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TRANSDERMAL DRUG DELIVERY SYSTEM: AN INNOVATIVE APPROACH IN DRUG DELIVERY

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ABSTRACT

Administration of medicines by the transdermal route has the advantage of being relative painless. The appeal of using the skin as a medicine entry point is in the case of access, which is huge underpinning circulatory and lymphatic networks, and Non-invasive mode of medicine delivery. Administration of medicines through the skin for systemic effect; So- called transdermal delivery was first used in his 1981 when Ciba geigy retailed the transdermal V(Now retailed as transdermal scop) Prevents associated nausea and vomiting sickness. Transdermal medicine delivery provides controlled release of medicines to the patient. It allows for a stable blood position profile, reduces systemic side goods, and is occasionally too. Present review represents the various novel approaches used in transdermal drug delivery of drug. Along with that how recent technology used for developing transdermal drug delivery system.

1. INTRODUCTION

1.1 Transdermal drug delivery system

Interest in developing new delivery systems for existing drugs in recent years the molecule has been updated. Molecules not only improve the performance of drugs in terms of efficacy and safety, Improved Significant patient compliance and overall treatment efficacy. If new delivery systems can be overcome if properly designed and engineered for specific drugs certain hurdles associated with traditional shipping methods. The drug is partially or partially treated complete degradation prior to reaching the site of action can be effectively achieved with improvement. Bioavailability using new concepts of timed release or pulsed release or enteric delivery. Advances in formulation and innovative routes of administration over the last 20 Years make.[1] Improved understanding of drug transport through tissues during the

present Products or drug delivery systems have been used for centuries to treat topical skin. The use of the skin as a pathway for disease and systemic drug delivery is of relatively recent origin. Drug administration by the transdermal route offers the advantage of being relatively painless. Orally administered drugs experience a hostile environment in the gastrointestinal tract where most drugs are degrades under changing pH conditions or faces solubility issues and most importantly, first-pass metabolism.[2] The appeal of using the skin as a drug entry port lies in access, its vast surface area, and Systemic access with underlying circulatory and lymphatic networks and non-invasive of drug delivery. Delivery of drugs through the skin for systemic action, so-called transdermal delivery first used in 1981 when Ciba-Geigy sold his transdermal V (now transdermal scop) to prevent nausea and vomiting associated with motion sickness.[1]

Over the past two decades, transdermal patches have evolved into a proven technology. Multiple significant clinical advantages over other dosage forms it represents a new trend The Controlled Delivery System has opened up new scientific horizons for innovation. Delivery from Drugs delivered transdermal (through the skin) offer several important advantages over conventional drugs Oral and intravenous routes of administration. Drugs administered transdermal avoid the risks and the inconvenience of intravenous therapy usually reduces the likelihood of overdosing. Allows for easy termination and allows for local and systemic therapeutic effects. Drug delivery innovation is on the rise place at a much faster pace compared to. For the last 20 years. Improve patient compliance and efficacy is an integral aspect of new drugs delivery system[3] Tramadol is a synthetic, potent, atypical, centrally acting analgesic with two distinct mechanisms of action[4] Transdermal medicine dosing provides controlled release of drug in patients and allows for constant blood levels. The result is less systemic side effects and sometimes more efficacy than others dosage form. The main purpose of transdermal drug delivery system is drug delivery minimal inter- and intra-patient systemic circulation through the skin at a defined rate change. In addition, transdermal patches are easy to use, convenient, and painless. Because they offer multi-day dosing, they are widely recognized to improve patient compliance.[1] A "patch" or the like is a dosage form designed to deliver a therapeutically effective amount of a drug through a patient's skin.

1.2 TRANSDERMAL PATCH

A transdermal patch is defined as a tenacious treated patch that's applied to the skin. Delivers a precise cure of medicine through the skin into the bloodstream at a destined rate release and

enter the body[5] presently, substantially transdermal systems are on the request it's grounded on a semipermeable membrane called a patch. transdermal medicine delivery a system (TDDS), also known as a" transdermal patch" or" dermal patch", is a lozenge form. Designed to deliver therapeutically effective quantities of medicine across and into the case's skin blood inflow motes pass through the SC in three ways optimal treatment results bear further than just the right medicine[6] Not just picky, but effective medicine delivery the skin on the average adult body occupies a face area of about 2 m 2 and contains about one- third of the blood that circulates in the body. Last 30 times[7] Trans cellular, intercellular, or adnexal pathways almost products reach the feasible epidermis resistant prolixity marvels.[8] Keep the patch in close contact with the skin, medicine- containing suspense.[9]

ADVANTAGES

• Hepatic first-pass metabolism, salivary metabolism, and intestinal metabolism are avoided.

• Ease of use allows patients to self-administer these systems.[10]

• In case of emergency, patch can be removed at any time during treatment Stop drug supply immediately.

• Can avoid first-pass metabolism and gastrointestinal incompatibilities.[15]

• Because skin composition is structurally and biologically the same for almost everyone human inter- and intra-patient variability is minimal.

• Adequate dosing of GI and absorbable drugs through the skin.

• For drugs with short biological duration, continuous non-invasive infusion is possible. A half-life the would otherwise require frequent dosing.

• Conventional oral dosage forms suffer from a significant drawback of low bioavailability due to hepatic first-pass metabolism.[11]

• Less frequent dosing improves patient compliance.

• Treatment failure related to irregular dosing with conventional agents treatment can be avoided.

• Consistent and optimal blood concentration times minimize side effects profile.

• Avoids the risks, pain, and discomfort associated with parenteral therapy. Release longer than oral sustained drug delivery systems.

DISADVANTAGES

• Possible skin irritation with one or more formulations component.

• Dose dumping can occur if the drug binds to the skin.

• For use only in chronic conditions where long-term drug therapy is desired periods that include hypertension, angina, and diabetes.[10]

• Delay time is variable and can vary from hours to days depending on the drug candidate.

• Skin metabolism influences the therapeutic performance of the system. Transdermal treatment can only be performed for certain strong drugs.

• Transdermal therapy is not suitable for ionic agents.

• Drug delivery cannot be pulsed.

• All types of adhesive may not stick well it is gentle on the skin and can be uncomfortable to wear.[12]

• Adhesion may vary depending on the type of patch and the environment.

2. TECHNOLOGY FOR DEVELOPING TRANSDERMAL DRUG DELIVERY SYSTEM

The technologies can be classified in four basic approaches.[13]

1. Polymer membrane partition controlled TDDS.
2. Polymer matrix diffusion controlled TDDS.
3. Drug reservoir gradient controlled TDDS.
4. Micro reservoir dissolution controlled TDDS.

2.1 Polymer membrane partition controlled TDDS

In this type of system the drug reservoir is completely encapsulated in a shallow compartment. Molded from a drug impermeable metal-plastic laminate and a rate-controlling polymer micro porous or nonporous membranes. E.g. Ethylene vinyl acetate (EVA) copolymers with defined drug permeation properties Sectional view of this system. Of drug molecules are released only through the rate-limiting membrane. In medicine in the reservoir compartment, the drug solids are dispersed in a solid polymer matrix or suspended in a non-leaching viscous liquid medium such as silicone fluid to form a paste suspension.[13]

A thin layer of drug-compatible, hypoallergenic, adhesive polymer silicone or poly acrylate adhesive can be applied to the outer surface of the rate control membrane adhesion between the transdermal drug system and the skin surface is realized release from this type of transdermal drug delivery system is polymer composition, permeability coefficient and thickness of the rate-limiting membrane, glue. Constant drug release rate is the main advantage of membrane permeation a controlled transdermal system. However, there is also a rare risk of accidental brekage.

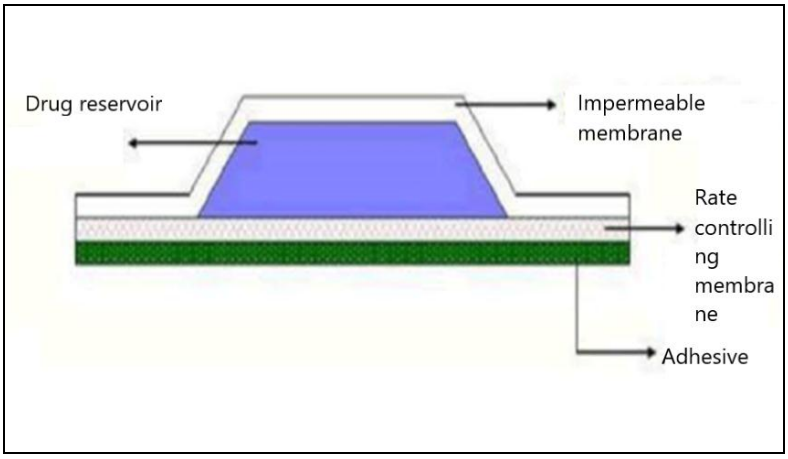

Fig. 1 Memrane permeation controlled system.

