

Comparison of a New Two-Part Transdermal Drug Delivery System, the Patch-Cap™, to Conventional Passive Transdermal Patches

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Mr Redding has seventeen years of experience in controlled-release product development and commercialisation. In 1988 he co-founded Encapsulation Systems, Inc., where he developed an extensive experience in technology transfer. In 1991 he joined M-Cap Technologies Intl as Co-President before becoming President, in 1995, for Delta Food Group. Since 2001, Mr Redding has led a highly innovative team to develop a non-invasive drug delivery technology, with an Insulin Patch being the ultimate goal. That technology is now in human clinical trials. In 2004, Dermisonics, Inc. was created to oversee the development of the U-Strip technology and Mr Redding serves as Executive Vice-President.

Introduction

The product development process for a transdermal drug delivery (TDD) system is multidisciplinary in nature. Much of the scientific literature in the field of transdermal delivery pertains to skin permeation and methods of skin penetration enhancement because these are the fundamental issues that must be addressed for any transdermal drug candidate. However, in addition to the basic questions of skin permeability and dose delivered, the development process must also address other basic questions, such as the following:

- What is the appropriate patch design?
- What are the appropriate materials to use in the patch construction?
- Will the target drug be compromised by either the design or the materials used in the patch construction.

The Basis Designs To Transdermal Patch Products

Reservoir Type Patch:

The Reservoir Type Patch is characterised by the inclusion of a liquid reservoir compartment containing a drug solution or suspension, which is separated from a release liner by a semi-permeable membrane and an adhesive. Commercial examples include Duralgesic (Fentanyl), Estraderm® (estradiol) and Transderm-Nitro® (Nitroglycerin).

Matrix Type Patch:

The Matrix Type Patch is similar to the Reservoir Type Patch design but has two distinguishing characteristics: the drug reservoir is provided within a semi-solid formulation and there is no membrane layer. Commercial examples include Habitrol® (Nicotine), Nitrodisc® (Nitroglycerine) and ProStep® (Nicotine).

Drug-In-Adhesive Type Patch: DIA

This type of patch is characterised by the inclusion of the drug directly within the skin-contacting adhesive (Wick, 1988). In this design the adhesive fulfils the adhesion-to-skin function as well as acting as the formulation foundation, containing the drug and all the excipients (Wilking *et al.*, 1994). This category has two sub-sections: Monolithic and Multilaminar. Commercial examples include Climara® (Estradiol) (Monolithic DIA); Nicoderm® (Nicotine) (Multilaminar DIA).

The DIA patch design has several advantages in reducing the size of the overall patch and provides a more concentric seal upon the skin. In addition, patches tend to be more comfortable to wear and very thin; a typical DIA patch is 165 to 200 µm thick. Major disadvantages include a longer drug delivery profile. The release of the drug from a DIA patch follows first order kinetics, namely, it is proportional to the concentration of drug within the adhesive. As the drug is delivered from the DIA patch the drug concentration will eventually begin to fall. Therefore, the delivery rate falls off over time and this fact needs to be considered in the clinical evaluation phase of development.

Patch Products

A major problem with all major forms of transdermal patches is the intermingling of the drug with adhesive compositions. These result in new profiles and, in many instances, the drug is degraded through the interaction with the adhesive composition. The chemistry of the adhesive can alter the stability, performance and function of certain drugs.

Furthermore, there are limits to the molecule size of drugs that can be delivered via a passive system. Typically, drug candidates are below 500 Daltons for DIA patches and below 1,000 Daltons for Matrix or Reservoir patches, even through the use of skin enhancers.

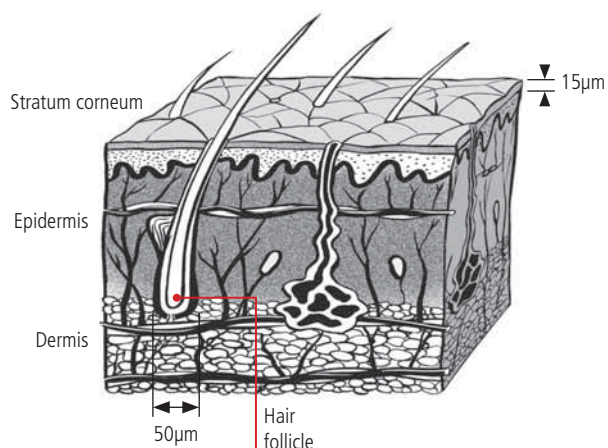


Figure 1.

Electronically-Assisted Transdermal Devices

Several approaches are used to assist electronically in transdermal delivery including iontophoresis and ultrasound. These systems are designed to increase the flow of metallic-based drugs across the stratum corneum, to microporate the skin or allow the delivery of macromolecules across the stratum corneum into the dermis or underlying tissue (Figure 1).

Such electronically-assisted TDDs often use an outside electronic system, which is not connected to a drug-containing patch, or the patch has electrodes within it to assist in ionic transfer. Direct connection to a disposable transdermal patch is often impractical because the electrodes or the ultrasonic transducer system are not disposable.

A new patented, two-part transdermal patch was developed to solve the problem of electronically-assisted transdermal drug delivery systems, enabling such systems to become more portable or wearable by the patient. It also avoids the disadvantages of conventional patch designs where drug contamination or denaturing may be caused through interaction with an adhesive or polymer component within the patch design.

