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Transdermal Patch: A New Approach to Tdds

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ABSTRACT
Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery systems. In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation. Transdermal drug delivery systems are polymeric formulations which when applied to skin deliver the drug at a predetermined rate across dermis to achieve systemic effects. Transdermal dosage forms, though a costly alternative to conventional formulations, are becoming popular because of their unique advantages. Controlled absorption, more uniform plasma levels, improved bioavailability, reduced side effects, painless and simple application and flexibility of terminating drug administration by simply removing the patch from the skin are some of the potential advantages of transdermal drug delivery. Development of controlled release transdermal dosage form is a complex process involving extensive efforts. This review article describes the methods of preparation of different types of transdermal patches, evaluation parameters and some available marketed products. Now a day about 74% of drugs are taken orally and are found not to be as effective as desired either due to bioavailability problems or degradation of drug in acidic pH of stomach. To resolve such problems, transdermal drug delivery system (TDDS) was emerged. Transdermal drug delivery systems are dosage forms involves drug transport to viable epidermal and dermal tissues of the skin for local therapeutic effect while a very major fraction of drug is transported into the systemic blood circulation. Transdermal drug delivery systems, also known as ‘‘patches,’’ are dosage forms designed to deliver a therapeutically effective amount of drug across a patient’s skin. This review article provides an overview of TDDS, advantages, limitations, various components of TDDS, methods of preparation, types of transdermal patches, factors affecting transdermal permeation, evaluation parameters and new approaches in TDDS.

KEYWORDS: Transdermal drug delivery system, transdermal patches, design of transdermal dosage form, evaluation of transdermal system.

I. INTRODUCTION

Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation. The relative impermeability of skin is well known, and this is associated with its functions as a dual protective barrier against invasion by micro-organisms and the prevention of the loss of physiologically essential substances such as water. Elucidation of factors that contribute to this impermeability has made the use of skin as a route for controlled systemic drug delivery possible. Basically, four systems are available that allow for effective absorption of drugs across the skin. The microsealed system is a partition-controlled delivery system that contains a drug reservoir with a saturated suspension of drug in a water-miscible solvent homogeneously dispersed in a silicone elastomer matrix. A second system is the matrix-diffusion controlled system. The third and most widely used system for transdermal drug delivery is the membrane-permeation controlled system. A fourth system, recently made available, is the gradientcharged system. Additionally, advanced transdermal carriers include systems such as iontophoretic and sonophoretic systems, thermosetting gels, prodrugs, and liposomes.

Many drugs have been formulated in transdermal systems, and others are being examined for the feasibility of their delivery in this manner (e.g., nicotine antihistamines, beta-blockers, calcium channel blockers, non-steroidal anti-inflammatory drugs, contraceptives, anti-arrhythmic drugs, insulin, antivirals, hormones, alpha-interferon, and cancer chemotherapeutic agents). Research also continues on various

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chemical penetration enhancers that may allow delivery of therapeutic substances. Transdermal drug delivery system is topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. These devices allow for pharmaceuticals to be delivered across the skin barrier.

This approach to drug delivery offers many advantages over traditional methods. As a substitute for the oral route, transdermal drug delivery enables the avoidance of gastrointestinal absorption, with its associated pitfalls of enzymatic and pH associated deactivation. This method also allows for reduced pharmacological dosage due to the shortened metabolization pathway of the transdermal route versus the gastrointestinal pathway. The patch also permitsconstant dosing rather than the peaks and valleys in medication level associated with orally administered medications. Multi-day therapy with single application, rapid notification of medication in the event of emergency, as well as the capacity to terminate drug effects rapidly via patch removal, are all further advantages of this route. However this system has its own limitations in which the drug that require high blood levels cannot be administered and may even cause irritation or sensitization of the skin. the adhesives may not adhere well to all types of skin and may be uncomfortable to wear. Along with these limitations the high cost of the product is also a major drawback for the wide acceptance of this product.

II. COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEMS

- Polymer matrix or matrices.
- The drug
- Permeation enhancers
- Other excipients

Polymer Matrix

The Polymer controls the release of the drug from the device. Possible useful polymers for transdermal devices are

Natural Polymers:

e.g. Cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.

