CASE STUDY

Active Material Science Innovations to Deliver Combination Moisture and Oxygen Protection for Transdermal Therapeutic Patches

Situation

Transdermal therapeutic patches (TTP) are a growing drug administration route, offering an easy-to-use, patient-friendly, and reliable method of delivering drugs to the body via skin absorption. Enabling convenient and pain-free self-administration for patients, TTPs allow the drug to bypass the first pass metabolism and can eliminate the need for frequent dosing by providing a consistent amount of API to the patient for long-term treatment. However, TTPs face unique challenges when it comes to integrating solutions to address moisture or oxygen sensitivity, odors, or VOCs that can impact shelf life and API stability. Solving for these challenges is a critical component to assuring accurate dosage and effective long-term treatment via this drug delivery system.

IDEA IN BRIEF

THE PROBLEM
A TTP was not meeting the 18 month shelf life needed and the source of degradation was unknown. Attempts to remove moisture and oxygen from the headspace independently failed to produce desired results.

THE CHALLENGE
A solution was needed to address moisture and oxygen sensitivity in tandem to maintain API stability. The solution could not impact packaging design or infrastructure and required use of pre-validated adhesives.

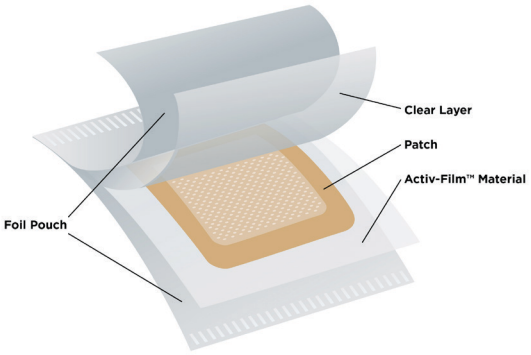
THE SOLUTION
Aptar CSP's Activ-Film™ material incorporates multiple chemistries into a singular polymer solution that can be seamlessly integrated into the TTP's current packaging design to deliver 18 months of shelf life.

Your product, actively protected™

Aptar CSP Technologies

CASE STUDY // ACTIVE MATERIAL SCIENCE INNOVATIONS TO DELIVER COMBINATION MOISTURE AND OXYGEN PROTECTION FOR TTPs

Challenge



A global top 10 pharmaceutical company was experiencing a unique degradation challenge with their TTP product. Housed in foil packaging, the TTP was not meeting the 18-month shelf life needed, and the cause of degradation was unknown. The drug developer performed studies focusing on moisture management in the headspace, and also attempted to independently remove oxygen from the packaging in an effort to identify the cause of degradation and solve it. Both efforts yielded only marginal improvement in drug stability and shelf life. It was suspected that a combination of both moisture and oxygen management was needed. However, mechanisms to simultaneously control both moisture and oxygen in the headspace are uncommon, and since most oxygen scavengers require moisture to activate, this creates an inherent conflict that can make it difficult for both forms of active protection to be achieved in a single solution.

In addition to the need to simultaneously control moisture and scavenge oxygen, the solution needed to integrate into the manufacturing infrastructure and packaging already in place to support production of the TTP. There was little tolerance for modification to manufacturing aspects. Lastly, since the drug was sensitive to many adhesives, any solution proposed needed to use adhesives the pharma developer already validated. In short, this company needed a solution to improve their TTP product's stability by simultaneously managing moisture and oxygen in a minimal headspace environment, without significantly impacting the current manufacturing infrastructure or packaging footprint, and while utilizing only validated adhesives.

Solution: Active Material Science Technology

Aptar CSP Technologies' active material science solutions are customizable to meet the needs of various application fields and therapeutic areas. The company's 3-Phase Activ-Polymer™ platform technology has the ability to incorporate multiple chemistries into a single polymer solution that can be deployed in a range of physical formats. This uniquely positioned Aptar CSP as the ideal partner to co-develop a solution to the challenges this TTP faced.

In order to seamlessly integrate into the TTP's current packaging design, the proposed Activ-Polymer™ solution needed to be deployed as Activ-Film™ material, an extruded film format, adhered to the foil pouch housing the patch. The film was engineered to incorporate multiple active properties into a single combination solution that can scavenge oxygen while simultaneously adsorbing moisture molecules. Most industry recognized oxygen scavengers require the presence of moisture to activate. Aptar CSP, however, has a unique offering where the oxygen scavenging function is not reliant on moisture and therefore can perform independent of the system's relative humidity (RH). