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Review of Transdermal Patches

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ABSTRACT

A transdermal patch is a medicated adhesive patch that is applied to the skin to deliver a specific amount of medication through the skin and into the bloodstream. The transdermal drug delivery system is a novel drug delivery system that overcomes the issues associated with traditional dosage. The domain "Transdermal Patches" consists of four modules dealing with different topics. The first module is about introduction. The second module demonstrates preformulation, excipient selection criteria, formulation, and preparation methods. The third module discusses the evaluation and stability studies. The fourth Module covers storage, packaging, and labelling.

SYSTEM FOR TRANSDERMAL DRUGS DELIVERY

One system that falls under the category of controlled drug delivery is the transdermal drug delivery system (TDDS), whose goal is to deliver the medication through the skin at a predetermined and controlled rate.Longer therapeutic effect, fewer side effects, increased bioavailability, better patient compliance, and simple drug therapy termination are just a few of its many benefits. For most molecules, the stratum corneum is thought to be the rate-limiting barrier in transdermal permeation.

ADVANTAGES

- extended period of time spent in action.
- decrease in the dosage's frequency.
- increased homogeneity of plasma levels.

DISADVANTAGES

- potential for skin irritation, contact dermatitis, or localized irritation at the application site brought on by the medication or its excipients.
- How many drugs can be delivered this way is limited by the permeability of skin.

TRANSDERMAL PATCHES.

A transdermal patch is used to administer a specific amount of medication through the skin and into the bloodstream. In 1981, the FDA approved the first transdermal patch products. Transdermal delivery provides controlled, consistent drug administration, allowing continuous input of drugs with short biological half-lives while eliminating pulsed entry into systemic circulation. TDDS has numerous advantages over standard injection and oral methods.

The main components to a transdermal patch are:

(1) Liner - Keeps the patch safe during stoThe liner is removed prior to use.

(2) Drug - The drug solution makes direct contact with

(3) Adhesive - Helps to hold the patch's components together while also adhering the patch to(4) Membrane - Controls drug release from reservoirs and multi-layer patches.

(5) Backing - protects the patch from the outside environment.

TYPES OF TRANSDERMAL PATCHES

A. Single-layer Drug-in-Adhesive

The drug is located in the system's adhesive layer.In this type of patch, the adhesive layer not only holds the various layers together and the entire system to the skin, but it is also responsible for drug release. A temporary liner and backing are used to surround the adhesive layer.

B. Multilayer drug-in adhesive

The multi-layer drug-in adhesive patch, like the single-layer system, is responsible for drug release through both adhesive layers.One layer is for immediate release of the drug, while the other is for controlled release of the drug from the reservoir. The multi-layer system differs in that it includes an additional layer of drug-in-adhesive, typically separated by a membrane. This patch also features a temporary liner layer and a permanent backing.

C. Reservoir

The reservoir transdermal system, as opposed to the single- and multi-layer drug-in-adhesive systems, has a separate drug layer.The drug layer is a liquid compartment that contains a drug solution or suspension and is separated by an adhesive layer. The backing layer provides additional support for this patch. This system's release rate is zero order.

C. Matrix

The Matrix system includes a drug layer made of a semisolid matrix that contains a drug solution or suspension.The adhesive layer in this patch surrounds and partially overlays the drug layer. Also called a monolithic device.

E. Vapour Patch

In this type of patch, the adhesive layer not only adheres the various layers together, but it also releases vapour.Vapour patches are new to the market and can release essential oils for up to 6 hours. The vapour patches release essential oils and are primarily used to relieve congestion.

ADVANTAGES

1. It is a simple method that requires only once a week application. Such a simple dosing regimen can help patients adhere to their drug therapy.

2. Transdermal drug delivery can be used to treat patients who are unable to tolerate oral dosage forms.

3. It is especially beneficial to patients who are nauseated or unconscious.

4. Drugs that cause gastrointestinal upset may be suitable for transdermal delivery because this method avoids direct effects on the stomach and intestine.

5. Drugs that are degraded by enzymes and acids in the gastrointestinal system may also be viable targets.

6. Transdermal administration allows for the avoidance of first pass metabolism, which is another limitation of oral drug administration.

