International Journal of Biomedical and Advance Research
ISSN: 2229-3809 (Online); 2455-0558 (Print)
Journal DOI: 10.7439/ijbar
CODEN: IJBABN **Review Article**

Transdermal drug delivery system: formulation, development and evaluation-An overview

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Abstract

In a transdermal drug delivery system the drug is applied in a relatively high dosage to the inside of a patch, which is worn on the skin for an extended period of time. Through a diffusion process, the drug enters the bloodstream directly through the skin. Since there is high concentration on the patch and low concentration in the blood, the drug will keep diffusing into the blood for a long period of time, maintaining the constant concentration of drug in the blood flow. Transdermal drug delivery system was introduced to overcome the difficulties of drug delivery through oral route. The conventional oral dosage forms have significant setbacks of poor bioavailability due to hepatic first pass metabolism. To improve characters of transdermal drug delivery system (TDDS) was emerged, which will improve the therapeutic efficacy and safety of drugs by specific sites within the body, thereby reducing both the size and number of doses. This review article describes the methods of preparation of different types of transdermal patches such as matrix patches, reservoir type, membrane matrix, drug-in-adhesive patches and micro reservoir patches.

Keywords: Transdermal Drug Delivery system, Bioavailability, Drug-In-Adhesive Patches, Reservoir Type, Membrane

1.Introduction

Optimum therapeutic outcomes require not only proper drug selection but also effective drug delivery. The human skin is a readily accessible surface for drug delivery. Over the past three decades, developing controlled drug delivery has become increasingly important in the pharmaceutical industry.Transdermal delivery systems are currently available containing scopolamine (hyoscine) for motion sickness, clonidine and nitroglycerin for cardiovascular disease, fentanyl for chronic pain, nicotine to aid smoking cessation. Transdermal delivery provides controlled, constant administration of the drug and allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation. TDDS offers many advantages over conventional injection and oral methods. It reduces the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliance and minimizes harmful side effects of a drug caused from temporary overdose. It is convenient, especially notable in patches which require only once weekly application. Such a simple dosing regimen aids in patient adherence to drug therapy. The transdermal drug delivery system has attracted considerable attention because of its many potential such as better patient compliance, avoidance of gastrointestinal disturbances, hepatic first-pass metabolism and sustained delivery of drugs to provide steady plasma profiles, particularly for drugs with short half-lives, reduction in systemic side effects and enhanced therapeutic efficacy.

The drugs administered across skin should have the three constraining characteristics:

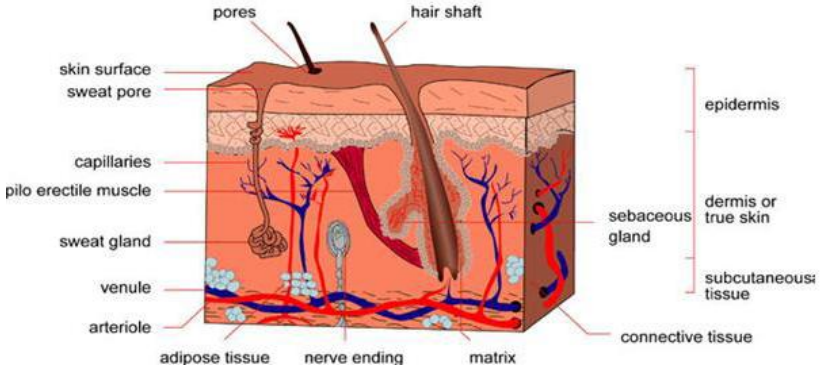
appropriate partition coefficient, low molecular mass (<500Da), and small required dose (uptomilligrams).

The physiology of skin illustrates the three feasible pathway exist for passive transport of active through the skin:

1. Intercellular diffusion through the lipid lamellae
2.Transcellular diffusion through both the keratinocytes and lipid lamellae
3. Diffusion through hair follicles and sweat ducts, It is documented that polar molecules mainly permeate.

