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DEVELOPMENT AND EVALUATION OF PANTOPRAZOLE SODIUM TRANSDERMAL PATCHES FOR ULCER THERAPY

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Abstract: A key component of novel drug delivery systems is the transdermal drug delivery system (TDDS). All topically applied medication formulations meant to release the active ingredient into the bloodstream are collectively referred to as transdermal delivery systems. Transdermal drug delivery systems are composed of polymeric formulations that, when applied topically, distribute the medication throughout the dermis at a predefined rate, resulting in systemic effects. Reduced adverse effects, more consistent plasma levels, better bioavailability, controlled absorption, easy application, and flexibility in stopping drug administration by only removing the patch from the body. Nowadays, a lot of topical, cosmetic, and transdermal delivery systems use transdermal patches. These patches are a significant result of the advancements in skin science, technology, and knowledge that have been made possible by clinical observation, trial and error, and evidence-based research that go all the way back to the earliest known human records.(1)

I. INTRODUCTION

Transdermal therapy systems are intended to deliver medications to the systemic circulation through the skin in a controlled, continuous manner.

There are essentially four methods that enable efficient medication absorption throughout the skin:

- The drug reservoir in the micro sealed system, a partition-controlled delivery system, holds a saturated drug suspension in a water-miscible solvent that is uniformly distributed throughout a silicone elastomer matrix.
- The matrix-diffusion controlled system is a second system.
- The membrane-permeation controlled system is the third and most used transdermal medication delivery method.
- Recently, the gradient charged system has been made available as a fourth system. (2)

Transdermal drug delivery systems are topical medications applied topically in the form of patches that distribute medications at a predetermined and regulated rate for systemic effects. An alternative method of delivering medication is offered by a transdermal drug delivery device, which can have an active or passive design. These devices facilitate the delivery of medications 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.(3)

COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEMS:

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

❖ **Polymer Matrix or matrices:** The Polymer controls the release of the drug from the device. Possible useful polymers for transdermal devices are

- Natural Polymers: eg. Cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.
- Synthetic Elastomers: e.g. Polybutadieine, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene butadieine rubber, Neoprene etc.
- Synthetic Polymers: e.g. Poly vinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinylpyrrolidone, Polymethylmethacrylate, Epoxy etc. (4)(5)

❖ **The Drug:** Carefully selecting the medicine is essential for the successful development of a transdermal drug delivery system.

Properties of drug:

a) The drug should have a molecular weight less than approximately 1000daltons.
b) The drug should have affinity for both – lipophilic and hydrophilic phases.
c) Extreme partitioning characteristics are not conducive to successful drug delivery via the skin.
d) The drug should have low melting point(6)

❖ **Permeation enhancers:** These substances change the skin's ability to act as a barrier to the flow of a desired penetrant, increasing skin permeability.

Permeation enhancers include:

I. Solvents : Examples include water alcohols – methanol and ethanol; alkyl methyl sulfoxides – dimethyl sulfoxide, alkyl homologs of methyl sulfoxide dimethyl acetamide and dimethyl formamide ; pyrrolidones – 2 pyrrolidone, N methyl, 2-pyrrolidone; miscellaneous solvents – propylene glycol, glycerol

II. Surfactants :

a) Anionic: e.g. Dioctyl sulphosuccinate, Sodium lauryl sulphate, Decodecylmethyl sulphoxide etc.

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

III. Biary system: These systems apparently open up the heterogeneous multi laminate pathway as well as the continuous pathways e.g. Propylene glycol-oleic acid and 1, 4-butanediol-linoleic acid.(7)

IV. Miscellaneous chemicals: These include urea, a hydrating and keratolytic agent; n-dimethyl-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.(8)(9)

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

II. TYPES OF TRANSDERMAL PATCHES:

There are different types of transdermal patches present in market some of types are:

1. Single layer drug in adhesive
2. Multilayer drug in adhesive
3. Drug reservoir in adhesive
4. Drug matrix in adhesive

Single layer drug in adhesive : The medicine is included directly into the skin-contacting adhesive in the Single-layer medicine-in-Adhesive technology. The adhesive in this transdermal system design acts as both the foundation for the formulation, holding the medicine and all of the excipients beneath one backing film, in addition to attaching the system to the skin. (10)

Multilayer drug in adhesive : Similar to the Single layer Drug-in-Adhesive, the Multi-layer Drug-in-Adhesive incorporates the drug directly into the adhesive. The term "multi-layer" refers to two different approaches of adding drug-in-adhesive layers adding a membrane between two different layers or adding drug-in-adhesive layers under one backing film.