2.2 ADHESIVE DISPERSION TYPE SYSTEMS

This is a simplified form of membrane permeation control system. As shown in drug reservoirs are formulated by dispersing the drug directly into the adhesive polymer. Poly (Isobutylene) or poly (acrylate) adhesive is applied followed by medicated adhesive with solvent. Poured or hot-melted onto a flat sheet of drug-impermeable metal-plastic carrier, thin drug reservoir layer[13] above the drug reservoir layer is a thin layer of non-drug material a regulated adhesive polymer with constant permeability and constant thickness is applied manufacture an adhesive diffusion controlled delivery system. On top of that there is a non-medical layer, applies a thickness of rate-limiting adhesive polymer manufacture of adhesive diffusion controlled drug delivery system.[8] Learn about the use of pressure sensitive adhesives (PSAs) for skin contact applications.

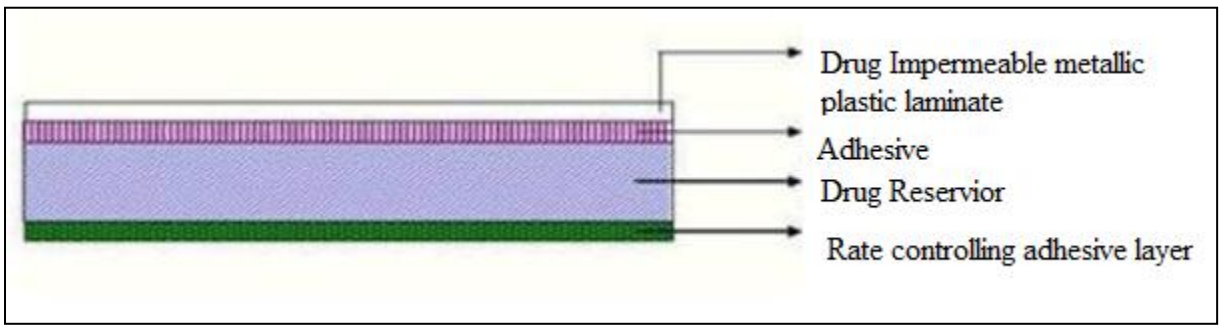

Fig. 2: Adhesive Dispersion Type System.

2.3 MATRIX DIFFUSION CONTROLLED SYSTEMS:

In this approach, drug reservoirs are created by uniformly dispersing drug particles. Hydrophilic or lipophilic polymer matrix the resulting drug-containing polymer is then drug discs of defined surface area and controlled thickness.[13] Drug distribution the particles in the

polymer matrix are liquid polymer or high viscosity base polymer followed by cloth milled drug particles link polymer chains or mix drug solids homogeneously with rubbery polymers high temperature. Drug reservoirs can also be formed by dissolving drugs Polymer in common solvent followed by solvent evaporation in the mold at high temperature under temperature and/or vacuum. Then glue this polymer disc containing the drug reservoir the occlusive polymer is then spread around to form a border strip of adhesive around medicinal intervertebral discs. Polymer discs containing drug reservoirs affixed to a sealed baseplate in the compartment of the drug.[14] Medicine is uniformly dispersed in hydrophilic or lipophilic solutions polymer matrix.[15]