2. Anatomy and physiology of skin[2-5]:

3. Figure 1: Structure of skin



2.1 Epidermis

The skin is the largest organ in the body and, on average, accounts for about 6 lbs of our body weight. Skin has as its primary function to keep the body hydrated or to keep water inside the body and also prevents foreign substances from entering the body from the environment. The major divisions of the skin, from top to bottom are the epidermis, dermis and the hypodermis. The hypodermis portion is where fat is stored, as shown by the ovals in the figure representing adipocytes. Therefore, in order to have drug delivery via the skin, the drug must pass through the epidermis into the dermis where it can be absorbed by capillaries into the circulatory system. Of the five layers of the epidermis, the most important barrier layer is the outer layer, or stratum corneum. The stratum corneum is made up of dead, keratinized cells called keratinocytes, or sometimes corneocytes. There are three possible ways that drug molecules can pass through stratum corneum. The drug can be absorbed by various pathways through the skin depending on the physicochemical properties of the drug. Both lipophilic and hydrophilic drugs are absorbed from different routes.

1) Transfollicular route: -Transfollicular route is the shortest pathway that drug has to follow to reach the systemic circulation that provides a large area for diffusion of drugs. These ducts offer a continuous channel across the stratum conium for drug transport but various factors like secretion from glands, content and amount of secretion etc., affect the transport of drugs through this route. However trans appendageal route occupies only 0.1% of total skin surface and therefore contributes a little.

2) Transcellular route: - Drug delivering through this route passes from corneocytes which has highly hydrated keratin creating hydrophilic pathway. Corneocytes are surrounded by lipids connecting these cells. So a drug requires a number of partitioning and diffusion steps. It is the most widely used route by various types of drugs. The highly hydrated keratin provide aqueous pathway to the hydrophilic drugs. A number of partitioning and diffusion steps are needed to pass the drug through the cell matrix.

3) Intercellular route: - As the name indicates intercellular the drug diffuses through the lipid bilayer between the cells. In this route, the molecule stays in the lipid bilayer and winds around the keratinocytes on its way to the dermis. Although both paths are possible, the most common route of drug penetration is the intercellular route because most drug molecules are more soluble in the lipid environment of the bilayer than in the protein environment of the keratinocytes.

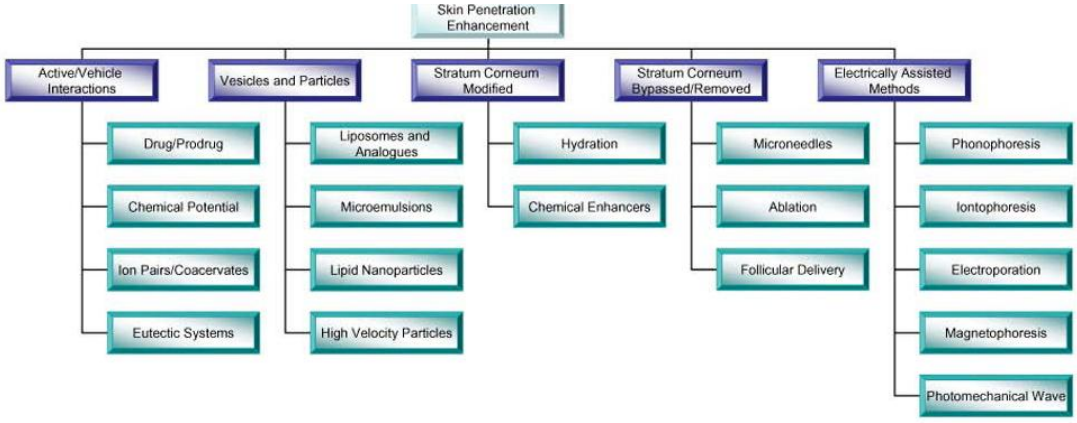
3.Methods for enhancing transdermal drug delivery [6,7]

3.1 Skin penetration can be enhanced by following methods:-

1. Drug/prodrug: The prodrug approach has been used to enhance the dermal and transdermal delivery of drugs with unfavorable partition coefficients the prodrug design involves addition of a promoiety to increase partition coefficient and also solubility and transport of the parent drug in the stratum conium. For example: The intrinsic poor permeability of the very polar 6-mercaptopurine was increased up to 240

times using S6- acyloxymethyl and 9-dialkylaminomethyl promoieties. The prodrug approach has also been investigated for increasing skin permeability of non-steroidal anti-inflammatory drugs, like naltrexone nalbuphine buprenorphin alpha-blocker and other drugs **[7]**.