7. Drugs that require relatively stable plasma levels make excellent candidates for transdermal drug delivery.

DISADVANTAGES

1. It is possible that local irritation will occur at the application site.

2. The drug, adhesive, or other excipients in the patch formulation can all cause erythema, itching, and local edema.

3. It is possible to develop allergic reactions.

4. It is essential that the molecular weight be less than 500 Da.

PREFORMULATION STUDIES.

Drug preformulation studies encompass a range of analytical techniques such as identification, thin-layer chromatography, drug-excipient interaction, melting point, calibration curve, Fourier Transform Infrared analysis, and solubility studies.

Drug Identification and Characterization Methods

a) Organoleptic properties**:** The color, odor, taste, and state of the drug were used to examine its organoleptic properties.

b) The melting point of the drug was determined by placing a small amount of drug in a capillary tube that was closed at one end and placed in a melting point apparatus, and the temperature at which the drug melts was recorded.

c) UV Absorption Maxima: A UV spectrophotometer was used to identify the drug. The drug's λmax was determined based on its spectra. The calibration curve for the medication was created using the spectral data obtained from this scan.

d) Fourier Transform Infra-Red analysis: To identify the compounds in the sample, FTIR analysis was performed. To avoid air entrapment, the drug powder was gently positioned over the sample holder, and the sample was scanned.

e) Solubility: The drug's solubility was assessed in a range of solvents, such as water, methanol, and ethanol.

DRUG EXCIPIENT COMPATIBILITY STUDIES

Study of drug-excipient compatibility is an important phase in the pre-formulation study of drug development.

Analytical Techniques Used to Detect Drug-Excipient Compatibility

Fourier Transform Infrared Spectroscopy (FT-IR)

Using the potassium bromide discs method, FT-IR spectra were recorded on an instrument Shimadzu FT-IR 8400S in the frequency range of 400–4000 cm-1 with a resolution of 4 cm-1.For one month, the medication and each of the chosen excipients (1:1 w/w) were kept at 40 ± 20C. The drug and excipient mixture were ground, as well as individual samples.

combined completely with potassium bromide in a mortar for three to five minutes, and then compressed into a disc for five minutes under five tons of pressure. The range of 0.2% to 1% is where the sample concentration in potassium bromide should be. After the disc was put in the path of light, the spectrum was collected and examined for signs of interaction.

Thermal methods of analyses

Thermal analysis is widely used to quickly assess physicochemical incompatibility and plays a crucial role in compatibility studies.We offer three distinct kinds of thermal analyses, namely:

Differential scanning calorimetry (DSC)

The DSC curves of pure components and those derived from a 1:1 physical mixture are contrasted.A significant shift in the melting of the components or appearance of a new exo/endothermic peak and/or variation in the corresponding enthalpies of reaction in the physical mixture indicate incompatibility.

Isothermal microcalorimetry

It makes it possible to measure minuscule amounts of heat that are absorbed or evolved.The calorimeter is used to measure the individual thermal activities of the API, excipient, and their mixtures as well as to monitor the thermal activity (heat flow) at a constant temperature.

Hot stage microscopy (HSM)

Using a visual thermal analysis technique called HSM, solid-state interactions that DSC might mistakenly interpret as incompatibility can be effectively monitored. Compatibility studies with this technique only require a very small number of samples.

(C) CRITERIA FOR EXCIPIENTS SELECTION

pharmacetical excipient are substances other than the active pharmaceutical ingredient(API). that have been appropriately evaluated for safety and then included in drug delivery system. Excipients are used as bulking agents, protective agents, and to increase the drug's bioavailability.

criteria

• They must be non-toxic

• low cost

• They have to be inert physiologically.

• They must be physically and chemically stable

Polymers

A polymer is a material or substance made up of many repeating subunits that combine to form a very large molecule known as a macromolecule.

1. The polymer should be chemically non reactive or it should be an inert drug carrier.

2. The polymer must not decompose on storage or during the life span.

3. Molecular weight, physical characteristic and chemical functionality of the polymer must allow the diffusion of the drug substance at desirable rate;

4. The polymer and its decomposed product should be nontoxic. It should be biocompatible with skin;

5. The polymer must be easy to manufacture and fabricate into desired product. It should allow incorporation of large amounts of active agent. Eg. HPMC,acrylate copolymer, polyisobutylene

Permeation enhancers

Penetration enhancers are the substances used to increase permeation of skin mucosa. Absorption promoters or enhancers are other names for penetration enhancers, which are substances that increase the amount of penetrant absorbed through the skin. Penetration enhancers used to increase the permeability of drug through skin

Properties

• It should have no pharmacological activity within body.