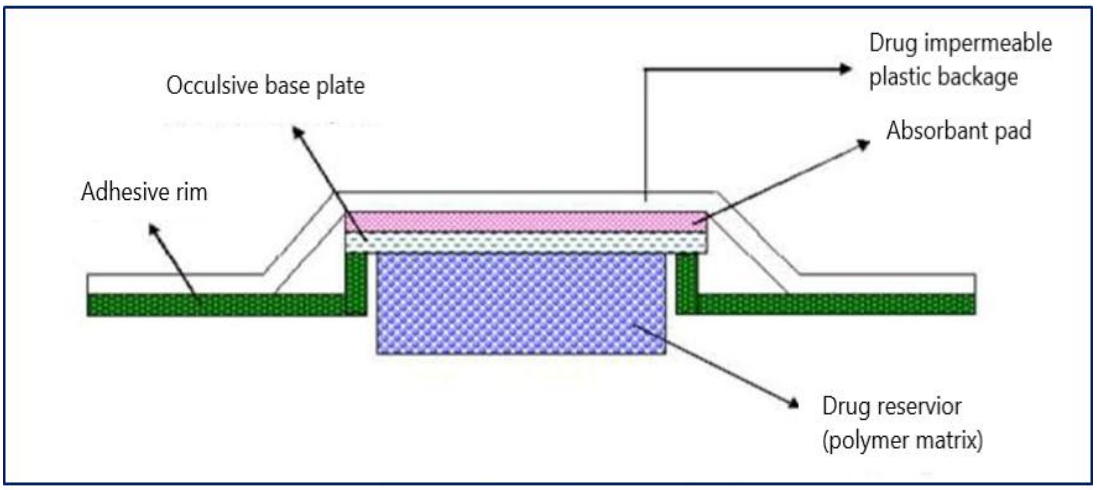

Fig. 3: Matrix diffusion controlled type TDDS.

2.4 MICRO-RESERVOIR TYPE OR MICRO-SEALED DISSOLUTION CONTROLLED SYSTEMS

This can be viewed as a combination of reservoir and matrix diffusion type drug delivery system. Here, a drug reservoir is formed by first suspending drug solids in an aqueous solution dissolves water-soluble liquid polymer and disperses drug suspension uniformity of lipophilic polymers, i.e. Silicone elastomers, by high-energy dispersion a technique for forming multiple discrete non-leaching microspheres of drug reservoirs.[13] This achieves rapid stabilization of this thermodynamically unstable dispersion. In situ instant cross-linking of polymer chains, creation of drug-loaded polymer discs constant surface area and constant thickness. According to physicochemical properties depending on the release of the drug and the desired rate of drug release, the device may further biocompatible polymers for modifying the mechanism and rate of drug release transdermal the treatment system is primed by placing

the disc containing the drug in the center Comes with sticky edges. This drug delivery system combines nation of reservoirs and matrix dispersion systems.[16]

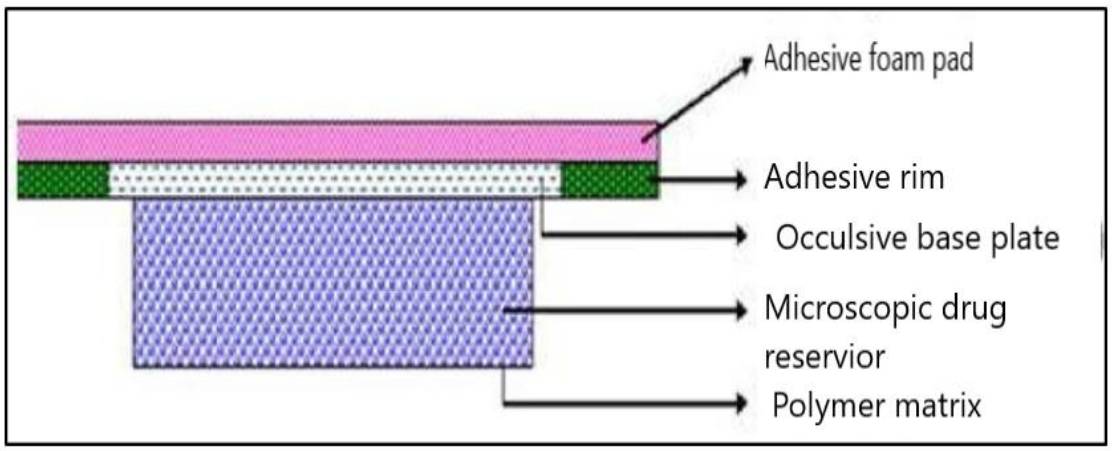

Figure 4: Micro reservoir type of TDDS.