Fig:- 2 Various methods used to enhance the Skin penetration



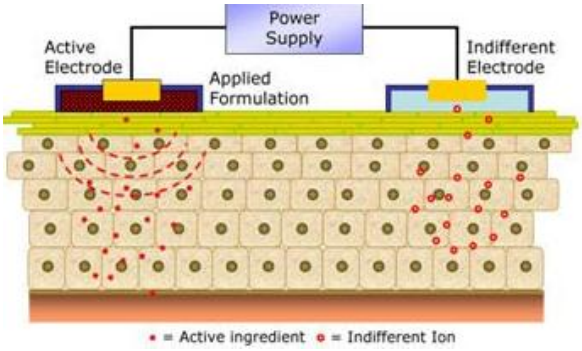
2. Eutectic system: A eutectic system is a mixture of chemical compounds or elements that has a single chemical composition that solidifies at a lower temperature than any other composition. According to regular solution theory, the lower the melting point, the greater the solubility of a material in a given solvent, including skin lipids **[7]**.

3. Liposomes and vehicles: Liposome is colloidal particles formed as concentric bimolecular layers that are capable of encapsulating drugs. There are many examples of cosmetic products in which the active ingredients are encapsulated in vesicles. These include humectants such as glycerol and urea, unscrewing and tanning agents, enzymes, etc. Phosphatidylcholine from soybean or egg yolk is the most common composition although many other potential ingredients have been evaluated. **[7]**

4. Solid lipid Nanoparticles: Solid lipid nanoparticles (SLN) have recently been investigated as carriers for enhanced skin delivery of sunscreens, vitamins A and E, triptolide and glucocorticoids. It is thought their enhanced skin penetration is primarily due to an increase in skin hydration caused by the occlusive film formed on the skin surface [8].

5. Iontophoresis: This method involves permeation of a topically applied therapeutic agent by application of low level electric current either directly to skin or indirectly via dosage form. Parameters that effect design of aionophoretic skin delivery system include electrode type, current intensity and pH of system. Increased drug permeation as a result of this methodology can be attributed to either one or a combination of the following mechanisms: Electro-repulsion (for charged solutes), electro-osmosis (for uncharged solutes) and electro-perturbation (for both charged and uncharged)**[9]**.

Fig. 3: Basic principle of Iontophoresis



6. Electroporation: It involves the application of high voltage pulses to the skin that has been suggested to induce the formation of transient pores. High voltages (100 V) and short treatment durations (milliseconds) are most frequently employed. The technology has been successfully used to enhance the skin permeability of molecules with differing lipophilicity and size (i.e. small molecules, proteins, peptides and oligonucleotides) including biopharmaceuticals with molecular weights greater that 7kDA**[9]**.

7. Ultrasound (sonophoresis and phonophoresis): This technique involves the use of ultrasonic energy to enhance the transdermal delivery of solutes either simultaneously or via pre-treatment. It uses low frequency ultrasound (55 kHz) for an average duration of 15 seconds to enhance skin permeability [9].

8. Laser radiation and photomechanical waves: Lasers are frequently used for treatment of dermatological conditions like acne and to confer facial rejuvenation. This method involves direct and controlled exposure of a laser to the skin that results in the ablation of the stratum corneum without significantly damaging the underlying epidermis **[11]**.

9. Radio frequency: It involves the exposure of skin to high frequency alternating current resulting in formation of heat induced micro channels in the membrane. The rate of drug delivery is controlled by number and depth of micro channels formed by device. Treatment duration takes less than a second **[12]**.

10. **Magnetophoresis**: It involves application of magnetic field that acts as an external driving force to enhance the diffusion of a diamagnetic solute across the skin. Skin exposure to a magnetic field might also induce structural alterations that could contribute to an increase in permeability **[12]**.

11. **Micro needle based devices**: The first ever patents for drug delivery for percutaneous administration of drug was based on this method. This micro needles length 50-110 micrometer will penetrate SC and epidermis to deliver drug.

12. **Skin Abrasion**: The abrasion technique involves the direct removal or disruption of the upper layers of the skin. These devices are based on techniques employed by dermatologists for superficial skin resurfacing which are used in the treatment of acne, scars, hyperpigmentation and other skin blemishes.