Synthetic Elastomers:

e.g.Polybutadiene, Hydrinrubber,Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrenebutadieine rubber, Neoprene etc

Synthetic Polymers:

e.g. Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinylpyrrolidone, Polymethylmethacrylate, Epoxy etc.

Drug

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

Physicochemical properties

- The drug should have a molecular weight less than approximately 1000dalton.
- The drug should have affinity for both – lipophilic and hydrophilic phases. Extreme partitioning characteristics are not conductive to successful drug delivery via the skin.
- The drug should have low melting point.

Enhancers

These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant.

Solvents

These compounds increase penetration possibly by swallowing the polar pathway and/or by fluidizing lipids. Examples include water alcohols – methanol and ethanol; alkyl methyl sulfoxides – dimethyl sulfoxide, alkyl homologs of methyl sulfoxide dimethyl acetamide and dimethyl formamide, pyrrolidone – 2 pyrrolidone,N-methyl, 2-purrolidone; laurocapram (A zone), miscellaneous solvents – propylene glycol, glycerol, silicone fluids, isopropyl palmitate.

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. Dioctyl sulphosuccinate, Sodium lauryl sulphate, decodecylmethylsulphoxide etc.

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Nonionic Surfactants:
e.g. Pluronic F127, Pluronic F68, etc. Bile Salts:e.g. Sodium ms taurocholate, Sodium deoxycholate,Sodium tauroglycocholate.

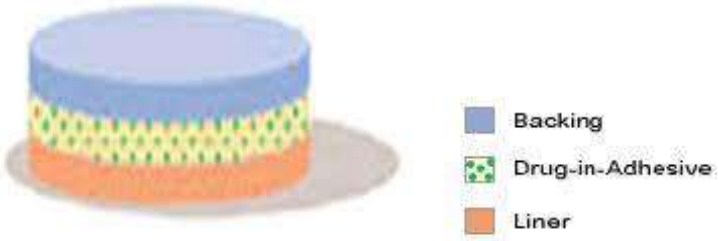
Binary system
These systems apparently open up the heterogeneous multilaminate pathway as well as the continuous pathwayse.g. Propylene glycol-oleic acid and 1, 4-butane diol-linoleic acid.

Miscellaneous chemicals
These include urea, a hydrating and keratolytic agent; N, Ndimethyl-m-toluamide; 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.

Other Excipients
Adhesives:
The fastening of all transdermal devices to the skin has so far been done byusinga pressure sensitive adhesive which can be positioned on the face of the device or in the back of the device and extending peripherally.

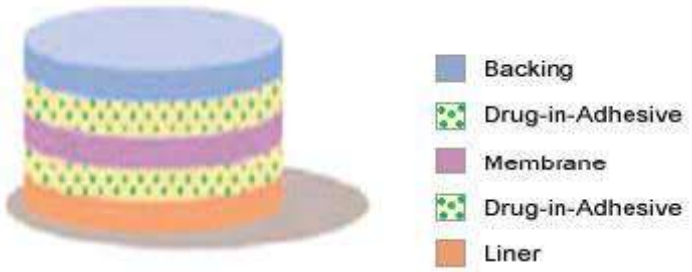
III. TRANSDERMAL PATCHES:

Single-layer Drug-in-Adhesive



The Single-layer Drug-in-Adhesive system is characterized by the inclusion of the drug directly within the skin-contacting adhesive. In this transdermal system design, the adhesive not only serves to affix the system to the skin, but also serves as the formulation foundation, containing the drug and all the excipients under a single backing film. The rate of release of drug from this type of system is dependent on the diffusion across the skin.

Multi-layer Drug-in-Adhesive



The Multi-layer Drug-in-Adhesive is similar to the Single layer Drug-in-Adhesive in that the drug is incorporated directly into the adhesive. However, the multi-layer encompasses either the addition of a membrane between two distinct drug-in-adhesive layers or the addition of multiple drug-in-adhesive layers under a single backing film.