• It should be cosmetically acceptable.

• It should be odorless, tasteless, colorless and inexpensive

• These materials should be non toxic, non irritating, pharmacologically inert, non allergic.

• It needs to be stable both physically and chemically.

Eg.1.synthetic:.Sulphoxides ,2.Natural:.Terpens-Menthol,3.Essential oil-Basil oil, Neem oil.

Adhesive

Serve to adhere the compound of the patch together along with adering the patch to the skin Properties

• Should not irritate the skin

• Should adhere to the skin aggresiveily

• Should easily removable

• Should have an intimate contact with skin

• Permeation of drug should not be affected

Eg,rubber based pressure sensitive adhesives, acrylic PSA, etc..

Backing membrane

To preserve system stability and protect the layer

Properties

• Flexible and provide good bond to drug reservoir

• It should be impermeable

Eg,metallic plastic laminate, plastic laminate with absorbent pad, occlusive base plate **Release liner**

Before applying the patch, remove and discard the film that covers the adhesive side of the transdermal drug delivery system.

Properties

• Usually, a very light touch of a finger is sufficient to adhere them to a surface, such as skin; • They can be removed from the skin easily and without leaving any residue on its surface.

Eg, polyacrylates (acrylates), polyisobutylene (PIB) or polydimethylsiloxane (silicone)

METHODOLOGY

1.Polymer membrane permeation controlled TDDS

This system embeds the drug reservoir between a rate-sensitive backing layer and an impermeable layer. regulating membrane. Only the rate-regulating membrane allows the medication to release, which can either non-porous or microporous. Within the drug reservoir compartment, the drug may take the following forms: in a solid polymer matrix as a suspension, solution, or dispersion.

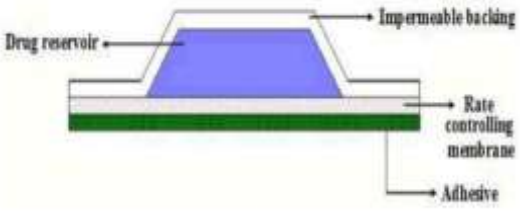

Fig.1: polymer membrane permeation controlled TDDS

2. Adhesive diffusion controlled TDDS

The medication reservoir is created by melting the adhesive onto an impermeable backing layer or by dispersing the medication in an adhesive polymer and then spreading the medicated polymer adhesives by solvent casting.After that, a non-medicated, constant-thickness adhesive polymer is applied to the drug reservoir layer. For example: Deponit (nitroglycerin).

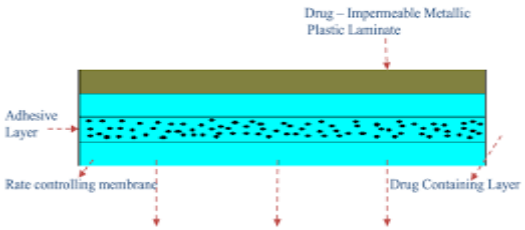

Fig.2: adhesive diffusion controlled TDDS

3. Matrix diffusion controlled TDDS

The medication is uniformly distributed within a hydrophilic or lipophilic polymer matrix.

containing polymer disk is subsequently secured to an occlusive base plate within a manufactured compartment.

impermeable backing layer of a medication, such as Nitrodur (nitroglycerine).

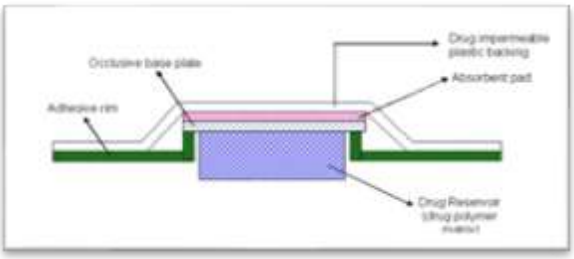

Fig.3: matrix diffusion controlled TDDS

4. Microreservoir controlled TDDS

The drug reservoir is created by combining the matrix dispersion system with the reservoir.

through the drug's suspension in an aq. water-soluble polymer solution, followed by the dispersion of the

uniformly dissolve in a lipophilic polymer to create tiny drug reservoir spheres.