13. **Needle-less Injection**: Transdermal delivery is achieved by firing the liquid or solid particles at supersonic speeds through the outer layers of the skin using a suitable energy source. The mechanism involves forcing compressed gas (helium) through the nozzle, with the resultant drug particles entrained within the jet flow reportedly traveling at sufficient velocity for skin penetration. This method avoids issues of safety, pain and fear **[13]**.

14. Application of pressure: The application of modest pressure i.e. 25kPa provides a potentially non-invasive and simplest method of skin permeability of molecules such as caffeine.

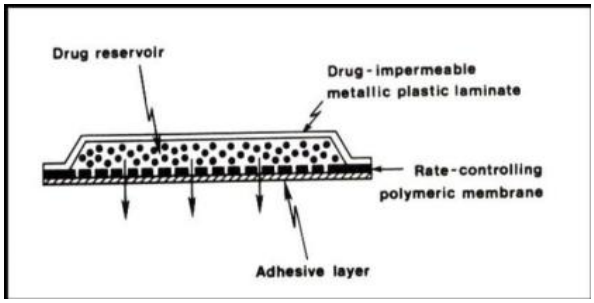
4. Approaches used in development of TDDS [14, 15, 16].

Several technologies have been successfully developed to provide a rate control over the release and the transdermal permeation of drugs. These technologies can be classified into four approaches as follows:

1. Membrane permeation – controlled systems
2. Adhesive dispersion – type systems.
3. Matrix diffusion – controlled systems.
4. Micro reservoir type or micro sealed dissolution controlled systems.

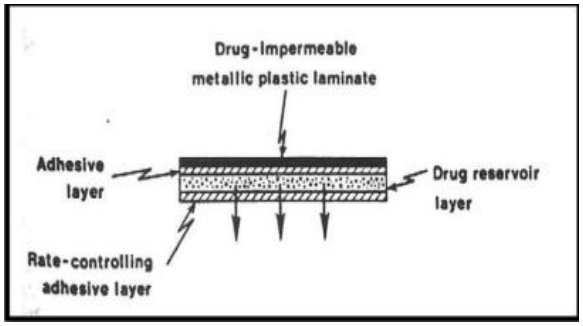
1. Membrane permeation – controlled systems: In this type of system, drug reservoir is encapsulated in a shallow compartment moulded from a drug-impermeable metallic plastic laminate and a rate controlling polymeric membrane which may be micro porous or non-porous as shown in fig.4. The drug molecules are permitted to release only through the rate – controlling polymeric membrane. In the drug reservoir compartment, the drug solids are either dispersed homogenously in a solid polymer matrix (e.g. Polyisobutylene adhesive) or suspended in anunbleachable, viscous liquid medium (e.g. Silicon fluids) to form a paste like suspension. Examples of thissystem are Transderm-nitro, Transderm-scop, Catapresand Estraderm etc.

Fig 4: Membrane permeation controlled system.



2. Adhesive Dispersion – Type Systems: This is a simplified form of the membrane-permeation controlled system. As shown in fig.5, the drug reservoir is formulated by directly dispersing the drug in an adhesive polymer e.g. Poly (isobutylene) or poly (acrylate) adhesive and then spreading the medicated adhesive, by solvent casting or hot melt, on to a flat sheet of drug impermeable metallic plastic backing to form a thin drug reservoir layer. On the top of the drug reservoir layer, thin layers of non-medicated, rate-controlling adhesive polymer of a specific permeability and constant thickness are applied to produce an adhesive diffusion – controlled delivery system.

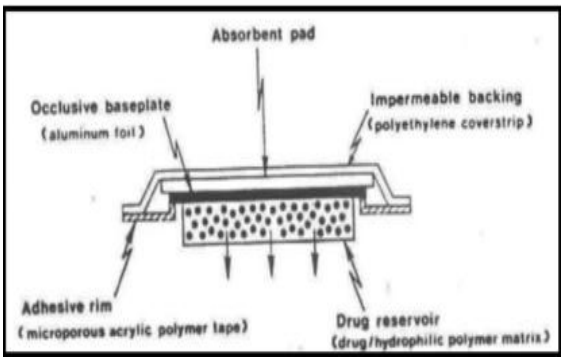
Fig 5: Adhesive dispersion type system



3. Matrix Diffusion- Controlled Systems: In this approach, the drug reservoir is formed by homogenously dispersing the drug solids in a hydrophilic or lipophillic polymer matrix. The resultant medicated polymer is then molded into a medicated disc with a defined surface area and

controlled thickness. Drug reservoir containing polymer disc is then pasted onto an occlusive base plate in a compartment fabricated from a drug-impermeable plastic backing membrane (fig.6). e.g. Nitro-Door: Delivers nitroglycerin for the treatment of angina pectoris.