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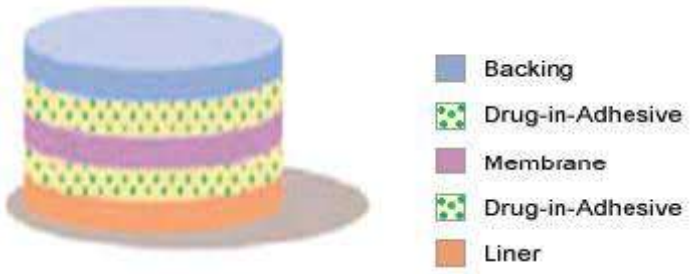
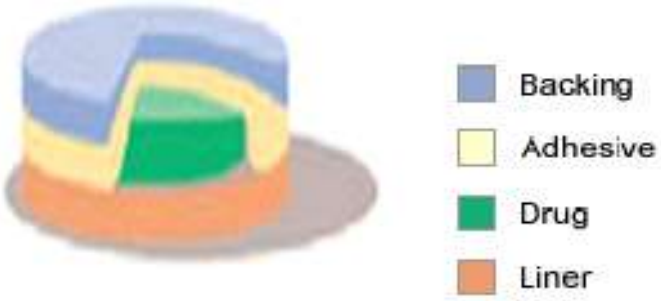
Drug Reservoir-in-Adhesive



The Reservoir transdermal system design is characterized by the inclusion of a liquid compartment containing a drug solution or suspension separated from the release liner by a semi-permeable membrane and adhesive. The adhesive component of the product responsible for skin adhesion can either be incorporated as a continuous layer between the membrane and the release liner or in a concentric configuration around the membrane.

Drug Matrix-in-Adhesive



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. The component responsible for skin adhesion is incorporated in an overlay and forms a concentric configuration around the semisolid matrix.

IV. EVALUATION OF TRANSDERMAL PATCHES

Transdermal patches have been developed to improve clinical efficacy of the drug and to enhance patient compliance by delivering smaller amount of drug at a predetermined rate. This makes evaluation studies even more important in order to ensure their desired performance and reproducibility under the specified environmental conditions. These studies are predictive of transdermal dosage forms and can be classified into following types:

- Physicochemical evaluation
- In vitro evaluation
- In vivo evaluation

1. Physicochemical Evaluation:

Thickness:

The thickness of transdermal film is determined by traveling microscope, dial gauge, screw gauge or micrometer at different points of the film.

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.

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.

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Content uniformity test:

10 patches are selected and content is determined for individual patches. If 9 out of 10 patches have content between 85% to 115% of the specified value and one has content not less than 75% to 125% of the specified value, then transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75% to 125%, then additional 20 patches are tested for drug content. If these 20 patches have range from 85% to 115%, then the transdermal patches pass the test.

Moisture content:

The prepared films are weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 h. The films are weighed again after a specified interval until they show a constant weight. The percent moisture content is calculated using following formula.

%Moisture content = Initial weight – Final weight X 100
Final weight

Moisture Uptake:

Weighed films are kept in a desiccator at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using saturated solution of Potassium chloride in a desiccator until a constant weight is achieved.

%Moisture uptake is calculated as given below.

% Moistureuptake = Final weight – Initial weight X 100

Initial weight 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 center 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 = I1 – I2 X 100
I1 I 2 = Final length of each strip
I 1 = Initial length of each strip

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 itbreaks. The number of times the films could be folded at the same place without breaking is folding endurance value.

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, is thickness of film, L is length of film, l is elongation of film at a break point.

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.

Thumb tack test:

The force required to remove thumb from adhesive is a measure of tack.

Rolling ball test: This test involves measurement of the distance that stainless steel ball travels along an upward facing adhesive. The less tacky the adhesive, the further the ball will travel.

Quick stick (Peel tack) test:

The peel force required breaking the bond between an adhesive and substrate is measured by pulling the tape away from the substrate at 90? at the speed of 12 inch/min.

Probe tack test:

Force required to pull a probe away from an adhesive at a fixed rate is recorded as tack.

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2. In vitro release studies:

Drug release mechanisms and kinetics are two characteristics of the dosage forms which play an important role in describing the drug dissolution profile from a controlled release dosage forms and in vivo performance. The dissolution data is fitted to these models and the best fit is obtained to describe the release mechanism of the drug. There are various methods available for determination of drug release rate of TDDS.