The Patch-Cap™

The Patch-Cap™ is a two-part transdermal patch consisting of a transducer coupler and a patch-cap, which actually holds the drug (Redding, 2005). The Patch-Cap™ is designed specifically for ultrasonic and other electronic drug delivery applications where a conventional patch is unsuitable due to its reliance on a drug/adhesive mixture. Such conventional patches run the risk of contaminating the drug. In the Patch-Cap™ an absorbent pad is used to store the drug until ultrasound, delivered from a snap-on transducer coupler, liberates the drug from the cap and onto the patient's skin surface. From there, ultrasound can be employed to expand the skin pores and deliver the drug into the dermis.



Figure 2 – The Patch-Cap™.

The transducer coupler (the black component in Figure 2) contains up to four miniature ultrasonic transducers and is powered by the U-Strip Ultrasonic Drug Delivery System. The patch-cap (the white component) contains the drug and is disposable. The current design holds 75 units of insulin, enough for a two-day supply for most diabetics for a U-Strip/insulin delivery system. The Patch-Cap™ is designed to be replaced every 24-36 hours.

Unique Adhesive Free Design

The Patch-Cap™ uses an absorbent pad to absorb the drug. The absorbency power of the pad is measured in factors of liquid water absorption; for example, many absorbent materials can hold up to twelve times their weight in liquid. Therefore, a patch-cap can contain far more liquid suspension of a particular drug composition.

The use of adhesives, which directly contact the drug, is eliminated in this design. Adhesives may be used in the border of the patch but the DIA, matrix or reservoir design are discarded in favour of an absorbent pad which is held in place in the cap by the use of an Inner Snap ring. The ring holds the drug-loaded absorbent pad within the cap (Figure 3). Additionally, the two-part system enables the more expensive ultrasonic emitter to be retained for future use while the patch-cap is disposable.

Connection to the Ultrasonic Signal Emitter

In conventional ultrasound systems a hydro-gel is used to provide a coupling agent format. The use of a gel-coupling agent could also contaminate an active drug substance liberated from the patch onto the skin surface. The Patch-Cap™ avoids the requirement for a coupling by using the liberated drug itself as the coupling agent. The sonic transmission is effected from the transducer to the patient's skin, by using the liberated drug as the coupling agent. In this design the ultrasonic transducer is designed to mate with the patch-cap directly; the transducer coupler is the permanent fixture while the patch-cap is the disposable component.

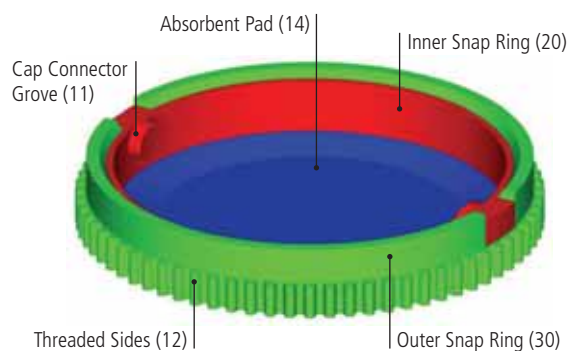


Figure 3 – The Patch-Cap design.

Use of Absorbent Pads to Contain the Drug

In the reservoir, matrix and DIA versions of a transdermal patch there is a very low concentration of drug possible. Often, the delivery is dependent upon the surface area of the patch. In the Patch-Cap™ design the thickness of the absorbent pad can be varied to marry with the absorbency factor. Therefore, more of the active drug can be contained within the fabric of the absorbent pad; for example, a 1 sq. cm of cellulosic pad can hold up to twelve times its weight in moisture at 1 mm thickness. The same pad thickness, but using a nylon pad, may hold only three times its weight in moisture. By varying the material used and altering its thickness the absorbent pad's holding capacity can be adjusted to meet a desired release rate and longevity, far exceeding that of conventional patches.

The U-Strip Drug Delivery System

The U-Strip system is a needle-free transdermal delivery system, which is capable of delivering large molecule drugs through the skin, non-invasively (Figure 4). Dermisonics is presently developing an insulin patch aimed at Type-1 and insulin-dependent Type-2 Diabetics (with a market potential of four million patients in the US). The patient can wear the insulin patch product, in the form of a two-part transdermal drug delivery device, the Patch-Cap™ and powered by an ultrasonic delivery controller, during their daily routine. The Patch-Cap™ regulates the dosing of insulin in both basal and bolus delivery needs (Figure 4).

The U-Strip Insulin Delivery System is a modified transdermal patch with an attached ultrasonic device. The ultrasound 'massages' the skin and enlarges the pore size of hair follicles, enabling large molecule drugs, such as insulin, to permeate through the skin into the bloodstream. Human Pilot Trials are underway and have shown significant results thus far (Figure 5).

Conclusion

The use of a two-part TDD, especially those that are electronically assisted, solves many of the critical concerns that limit the use of transdermal patches in drug delivery applications. Critical advantages include:

- Avoidance of interaction with adhesive chemistry and potential drug degradation
- The absorbent pad approach enables a far greater quantity to be stored within a TDD
- The use of a propagation source, i.e. the ultrasonic coupler still provides the Patch-Cap™ with disposability.



Figure 4 – The arm mounted control device enables basal and bolus delivery.



Figure 5 – Human volunteer from HPT-1 insulin delivery pilot trial, part of the Phase I clinical programme.

References

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