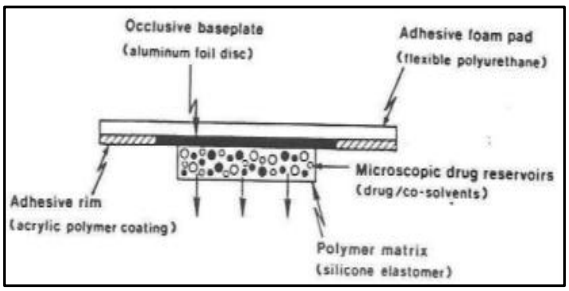
Fig.6: Matrix diffusion controlled system



4. Micro reservoir type or Micro sealed Dissolution:-

The micro reservoir type drug delivery system can be considered a combination of the reservoir and matrix diffusion type drug delivery systems. This transfer maltherapeutic system is then produced by positioning the medicated disc at the centre and surrounding it with an adhesive rim (fig. 7). E.g. nitroglycerine.

Fig.7: Micro reservoir type controlled system

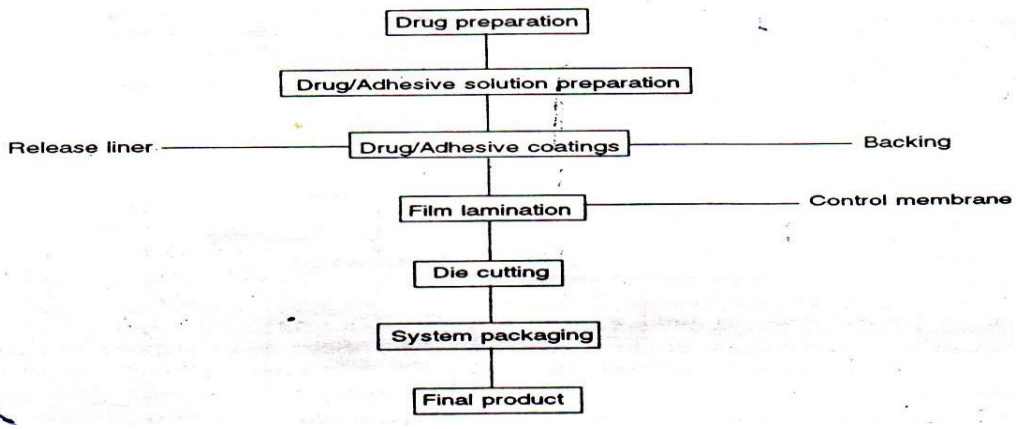


The Matrix system design is characterized by the inclusion of a semisolid matrix containing a drug solution or suspension which is in direct contact with the release liner.

5. Formulation methods for transdermal drug delivery [17, 18, 19, 20]:-

(A) Membrane permeation – controlled system: These system can be multilaminate process e.g. Transdermal Nitro. These products consist of three substrates held together by two layers of drug containing adhesive. First the drug is processed into the physical / chemical form required for incorporation into the product. Then the drug adhesive components and excipients are mixed with a solvent to achieve uniform solution. These adhesive compositions are deposited as a thin film on moving substances rate which are subsequently dried to remove solvent. Then lamination of the dried adhesive film and other layer to form the five layer product consisting of release linear contact adhesive control membrane, drug reservoir and backing substrate. The lamination then printed and die cut into final dosage form. The production is then packed in individual foil pouches. After inspection the products are automatically inserted into a continuously moving web of pouch stock which is sealed around the dosage form.

Fig.8:-Multilaminate transdermal dosage from manufacturing process flow diagram



(B) Adhesive dispersion type system: The manufacturing process these systems can be divided into following parts.

