of the abidance.[30] .

5. Percentage Moisture Content : The set of films are to be counted collectively and to be kept in a desiccators containing fused calcium chloride at room temperature for 24 hours. After 24 hours the films are to be revalidated.

%Moisture content = (Initial weight –Final weight) x 100 Final weight

6. Content Uniformity Test:Ten patches are chosen, and each patch's content is decided. Transdermal patches, however, also pass the content uniformity test. Fresh 20 patches are also tested for the presence of medication if nine out of ten patches have content between 85% and 115% of the stipulated value and bone has content not lower than 75% to 125% of the specified. Still, the transdermal patches pass the test as well. If the range of these 20 patches is between 85% and 115%.[28,29]

7. Moisture Uptake : Counted films are kept in desiccators at room temperature for 24 hours. These are also taken out and exposed to 84 relative moisture using impregnated result of potassium chloride in desiccators until a constant weight is achieved. Humidity uptake is calculated as given below[28,29] %Moisture Uptake = Final weight – Initial weight x 100 Initial weight

8. Drug Content : A specified zones of patch is to be dissolved in a suitable solvent in specific volume. also the result is to be filtered through a purifier medium and analyze the medicine contain with the suitable system.[28,30]

9. Shear Adhesion Test:This test is intended to determine an adhesive polymer's cohesive strength dimension. The molecular weight, degree of cross-linking, polymer composition, type, and amount of tackifier applied can all have an impact. A clean steel plate is covered with an adhesive-coated tape, and to make the tape drag parallel to the plate, a specific weight is suspended from it. The time it takes to drag the tape off the plate can be used to calculate the shear adhesion strength. The shear strength decreases with increasing discarding time. [31]

10. Peel Adhesion Test : In this test, the force needed to remove an adhesive coating form a test substrate is referred to as peel adhesion. Molecular weight of adhesive polymer, the type and quantity of complements are the variables that determined the peel adhesion properties. A single tape is applied to a stainless steel plate or a backing membrane of choice and also tape is dragged from the substrate at a 180º angle, and the force needed for tape removed is measured.[31]

11. Water vapor transmission studies(WVT) :Weigh one gramme of calcium chloride and put it in previously dried, empty vials with the same diameter to determine WVT. Using an adhesive such as silicon adhesive grease, the polymer films are adhered to the brim and left for five minutes to solidify. The vials are also immediately counted and put in a moisture chamber with a constant relative humidity of 68. The vials are counted once more at the conclusion of the first, second, and third days throughout a period of seven days, and an increase in weight was taken into consideration as a quantitative indicator of the amount of humidity transferred through the patch. In a different approach that was published, vials containing 200 mL of impregnated potassium chloride and sodium bromide were placed in desiccators.The desiccators were sealed tightly, and a hygrometer was used to assess the moisture content within. The process was repeated with the tallied vials in desiccators. W stands for weight gain in a day, S for exposed film area (in centimetre square), and T for exposure time.[32]

12. Rolling Ball Tack Test : This test measures the softness of a polymer that relates to speak. In this test, stainless steel ball of7/16 elevation in diameter is released on an inclined track so that it rolls down and comes into contact with vertical, upward facing adhesive. The distance the ball travels along the tenacious provides the dimension of technique, which is expressed in inch.[33]

13. Quick Stick (Peel-Method) : In this test, the tape is dragged down from the substrate at 90ºC at a speed of 12 inches/ min. The peel force needed breaking the bond between adhesive and substrate is measured and recorded as method value, which is expressed in ounces or grams per inch range.[33]

14. Probe Tack Test : In this test, the tip of a clean probe with a defined surface roughness is induced into contact with adhesive, and when a bond is formed between probe and adhesive. The posterior discarding of the probe mechanically breaks it. The force needed to drag the probe down from the adhesive at fixed rate is recorded as method and it's looked in grams.

15. In Vitro Skin Saturation Studies :Diffusion cell can be used for an in vitro saturation research. Complete thickness of the abdomen skin in male Westar rats weighing 200–250 grammes. The dermal side of the skin is thoroughly gutted with distilled water to remove any clinging apkins or blood vessels, and is equalised for an hour in dissolution medium or phosphate buffer pH7.4 before starting the trial. It is then placed on a glamorous stirrer with a small glamorous needle for invariant distribution of the diffusant. The hair from the abdominal region is to be precisely removed using an electric clipper. The heater is thermostatically controlled to maintain the cell's temperature at 32 ±0.5 °C.

At regular intervals, a column with a defined volume must be taken out of the receptor cube and replaced with an equivalent amount of new media. Samples must pass through a filtering media before being subjected to HPLC or spectrophotometric analysis. The permeability fractions were produced by dividing the flux by the initial medication payload (mg cm–2), and flux can be directly estimated as the pitch of the curve between the steady-state values of the amount of medicine penetrated (mg cm–2) vs. time in hours.[34, 35]

16. Skin Irritation Study : Skin irritation and sensitization testing can be performed on healthy rabbits(average weight1.2 to1.5 kg). The rearward surface(50cm2) of the rabbit is to be cleaned and remove the hair from the clean rearward surface by shaving and clean the surface by using rectified spirit and the representative formulations can be applied over the skin. The patch is to be removed after 24 hrs. and the skin is to be observed and classified into 5 grades on the base of the inflexibility of skin injury. [31]

17. Stability Studies : Stability studies are to be conducted according to the ICH guidelines by storing the TDDS samples at 40 ±0.5 ° c and 75 ± 5 RH for 6 months. The samples are withdrawn at 0, 30, 60, 90 and 180 days and analyze suitably for the medicine content.[34]

CONCLUSION:

The transdermal drug delivery method has grown in importance in recent years. Transdermal administration is an extremely attractive way to provide a drug that has the right physical chemistry and pharmacology. In addition to maintaining a steady blood level for extended periods of time and avoiding hepatic first pass metabolism, the transdermal drug delivery method may also improve bioavailability, lessen gastrointestinal irritation from local contact with the stomach mucosa, and improve patient compliance. It appears that the benefits of intravenous medication infusion can now be nearly mimicked by using the skin to provide medicines without the associated hazards.

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