Drug reservoir in adhesive :

A liquid compartment holding a medication solution or suspension and kept apart from the release liner by an adhesive and semi-permeable membrane define the Reservoir transdermal system design.

Drug matrix in adhesive :

A semisolid matrix containing a medication solution or suspension in direct contact with the release liner characterizes the design of the Matrix system. The skin-adhering component is integrated into an overlay and surrounds the semisolid matrix in a circular pattern.(11)(12)

III. EVALUATION OF TRANSDERMAL PATCHES :

Transdermal patches, which administer a lower dose of the medication at a predefined rate, have been created to increase patient compliance and improve the clinical efficacy of the treatment. Because of this, evaluation studies become even more crucial to ensuring the intended performance and repeatability of the system within the designated environmental parameters. These studies fall into the following categories:

1. Physicochemical evaluation
2. In vitro evaluation
3. In vivo evaluation (13)

1. **Physicochemical evaluation** :

I. **Thickness:** The thickness of transdermal film is determined by dial gauge, screw gauge or micrometer at different points of the film.

II. **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.

III. Uniformity of weight: Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not be different from the average weight.(14)

IV. Moisture content: The prepared films are weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 hrs. 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

For Final weight Moisture Uptake:

For a full day, weighed films are stored at room temperature in a desiccator. After that, they are removed and placed in a desiccator with a saturated potassium chloride solution at 84% relative humidity, or until a consistent weight is reached.% moisture uptake is calculated as .(15)

% Moisture uptake = Final weight – Initial weight X 100

For Initial weight Moisture Uptake :

- **Flatness :**

The surface of a transdermal patch should be smooth and should not shrink over time. To determine the flatness of the patches, two strips are cut from each side and one from the center. Every strip is measured for length, and any variations in length are calculated by calculating the percentage of constriction. on.

Zero percent constriction is equivalent to 100 percent flatness. (16)(17)

% constriction = $I_1 – I_2$ X 100

I_2 = Final length of each strip

I_1 = Initial length of each strip

- **Folding endurance :**

The process of evaluating folding endurance is figuring out how well films that are frequently folded under harsh conditions can fold. The film is folded at the same spot repeatedly until it breaks to assess the folding endurance. Folding endurance value is the number of times a film might be folded in the same direction without breaking. (18)(19)

- **Tensile Strength:**

Polymeric films are sandwiched separately between corked linear iron plates in order to measure tensile strength. An iron screen holds one end of the films in place, while a pulley connects the other end to a freely moveable thread. The pan is gradually filled with weights by attaching the hanging end of the thread to it. The film's elongation is measured using a pointer on the thread. It is remarked that the weight is just right to shatter the film. The following formula can be used to determine the tensile strength(20)(21)(22)

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

F= force required to break

a = width of film

b = thickness of film

L = length of film

l = elongation of film at break point.(23)

- **Tack properties :**

The amount of tack in a polymer is determined by its molecular weight, composition, and usage of tackifying resins.

A. **Thumb tack test:**

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

B. **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.(24)(25)

C. **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.(29)

2) In vitro drug release studies :

For the in vitro drug release experiments, a **Franz diffusion cell** with a receptor compartment capacity of 60 ml was employed. Using a cellulose acetate membrane from the transdermal matrix-style patches that were manufactured, the medication was identified.

The donor and receptor compartments of the diffusion cell were divided by a cellulose acetate membrane with a pore size of 0.45 µ. The cellulose acetate membrane was covered with the manufactured transdermal patch and sealed with aluminum foil. The receptor compartment of the diffusion cell was filled with 7.4 pH phosphate buffer. (30)(31)(32)

The entire assembly was placed on a hot plate magnetic stirrer, and during the experiments, the solution was continuously stirred at 50 rpm in the receptor (27)(28)compartment using magnetic beads, as stated by Simon et al. The temperature was kept at 37±0.5 °C, which is the average temperature of a human body.

The samples were collected at different times and their drug content was determined using spectrophotometry. Air bubbles can readily enter the receiver compartment during manual sampling, so it is necessary to pay close attention to it the entire time during the experiment.

The receptor step was refilled with an equivalent volume of phosphate buffer for each sample removal.(32)

Skin preparation for permeation studies:

Skin from human cadavers and hairless animals are employed in these investigations. Given that humans would use the finished product, using the skin from cadavers as the skin model makes sense. However, it is not readily accessible. Therefore, hairless animal skin is typically preferred since it may be easily obtained from animals of a particular age or gender. (31)(34)

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