(I) Preparation of individual matrix solution Raw material [Polymer, tackifier, softening Agent] is dissolved in an organic solvent to obtain a standard or stock soln. The matrix solution then prepared from the stock solution by mixing it with ingredients specified by the formulation. The active ingredient and other non-soluble additives are added.

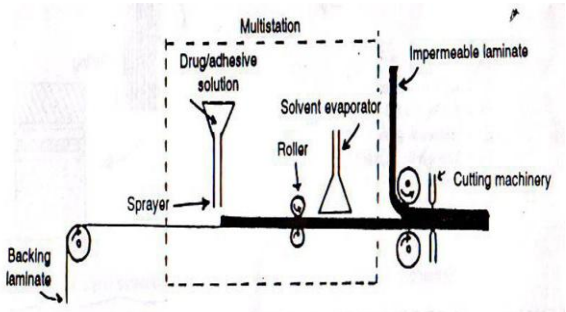
(II) Coating the individual matrix layers: -The individual layers are made by coating the solution (above). On the smooth paper or film web and removing the solvent by drying using Coating machine. This machine consists of two units

(a)Coating unit and (b) Drying unit.

(a)Coating unit:-The solvent based formulations are coated onto the appropriate web. Depending on the viscosity, solid contents, flow ability and surface tension of the matrix solution.

(b) Drying Unit: Closed to the environment and is directly connected to the drying unit to avoid solvent and this active agent evaporation. The solvent is evaporated from the adhesive mars by running the coated web through a drying channel using a transport system like cranked shaft, conveyor belt.

Fig.9: The process and equipment involved in the manufacture of an adhesive dispersion system



I) Building the multilayer laminate: - Lamination is used to build up the multilayer matrix system. Here two matrix layers, each adhering to one side of the web are laminated., Then a carrier material of this two layer laminate is removed and a third layer, with the laminated side to the laminated side of the two layer laminate is pressed. This procedure is repeated until the final laminate is complete.

(II) Separating unit of the multilayer laminate:- The bulk product is slit longitudinally and the individual unit is punched quit from the narrow rolls so obtained. Precision of the operations is of paramount importance here hence it affects the release rate of the active ingredient. Then the liner is applied with the necessary release aids to the system.

(III) Packaging: - Primary packaging is done using sealed, four cornered while secondary packaging in cardboard boxes precedes shipment.

(C) Matrix diffusion controlled system: - The drug is dispersed in an insoluble matrix of rigid non swellable hydrophobic material. Materials used for rigid matrix are insoluble plastics such as PVC and fatty and materials like stearic and beeswax. With the plastic materials the drug is generally kneaded with the solution of Polyvinyl chloride in an organic solvent and granulated waxy matrix is prepared by dispersing the drug in molten fat followed by congealing. The granules are then compressed into tablets swellable matrix system are popular for sustaining the release of highly water soluble drug. The material for such matrices are generally hydrophilic gums and may be of natural origin (guar gum, tragacanth) semi synthetic (HPMC, CMC) or synthetic (poly cryamides) The drug and the gum are granulated together with a solvent such as alcohol and compressed into tablets. The release of drug from such initially dehydrated hydro gels involves simultaneous absorption of water and desorption of drug via a swelling controlled diffusion mechanism. The gum swells and the drug diffuse out of it the swollen mars devoid of drug appear transport.

(D) Microsealed dissolution–Controlled system or Encapsulation: - The drug particles are coated or encapsulated by one of the several micro encapsulation techniques with slowly dissolving materials like cellulose, PEGs, polymethacrylates, waxes. The resulting pellets may be filled as such in hard gelatin capsule. The dissolution role of coat depends upon the solubility and thickness of the coating which may range from 1 to 200 microns.

6. Evaluation of transdermal patches [21,22,23]

1. Physicochemical evaluation
2. *In vitro* evaluation
3. *In vivo* evaluation

1. Physicochemical Evaluation:-

a) Thickness: The thickness of transdermal film is determined by travelling microscope, dial gauge, screw gauge or micrometer at different points of the film.

b) Uniformity of weight: Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.

c) Drug content determination: An accurately weighed portion of film (about 100 mg) is dissolved in 100 mL of suitable solvent in which drug is

soluble and then the solution is shaken continuously for 24 h in shaker incubator. Then the whole solution is sonicated. After sonication and subsequent filtration, drug in solution is estimated spectrophotometrically by appropriate dilution.