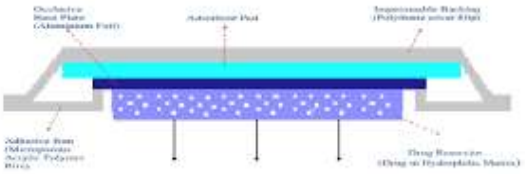

Fig.4: microreservoir controlled TDDS

The process of developing a drug's dosage forms rationally begins with pre-formulation testing.

It can be characterized as an examination of the chemical and physical characteristics of the drug substance both on its own and in combination with excipients.The overall objective of the pre-formulation testing is to generate information useful to the formulator in developing stable and bioavailability dosage forms which can be mass produced.

IDENTIFICATION AND CHARACTERISATION OF DRUG

a) Organoleptic properties

Organoleptic characteristics of the drug were investigated on the basis of color, odor, taste and State.

b) Melting Point:

Melting Point Apparatus was used to determine quercetin's melting point.c) UV Absorption Maxima :

The drug was identified using the UV spectrophotometric method. The spectra revealed that quercetin's λmax was measured at 256 nm. The quercetin calibration curve was created using the spectral data from this scan.

d) Fourier Transform Infra-Red analysis:

To identify the compounds in the sample, FTIR analysis was done.After making sure there was no air trapping beneath the powdered medication, the sample was carefully placed over the sample holder and scanned.

e) Solubility:

Quercetin's solubility was examined in a variety of solvents, including water, methanol, and ethanol.

f) Partition Coefficient:

Quercetin's partition coefficient was determined using the straightforward Shaking Flask method.10 milligrams. 10 milliliters of drug was dissolved. of 10 ml and a pH 7.2 phosphate buffer system. in a separating funnel of octanol. After being vigorously shaken for a full day by an orbital shaker, it was left to stand for total phase seThe UV spectrophotometric method was used to measure the drug's concentration.

Excipient drug compatibility studies

Compatibility studies for drug excipients are a crucial part of the preformulation phase of drug development.Drug-excipient interactions may have an impact on the dosage form's stability, bioavailability, chemistry, and physical characteristics.

EVALUATION OF FORMULATION

It takes a lot of research and a complex process to develop a transdermal dosage form with controlled release.Transdermal patches, which administer a lower dose of the medication at a predetermined rate, have been developed to increase patient compliance and improve the clinical efficacy of the drug. The study can be categorized into three types: physicochemical evaluation, in-vitro evaluation, and in-vivo evaluation. It is predictive of transdermal dosage forms.

1.Evaluation of physical parameters

a. Patch thickness: To verify the thickness of the prepared drug patch, the thickness is measured at various points along the patch using a digital micrometer. The average thickness and standard deviation are then calculated.

b. Physical Appearance and Surface Texture: These factors encompass both the patch's visual examination and the assessment of its texture through tactile or feel assessment.

c. Folding endurance involves cutting a particular section of the strip and folding it in the same spot repeatedly until it breaks. The number of times the film could be folded without breaking gave the value of endurance

d. Weight variation test:

figuring out the irregular drug distribution

Weight variation was calculated using the formula -

(Initial weight - Average weight)/Average weight X 100

e. Moisture absorption: The patches were precisely weighed and put in a desiccator with 100 milliliters of a saturated aluminum chloride solution to keep the humidity level constant.After 3 days the film s were taken out and weighed. Using the formula, the percentage of moisture absorption was determined.

Moisture absorption =[final weight –initial weight/initial weight x 100]

2.In vitro Evaluation of TDDS

a. In vitro

- The drug release from the prepared patches can be evaluated using the paddle over disc method (• Dry films with a known thickness need to be weighed, cut into a specific shape, and adhered to a glass plate using an adhesive.
- After the apparatus was equilibrated, the glass plate was submerged in 500 mL of the phosphate buffer or dissolution medium.
- Next, the paddle was moved at a speed of 50 revolutions per minute and positioned 2.5 centimeters away from Samples can be taken out at suitable intervals for up to 24 hours, and UV spectrophotometer or HPLC analysis can be performed.
- The mean value of the experiment can be computed, and it must be carried out in triplicate.