3. TYPES OF TRANSDERMAL DRUG DELIVERY SYSTEM:

3.1 Single layer drug in adhesive

This is a type that contains a drug in the adhesive layer. The adhesive layer does not end there different layers adhere to each other and are also involved in the release of active ingredients skin. The adhesive layer is surrounded by a temporary liner and backing.[12]

3.2 Multi -layer drug in adhesive

This type is also similar to monolayer, but one layer provides immediate release of the drug and another layer provides controlled release with an adhesive layer. Of the adhesive layer is responsible for the release of active ingredients. This patch also has one: Temporary liner layer and permanent underlay.

3.3 Vapor patch

Patches containing an adhesive layer are not only used to adhesive various surfaces at the same time, it also plays the role of releasing steam. The steam spot is market commonly used to release essential oils during decongestion. Various steam patch type used for health promotion is also available on the market. Reduces sleep quality and smoking status.

3.4 Reservoir system

In this system, the drug reservoir is an impermeable backing rate-limiting membrane. Drug is released only by rate control micro porous or nonporous membranes. Inside chemical storage drugs may be in the form of solutions, suspensions, gels, or dispersed in solid polymers

matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymer drug compatible membrane.

3.5 Matrix system

This type of patch is formulated by mixing the drug with an adhesive polymer to form a drug reservoir. This is followed by streaking onto a solvent-impermeable backing. Casting or melting process. The upper part of the reservoir is protected from sudden impacts adhesive polymer layer. Further, it can be classified into single-layer and multi-layer. Drag-in loop.

ii. Matrix-dispersion system

Drugs are uniformly dispersed in a hydrophilic or lipophilic polymer matrix. That is it is then converted into a medicinal disc of determined shape and thickness. This medicine Fixed in one compartment of the sealed baseplate using a polymer disc a drug-impermeable backing sheet is used. Instead of applying glue at the front of the drug reservoir, spread along the perimeter to form a strip glued edge.

3.6 Micro reservoir system

The system consists of tiny beads of drug reservoirs that release the drug. Zero-order rate to Maintain constant drug levels.

4. BASIC COMPONENT OF TDDS

4.1 Backing Films

Carrier films play an important role in transdermal and transdermal patches with the system. The role of the membrane is to protect and protect the active layer affects system stability and skin permeability and tolerability. To avoid any kind of incompatibilities the release liner it should also be flexible, convenient, and indispensable good compatibility with adhesives and excellent printability. Most popular version are Liners polypropylene, polyester, PVC and nylon.[17,18]

4.2 Release Liners

A non-stick coating covers the release liner. The role of a release liner is designed to protect the system while in the box and is easily removed before applying TDDS to the skin. Release films play an important role Patch stability, safety, and effectiveness most abundantly used release liner are polyester.

4.3 Pressure Sensitive Adhesives

For both types of TDDS, pressure-sensitive adhesive(PSAs)play an important role, by serving as the matrix that carries the active like additives and permeation enhancers and the means for making the patch stick to the skin. Widely used pressure sensitive adhesives are Natural Rubber PSAs, Synthetic Rubber PSAs, Acrylic PSAs, and Silicone PSAs.

4.4 Penetration Enhancers

These are completely different chemicals they belong to the same family according to their characteristics. They increase the penetration rate Several times the active ingredient through the skin. Although transdermal delivery has proven to be the greatest target for these drugs, the skin is very efficient at clearing such high molecular weight compounds and reaching therapeutic concentrations by passive absorption is unlikely.[19] The skin is of great interest as a site of drug application for topical and medical systemic effect.[20]The effects of various concentrations of permeation enhancers such as dimethyl sulfoxide and propylene glycol were investigated on skin permeation kinetics using a keshary -chein diffusion cell.[21] Mostly used permeation enhancers are Sulphoxides, Fatty acid and alcohols, azone and its derivative.

4.5 Micro porous or Semi-Permeable Membranes

Porous membranes are a special type of membrane primarily used in all liquid transdermal applications. Patches and some matrix type patches. Its job is to regulate the flow of semi-solid contents from the liquid reservoir and act as a rate-limiting membrane system. Example of Micro porous or Semi-Permeable Membranes are polyethylene and polypropylene.

5. Physicochemical evaluation

5.1 Thickness

The thickness of transdermal patches made with drugs is determined in another way using a digital micrometer check the patch points and determine the mean and standard deviation for the same thickness to ensure prepared patch thickness.[13]

5.2 Weight Uniformity

Examine weight variability by weighing 10 randomly selected patches individually average weight calculator. Individual weights should not deviate significantly from the average weight.