d) Content uniformity test: 10 patches are selectedand content is determined for individual patches.If 9 out of 10 patches have content between 85%to 115% of the specified value and one hascontent not less than 75% to 125% of thespecified value, then transdermal patches pass thetest of content uniformity. But if 3 patches havecontent in the range of 75% to 125%, thenadditional 20 patches are tested for drug content.If these 20 patches have range from 85% to115%, then the transdermal patches pass the test.

e) Moisture content: The prepared films areweighed individually and kept in a desiccatorscontaining calcium chloride at room temperaturefor 24 h. The films are weighed again after aspecified interval until they show a constantweight. The percent moisture content iscalculated using following formula:

% Moisture content = Initial weight – Finalweight X 100

f) Flatness: A transdermal patch should possess a smooth surface and should not constrict with time. This can be demonstrated with flatness study. For flatness determination, one strip is cut from the centre and two from each side of patches. The length of each strip is measured and variation in length is measured by determining percent constriction. Zero percent constriction is equivalent to 100 percent flatness. % constriction = $I_1 – I_2$ X 100

I_2 = Final length of each strip, I_1 = Initial length of each strip

g) Folding Endurance: Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. Folding endurance is determined by repeatedly folding the film at the same place until it break. The number of times the films could be folded at the same place without breaking is folding endurance value.

h) Tensile Strength: To determine tensile strength, polymeric films are sandwiched separately by corked linear iron plates. One end of the films is kept fixed with the help of an iron screen and other end is connected to a freely movable thread over a pulley. The weights are added gradually to the pan attached with the hanging end of the thread. A pointer on the thread is used to measure the elongation of the film. The weight just sufficient to break the film is noted. The tensile strength can be calculated using the following equation.

Tensile strength= F/a.b (1+L/l)

F is the force required to break; a is width of film; b is thickness of film; L is length of film;

l is elongation of film at break point.

i) Tack properties: It is the ability of the polymer to adhere to substrate with little contact pressure. Tack is dependent on molecular weight and composition of polymer as well as on the use of tackifying resins in polymer.

2. *In vitro* evaluation:-

a)The Paddle over Disc: (USP apparatus 5/ Ph Eur 2.9.4.1) this method is identical to the USP paddle dissolution apparatus, except that the transdermal system is attached to a disc or cell resting at the bottom of the vessel which contains medium at 32 ±5°C.

b) The Cylinder modified USP Basket: (USP apparatus 6 / Ph Eur 2.9.4.3) this method issimilar to the USP basket type dissolution apparatus, except that the system is attached to

The surface of a hollow cylinder immersed in medium at 32 ±5°C.

c) The reciprocating disc: (USP apparatus 7) in this method patches attached to holders are oscillated in small volumes of medium, allowing the apparatus to be useful for systems delivering low concentration of drug. In addition paddle over extraction cell method (Ph Eur 2.9.4.2) may be used.

d) Horizontal-type skin permeation system: This has been widely used for the evaluation of drug permeation across skin. The cell is divided in receptor and donor compartments with a low solution volume (3.5ml) for each compartment and a small membrane area (0.64cm2). They are continuously stirred by matched set of star-head magnets, which are rotated at a speed of 600rpm. The system is controlled by thermostated water through a water jacket surrounding the two compartments.

e) Franz diffusion cell: The cell is composed of two compartments: donor and receptor. The receptor compartment has a volume of 5-12ml and effective surface area of 1-5 cm2. The diffusion buffer is continuously stirred at 600rpm by a magnetic bar. The temperature in the bulk of the solution is maintained by circulating thermostated water through a water jacket that surrounds the receptor compartment.

f) Flow-through diffusion cell: flow through diffusion cells have the advantage that they can be used when the drug has lower solubility in the

receptor compartment. This cell can be fully automated and connected directly to HPLC. They have large capacity donor chamber to aloe appropriate loading of the applied compound and a low volume (0.3ml) receiving chamber that ensures rapid removal of penetrant at relatively low pumping rates.