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.

The Cylinder modified USP Basket:

(USP apparatus 6 / Ph Eur 2.9.4.3) This method is similar 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.

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 additionpaddle over extraction cell method (Ph Eur 2.9.4.2) may be used.

3. In vitro permeation studies:

The amount of drug available for absorption to the systemic pool is greatly dependent on drug released from the polymeric transdermal films. The drug reached at skin surface is then passed to the dermal microcirculation by penetration through cells of epidermis, between the cells of epidermis through skin appendages.

Usuallypermeation studies are performed by placing the fabricated transdermal patch with rat skin or synthetic membrane in between receptor and donor compartment in a vertical diffusion cell such as franz diffusion cell or keshary-chien diffusion cell. The transdermal system is applied to the hydrophilic side of the membrane and then mounted in the diffusion cell with lipophillic side in contact with receptor fluid. The receiver compartment is maintained at specific temperature (usually 32±5°C for skin) and is continuously stirred at a constant rate. The samples are withdrawn at different time intervals and equal amount of buffer is replaced each time. The samples are diluted appropriately and absorbance is determined spectrophotometrically. Then the amount of drug permeated per centimeter square at each time interval is calculated. Design of system, patch size, surface area of skin, thickness of skin and temperature etc. are some variables that may affect the release of drug. So permeation study involves preparation of skin, mounting of skin on permeation cell, setting of experimental conditions like temperature, stirring, sink conditions, withdrawing samples at different time intervals, sample analysis and calculation of flux i.e., drug permeated per cm2 per second.

V. PREPARATION OF SKIN FOR PERMEATION STUDIES:

Hairless animal skin and human cadaver skin are used for permeation studies. Human cadaver skin may be a logical choice as the skin model because the final product will be used in humans. But it is not easily available. So, hairless animal skin is generally favored as it is easily obtained from animals of specific age group or sex.

Intact Full thickness skin:

Hair on dorsal skin of animal are removed with animal hair clipper, subcutaneous tissue is surgically removed and dermis side is wiped with isopropyl alcohol to remove residual adhering fat. The skin is washed with distilled water. The skin so prepared is wrapped in aluminum foil and stored in a freezer at -20C till further use. The skin is defrosted at room temperature when required.

Separation of epidermis from full thickness skin: The prepared full thickness skin is treated with 2M sodium bromide solution in water for 6 h. The epidermis is separated by using a cotton swab moistened with distilled water. Then epidermis sheet is cleaned by washing with distilled water and dried under vacuum. Dried sheets are stored in desiccators until furtheruse.

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Table 1: Available medications for transdermal delivery

Drug	Trade name	Type of transdermal patch	Manufacturer	Indication
Fentanyl	Duragesic	Reservoir	Alza / Janssen Pharmaceutica	Moderate/ Severe pain
Nitroglycerine	Deponit ,Minitran, Nitrodisc,Nitrodur, Transderm,Nitro	Drug in adhesive, Drug adhesive, Micro reservoir In Matrix Reservoir	Schwarz Pharma,3M, Key Pharmaceuticals Searle, USA Pharmaceuticals, Alza/Novartis	Angina Pectoris
Nicotine	Prostep,Nicotrol , Habitraol	Reservoir,Drug in, adhesive Drug in adhesive	ElanCorp/Lederle Labs, Cygnus Inc /McNeil Consumer	Smoking Cessation
Testosterone	Androderm ,Testoderm TTS	Reservoir, Reservoir Thera Tech	Products Ltd, Novartis GlaxoSmithKline ,Alza in males	Hypogonadism
Clonidine	Catapres-TTS	Membrane matrix hybrid type	Alza/Boehinger Ingelheim	Hypertension
Lidocaine	Lidoderm	Drug in adhesive	Cerner Multum, Inc.	Anesthetic
Scopolamine	Transderm Scop	Membrane matrix hybrid type	Alza/Novartis	Motion sickness
Estradiol, Ethinyl Estradiol	Climara ,Vivelle,Estraderm Esclim,OrthoEvra	Drug in adhesive Reservoir, Labs, Novel Pharma/Novartis	3M Pharmaceuticals/ First syndrome Berlex, Alza /Novartis, Women Healthcare, Inc., Johnson & Johnson	Postmenstrual

4. 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.