3.In vivo Evaluation

The most accurate representation of a drug's performance comes from in vivo tests.In vivo studies allow for the full exploration of variables that are not possible to account for in vitro studies.

STABILITY STUDIES

When designing a TDDS, stability is a crucial factor to take into account as it impacts both patient compliance and the system's therapeutic efficacy.In this instance, prepared patches were stored for 30 days at room temperature after being wrapped in aluminum foil. The patches were examined for their drug release profile over the course of 30 days on the skin of the rats. Formulation P1 was chosen for this investigation because, based on all previous evaluation studies conducted on this formulation, it appeared to be quite promising.

TYPES OF STABILITY STUDIES ON DRUG SUBSTANCES

Physical stability

The appearance, color, dissolveability, palatability, and suspendability of the original physical attributes are preserved.Physical stability is crucial for the product's safety and effectiveness because it can influence uniformity and release rate.

Chemical stability

It is the propensity to resist alteration or breakdown brought on by reactions brought on by temperature, air, atmosphere, etc.

Microbiological stability

The propensity of the medications to become resistant to microbial growth and sterility is known as their microbiological stability.Within predetermined bounds, the antimicrobial agents utilized in the preparation maintain their efficacy. The sterile pharmaceutical product may be at risk due to this microbiological instability.

Therapeutic stability

The medication's therapeutic effect (Drug Action) is unaltered.

Toxicological stability

There is no appreciable increase in toxicity associated with toxicological stability.

STABILITY TESTING METHODS

At different phases of the product development process, stability testing is a procedure carried out for all pharmaceutical products.

1. Real-time stability testing

Under the suggested storage conditions, real-time stability testing is typically carried out for an extended period of time to allow for notable product degradation.The period of time for the test of the product depends on the stability of the product which clearly tells that the product is not degraded or decomposed for a long time.

2. Accelerated stability testing

Higher temperatures are used for this kind of stability testing, which determines how the product decomposes.The data is used to compare the relative stability of different formulations or to forecast the shelf life.

The Arrhenius equation predicts the accelerated stability studies with ease.

$K = Ae^{-Ea/RT}$ Log

where

K= Specific rate constant

A= Frequency factor or Arrhenius factor

Ea= Energy of activation

R= Real gas constant 4.184 j/mol. k

T= Absolute temperature

The medications are kept using this method at a variety of temperatures, including 40, 60, 70, 80, and 100 degrees.

3. Retained sample stability testing

Both room temperature and refrigerator temperature are to be used for these investigations.To test for stability, a single batch is chosen and kept under observation for a full year. Two batches of samples are created if there are more than fifty samples total. The shelf life is predicted in part by the stability studies of the samples. Every product could have a maximum shelf life of five years, which is five years longer than the test samples' three to six years. 36, 48, 60, 12, 18, and 24 months. Another name for this testing technique is the constant interval method.

3. Cyclic temperature stress testing
4. Product sampling is not a common application for this technique.Using this approach, cyclic temperature stress tests are created with product knowledge to replicate possible market-place storage conditions. In this testing, the sampling is thought to be carried out in a 24-hour cycle, or what is known as the earth's 24-hour rhythm.

PACKAGING AND LABELLING

PACKAGING

Materials and processes for making laminate materials that can be used to package a transdermal drug delivery system that includes a polyester film and a rubber-modified acrylonitrile methyl acrylate copolymer film, either separately or in combination. The polyester film ensures that the active drug included in the transdermal system is stable and largely soluble in the system while being stored before use.The packaging laminate is preferably translucent to allow visual inspection of its contents, and has sufficient tear resistance to substantially provide child resistant and/or proof properties.

Packaging of transdermal patches

LABELLING

Particulars to appear on the outer packaging and minimum particulars to appear on pouch for individual patch sachet

1. NAME OF THE MEDICINAL PRODUCT

2. STATEMENT OF ACTIVE SUBSTANCE(S)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

5. METHOD AND ROUTE(S) OF ADMINISTRATION

• Transdermal use.

• Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

• Keep unused and used patches out of children's sight and reach.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

• Do not store above 25ºC.

• Store in the original sachet in order to protect from moisture

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

12. MARKETING AUTHORISATION NUMBER(S)

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16.INFORMATION IN BRAILLE

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