3. *In vivo* studies:-

In vivo evaluations are the true depiction of the drug performance. The variables which cannot be taken into account during in vitro studies can be fully explored during in vivo studies. In vivo evaluation of TDDS can be carried out using animal models human volunteers.

a) Animal models: Considerable time and resources are required to carry out human studies, so animal studies are preferred at small scale. The most common animal species used for evaluating transdermal drug delivery system are mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit, guinea pig etc. Various experiments conducted lead us to a conclusion that hairless animals are preferred over hairy animals in both in vitro and in vivo experiments. Rhesus monkey is one of the most reliable models for in vivo evaluation of transdermal drug delivery in man.

b) Human models: The final stage of the development of a transdermal device involves collection of pharmacokinetic and pharmacodynamic data following application of the patch to human volunteers. Clinical trials have been conducted to assess the efficacy, risk involved, side effects, patient compliance etc. Phase I clinical trials are conducted to determinemainly safety in volunteers and phase II clinical trials determine short term safety and mainly effectiveness in patients. Phase III trials indicate the safety and effectiveness in large number of patient population and phase IV trials at post marketing surveillance are done for marketed patches to detect adverse drug reactions. Though human studies require considerable resources but they are the best to assess the performance of the drug.

7. Recent advances in transdermal delivery system [24, 25, 26, 27]:-

Latest research done in field of transdermal patches is stated below:

1. Patch technology for protein delivery:- Transdermal delivery of large protein is a novel and exciting delivery method trans pharma uses its unique printed patch technology for transdermal delivery of protein thereby complementing its via Derm delivery technology. It is postulated that the highly water soluble proteins are dissolved by the interstitial fluid that is secreted from the skin through the RF-MicroChannels, forming a highly concentrated protein solution in situ.The delivery of the dissolved molecules is then carried out, via the RF-Micro Channels, into the viable tissues of the skin, diffusing across a steep concentration gradient.

2. Testosterone transdermal patch system in young women with spontaneous premature ovarian failure:-In premenopausal women, the daily testoterone production is approximately 300 µg, of which approximately half is derived from the ovaries and half from the adrenal glands. Young women with spontaneous premature ovarian failure (sPOF) may have lower androgen levels, compared with normal ovulatory women. Testosterone transdermal patch (TTP) was designed to deliver the normal ovarian production rate of testosterone.

3. Transdermal patch of oxybutynin used in overactive bladder:- The product is a transdermal patch containing Oxybutynin HCl and is approved in US under the brand name of Oxytrol and in Europe underthe brand name of Kentera. OXYTROL is a thin, flexible and clear patch that is applied to the abdomen, hip or buttock twice weekly and provides continuous and consistent delivery of oxybutynin over a three to four day interval

4. Nanotechnology gaining hold:-This technology combines the advantage of a needle and the transdermal patch. The devices are dime-sized pieces of polymer with hundreds of hollow microneedles between 100 and 1,000 micrometers long.These small needles penetrate the top layers of skin and allow the drug to pass through with ease.

5. Pain relief: - Pain relief routinely benefits from transdermal patch technology. Most of the readers are aware of the Duragesic patch. One is Lidoderm, a lidocaine percent patch, which is used for post herpetic neuralgia. Other exciting advancements in pain control include the E-Trans fentanyl HCl patch. . This credit card-size patch is an active delivery device that has a self-contained battery that delivers pulses of fentanyl HCl, a strong narcotic. This mimics the use of intravenous self-controlled analgesic systems that are very expensive

6. Poke with patch approach: - Involves piercing into the skin followed by application of the drug patch at the site of treatment.

7. Coat and poke approach: - Needles coated with the drug are inserted into the skin and release of medicament is then occurs by dissolution.

8. Biodegradable micro needles: - Involves encapsulation of the drug within the biodegradable,

polymeric microneedles, which is then inserted into the skin.

9. Hollow micro needles: - Involves injecting the drug through the needle with a hollow bore.

8. Conclusion

Transdermal drug delivery systems represent a beneficial innovation for drug delivery, particularly in patients who cannot swallow or remember to take their medications. Clinicians and other allied health professionals should understand the appropriate administration techniques for transdermal systems to ensure optimal patient outcomes and to ensure the safety of all who encounter patients who use TDDS. Future developments of TDDSs will likely focus on the increased control of therapeutic regimens and the continuing expansion of drugs available for use. Transdermal dosage forms may provide clinicians an opportunity to offer more therapeutic options to their patients to optimize their care.

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