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 determine mainly 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.

VI. FACTORS AFFECTING TRANSDERMAL PERMEATION

1. Penetrate concentration

Increasing concentration of dissolved drug causes a proportional increase in flux. At concentration higher than the solubility, excess solid drug functions as a reservoir and helps to maintain a constant drug concentration for a long period of time.

International Journal of Pharmaceutical Research and Applications
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2. Partition coefficient

A lipid/water partition coefficient value of 1 or greater is required for optimal transdermal permeability. It may be altered by chemical modification without affecting the pharmacological activity of the drug.

3. pH conditions

Applications of solutions whose pH values are either in high or low extremities can be destructive to the skin. With moderate pH values, the flux of ionizable drugs is affected by changes in pH that alter the ratio of charged and uncharged species and their transdermal permeability.

4. Release characteristics

Solubility of the drug in the vehicle affects the release rate. The mechanism of drug release depends on the following factors:

a. Whether the drug molecules are dissolved or suspended in the delivery systems.
b. The interfacial partition coefficient of the drug from the delivery system to the skin tissue.
c. pH of the vehicle

5. Composition of the drug delivery systems

The composition of the drug delivery system which includes boundary layers, thickness, polymers and vehicles which not only affects the rate of drug release, but also the permeability of the stratum corneum by means of hydration, making with skin lipids, or other sorption promoting effects e.g., benzocaine permeation decreases with PEG of low molecular weight.

VII. EVALUATION PARAMETERS

1. Interaction studies

Excipients are an essential part of any formulation. No dosage form is possible to formulate with only drug. Interaction studies are performed to confirm the absence of any chemical reaction between drug and excipients of the formulation during various stages of manufacturing process. Interaction studies are performed by various analytical techniques like:

A. UV spectroscopy.
B. Thermal analysis.
C. FT-IR spectroscopy.
D. Chromatographic techniques.

2. Weight uniformity

The prepared patches are dried for 4 hours at 60C before performing the test. A specific part of a definite dimension is cut from various parts of the patch and weighed on a digital balance. The average weight and standard deviation values are then calculated.

3. Thickness of the patch

The thickness of the drug loaded patch is determined at different points by using a digital micrometer. The average thickness and standard deviation are then calculated from individual values.

5. Percentage Moisture content

The drug loaded patches are weighed individually and kept in a desiccator containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs the films are reweighed. Determine the percentage moisture content from the below mentioned formula:

% moisture content = [Initial weight- Final weight/ Final weight] ×100.

5. Percentage Moisture uptake

The drug loaded patches are weighed and kept in a desiccator at room temperature for 24 hrs containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 hrs the films are reweighed and the percentage moisture uptake is determined from the below mentioned formula:
% moisture uptake = [Final weight- Initial weight/ initial weight] ×100.

6. Folding endurance

A strip of specific dimension is cut evenly and repeatedly folded at the same place until it breaks. The number of times the film could be folded at the same place without breaking indicates the magnitude of folding endurance. Usually the test is repeated for 5 patches selected at random. The average value and standard deviation are then calculated.

7. Water vapour permeability (WVP) evaluation

Water vapour permeability is determined by foam dressing method. The air forced oven is replaced by a natural air circulation oven. The WVP can be determined by the following formula:

WVP=W/A

Where, WVP is expressed in gm/m2 per 24hrs, W is the amount of vapour permeated through the patch expressed in gm/24hrs and A is the surface

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area of the exposure samples expressed in m^2.

8. Uniformity of dosage unit test

An accurately weighed portion of the patch is cut into small pieces and transferred to a volumetric flask. Contents of the flask are dissolved in a suitable solvent and sonicated for complete dissolution of drug from the patch and made up to the mark with same. The resulting solution was allowed to settle for about an hour, and the supernatant was suitably diluted to give the desired concentration with suitable solvent. The solution was filtered using 0.2µm membrane filter and analyzed by suitable analytical technique (UV or HPLC).

