



THE CRITICALITY OF ADHESIVE SELECTION FOR OPTIMAL TRANSDERMAL DRUG DELIVERY SYSTEMS

In this piece, Megan Greth, Business Manager, ARx, LLC, and Gozde Karabiyik, PhD, Product Development Scientist, Adhesives Research, discuss why selecting the right adhesive for body-worn drug delivery systems – be they transdermal patches or wearable injection devices or pumps – is critical for a successful outcome.

The adhesive is an integral part of any active transdermal delivery device and passive short- and long-term wear transdermal patch. It is critical that an adhesive is selected or custom developed in consideration of the following key attributes when developing an effective and robust drug delivery system.

SKIN-FRIENDLY ADHESIVES FOR ADVANCED DRUG DELIVERY SYSTEM PERFORMANCE

Drug delivery methods have expanded in scope and capability, which has created a need for new adhesive technologies to overcome skin bonding challenges. Development of new active transdermal

importance in the delivery of insulin and other biologics to subcutaneous tissue.

Skin adhesives are critical components for both transdermal patches and drug delivery device applications to ensure firm bonding on skin to deliver target therapeutic dose. Adhesive and skin bond must withstand moving and lifting due to physical activity, constant friction from clothing, moisture exposure and varying degrees of skin oil levels. In drug delivery device applications, such as patch pumps and infusion sets, further challenges arise from the weight of the device filled with drug and limited moisture vapour transmission of skin adhesive under the device. It is also important to note that a number of factors

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drug delivery systems (TDDS) has enabled the delivery of larger compounds through the *stratum corneum*. Additionally, body-worn drug delivery devices have gained

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Figure 1: Biocompatible, skin-friendly adhesive.



Figure 2: Application of a SoftWear® low-trauma adhesive transdermal patch.

wear performance. All of these factors must be considered by an adhesives expert in order to achieve a consistent delivery profile across a specified patient population.

ADHESIVE REQUIREMENTS: BIOCOMPATIBILITY & BREATHABILITY

Adhesive biocompatibility is a significant concern in skin adhesive applications. Presence of any residual monomers and leachable components, particularly acrylics and natural rubber-based adhesives, could potentially cause skin irritation and sensitisation. Skin adhesives should be formulated carefully to provide a biocompatible adhesive system to prevent

any adverse skin reaction (see Figure 1). In addition, skin breathability through the adhesive is essential to prevent maceration during wear.

In some applications, maintaining a certain hydration level at skin and adhesive interface is critical for enhancing drug flux. In this case, the skin becomes weak due to maceration and it can result in potential tearing and pain during device removal. Adhesive breathability depends on the moisture vapour transmission rate (MVTR) of the skin patch and body-worn device design as well as the adhesive construction. Breathability of a skin adhesive can be increased via substrate selection, lowering adhesive coat weight and zone or pattern coating.

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SKIN-FRIENDLY, AGGRESSIVE ADHESIVES FOR LONG-TERM WEAR

Several currently available transdermal patches are designed to be removed within 24 hours of application. However, new applications are designed for longer wear time extending wear duration up to multiple days for continued controlled release. Current seven-day, passive transdermal patches on the market are provided with an adhesive overlay to assist with bonding for the desired time period. In addition, several body-worn drug delivery devices are designed to adhere on the skin beyond seven days.

Adhesives Research has designed a tailorable, pharmaceutical-grade, acrylic-based adhesive technology that provides an aggressive long-term wear (LTW) adhesive platform to secure a drug delivery patch or device on skin for up to seven days. This adhesive platform ensures bonding of the tape to skin with minimal edge lift during the course of wear and removes from the skin cleanly without leaving any residue. This adhesive platform provides high MVTR for breathability and good wear properties with no edge residue or cold flow.

Aggressive adhesion on skin offers a secure bond to prevent lifting or moving of the patch. In spite of the aggressiveness of the LTW, it has a pain index of <2.5 on the Wong-Baker FACES® Pain Rating Scale and pain experienced upon removal of the tape is tolerable. Studies have also shown that removal of the adhesive tape does not cause disruption of stratum corneum. This adhesive formulation can be further tailored to customise the wear time and pain level depending on the wear duration and the delivery application.

SOFTWEAR® LOW-TRAUMA ADHESIVES FOR SHORT-TERM WEAR

There is a growing need for low-trauma adhesives to provide reliable adhesion on different skin conditions and age groups with gentle removal from skin. Moreover, treatments for chronic conditions require repeated application (see Figure 2) and removal of a skin patch on specific skin site. Adhesives Research is addressing the growing need for gentle and repositionable skin adhesives through the development of low-trauma adhesive (LTA) technology

The adhesive is formulated to release from hair and the top layer of skin cleanly, with a pain index of <2.5 on the Wong-Baker FACES® Pain Rating Scale.

For comparison purposes, a standard skin-friendly adhesive has a pain index rating of 4–5 on this scale, based on Adhesives Research's studies. In addition, LTA formulations exhibit resistance to radiation sterilisation techniques. This is important in applications such as microneedles and abrasion, providing an advantageous alternative to standard adhesives available on the market.

approximately 35 years. However, the issue of cold flow still exists and has received heightened attention in recent years. As both time from date of manufacture and wear time increase, so does the ability for the adhesive matrix to flow outside of the patch backing layer and seep into the packaging foil or form a ring of residue on the skin. This phenomenon is not only aesthetically displeasing and inconvenient, but it can also impact the drug flux of the patch.

In recent years, the US FDA and various journals have discussed mechanisms to characterise cold flow. The FDA also references cold flow as a consideration in the Quality by Design section of its August 2011 guidance, "Residual Drug in Transdermal and Related Drug Delivery Systems". As with all Critical Quality Attributes, the minimising of cold flow has to be designed into the patch. Scientists must take careful consideration in selecting the appropriate adhesive chemistry, as well as the interaction with the active pharmaceutical ingredients and any other enhancers. Adhesives Research and ARx scientists have the advantage of over 35 years of foundational expertise in adhesive polymers and the selection thereof when formulating transdermal patches.

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for gentle removal. This customisable, pressure-sensitive adhesive (PSA) platform technology, known as SoftWear®, maintains intimate skin contact for up to three days with residue-free, gentle removal from skin.

COLD FLOW CONSIDERATIONS FOR PASSIVE TRANSDERMAL PATCHES

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