5.3 Drug content determination

Drug content is important in determining the percent potency of a drug product. Correct weigh drug material and add to 100 mL of appropriate solvent mixture of shake the solvent continuously for 24 hours in a shaking incubator. Complete mixture of drugs contains certain dilutions.

5.4 Percent Moisture content

Prepared films are individually weighed and stored in a desiccator containing calcium chloride 24 hours at room temperature. Slides are weighed again at set intervals until displayed constant weight.

5.5 Percentage moisture uptake

The weighed film is stored in a desiccator containing saturated potassium chloride solution maintain 84% relative humidity. After 24 hours, the patch is weighed again to determine moisture content. Inclusion from the following expressions

5.6 Flatness

Three longitudinal strips are cut from different sections of film length of each strip and measure the change in length due to unevenness of flatness. Determining the necking ratio, where 0% necking corresponds to 100% flatness.

5.7 Folding Endurance

Cut strips of given area evenly and fold repeatedly in the same place until it breaks number the bending resistance is the number of times the film can be folded at the same place without breaking.

5.8 Peel adhesion test

This test expresses the force required to remove the adhesive coating from the substrate as: peel adhesive. Apply a piece of tape to a stainless steel plate or support film of your choice the tape is peeled off from the substrate at an angle of 180° and the time until the tape is peeled off is measured.

5.9 Thumb tack test: This test was used to determine the adhesive properties of the adhesive just press with your thumb adhesive and relative cohesive properties are recorded.

5.10 Probe tack test

A probe tip with a defined surface roughness is in contact with the adhesive once a bond is formed between the glue and the probe release the probe at a constant speed.

5.11 Tensile strength

Strength was measured using a modified roller system. Includes two clamps are fixed, others are movable. Plaster strip (2x2 cm2) and placed it between the two shells. We gradually increased the pan weight to increase traction until the patch broke. Violence tensile strength required for the film to break (kg/cm2).

5.12 Flux and Permeability coefficient

The flux of meclizine (mg cm -2 h -1) was calculated from the slope of the plot of cumulative amounts of meclizine steady state permeated meclizine per cm2 of skin versus time using linear regression analysis.

5.13 In-vitro Permeation study

In vitro permeation studies can be performed using diffusion cells. Belly full his skin of male rate weighing 200–250 g. be careful with electric clippers. Thoroughly cleansed the dermal the skin equilibrate for 1 hour in distilled water to remove adherent tissue or blood vessels. Add medium or phosphate buffer pH 7.4 before starting the experiment. Furosemide transdermal films were developed using ethyl cellulose as film formers. The performance may be estimated by a scoring based on patch lift.[27]

6. Future

Transdermal drug delivery is the movement of drugs across the skin for absorption into the systemic circulation. Drug delivery is passive or active. Passive transdermal products do not destroy the stratum to facilitate delivery, but active technologies do.

The very specific physics required for successful passive transdermal drug delivery Due to their chemical properties, this segment of the pharmaceutical.[24] The transdermal absorption device market is $2 billion (Barry 2001) and this figure is The total US drug delivery market is $28 billion. Numbers like that the first transdermal patch was approved by the FDA in 1979, and only nine of his drugs have been approved since. Very short "Performance" list highlights physicochemical limitations imposed on skin release. Transdermal drug delivery had a strong year with a growth rate of 25%, it surpasses oral drug delivery (2%). Inhalation

market (20%). The number is certainly.[25] Delivery of drugs to the systemic circulation via the skin is considered a desirable alternative to oral intake. Patients often forget to take their medications, and even the most loyal patients get fed up with swallowing pills, especially if they have to take several each day.[24]

7. CONCLUSION

Transdermal drug delivery systems represent a beneficial innovation in drug delivery. Especially in patients who cannot swallow or remember to take their medications transdermal drug delivery provides controlled delivery of drugs to patients and allows for constant blood levels. The result is reduced systemic side effects and sometimes improved efficacy other dosage forms. Can provide delivery of drugs at low doses and save recipients from it large-dose injury with improved bioavailability. All-in-one transdermal patch it is a proven technology that offers many important clinical advantages over other dosage forms.

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