9. Drug content

A specified area of patch is to be dissolved in a suitable solvent in volumetric flask. The solution is then filtered through a filter medium and analyzed using suitable method (UV or HPLC technique).

10. Shear Adhesion

This test is to be performed for the measurement of the cohesive strength of adhesives. It dependent on molecular weight, the degree of cross linking and the composition of polymer, type and the amount of tackifier added. An adhesive coated tape is applied onto a stainless steel plate; a specified weight is hung from the tape, to affect its pulling in a direction parallel to the plate. Shear adhesion strength is determined by measuring the time it takes to pull the tape off the plate. The longer the time take for removal, greater is the shear strength.

11. **Polariscopeexamination**

This test is performed to examine the drug crystals from patch by using a polariscope. A specific surface area of the piece is to be kept on the object slide and observed for drug crystals to distinguish whether the drug is present in crystalline form or amorphous form.

12. **Thumbtacktest**

It is a qualitative test to evaluate tack property determination of adhesive. The thumb is simply pressed on the adhesive and the relative tack property is detected.

13. Flatness test

Three longitudinal strips are cut from each film from different portion like one from the center, other one from the left side, and another one from the right side. The length of each strip was measured and the variation in length because of non-uniformity in flatness was measured by determining percent constriction, with 0% constriction equivalent to 100% flatness. The average value and standard deviation are calculated.

14. Peel Adhesion test

In this test, the force required to remove an adhesive coating form a test substrate is determined. Molecular weight of adhesive polymer, the type and amount of adhesives are the variables that determined the peel adhesion properties. A single tape is applied to a stainlesssteel plate or a backing membrane and then the tape is pulled from the substrate at 180º. The force required to remove the tape is measured.

15. Rolling ball tack test

This test measures the softness of a polymer that relates to tack. In this test, stainless steel ball of 7/16 inches in diameter is released on an inclined track so that it rolls down and comes into contact with horizontal, upward facing adhesive. The distance travelled by the ball along the adhesive provides the measurement of tack, which is expressed in inch.

16. Percentage Elongation break test

The percentage elongation break is determined by noting the length just before the break point, the percentage elongation can be determined from the below mentioned formula:

Elongation percentage = L1-L2/ L2 × 100

Where, L1is the final length of each strip and L2 is the initial length of each strip.

17. Probe Tack test

In this test, the tip of a clean probe with a defined surface roughness is brought into contact with adhesive. A bond is formed between probe and adhesive during this contact time. The subsequent removal of the probe mechanically breaks it. The probe is pulled away and force required to pull the probe away is determined.

18. Quick Stick (peel-tack) test

In this test, the tape is pulled away from the substrate at 90ºC at a speed of 12 inches/min. The peel force required to break the bond between adhesive and substrate is measured and recorded as tack value, which is expressed in ounces or grams per inch width.

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19. In vitro drug release studies

This test was performed using franz diffusion cell. The dissolution medium used was phosphate buffer (pH 7.4). Samples were withdrawn maintaining sink conditions and were evaluated for drug content using suitable analytical techniques.

20. Skin Irritation study

This test is performed on animals and human volunteers. Relevant approvals and permissions form various regulatory boards are a must to proceed with the test. Pre-treatment of the animal to remove the hair is necessary. Various dehairing techniques can be employed. The patch is to be removed after 24 hr and the skin is to be observed and classified into 5 grades on the basis of the severity of skin injury.

21. 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 were withdrawn at 0, 30, 60, 90 and 180 days and analyze suitably for the drug content

VIII. CONCLUSION

- Transdermal drug delivery is hardly an old technology, and the technology no longer is just adhesive patches. Due to the recent advances in technology and the incorporation of the drug to the site of action without rupturing the skin membrane transdermal route is becoming the most widely accepted route of drug administration.
- A rich area of research over the past 10 to 15 years has been focused on developing transdermal technologies that utilize mechanical energy to increase the drug flux across the skin by either altering the skin barrier (primarily the stratum corneum) or increasing the energy of the drug molecules.

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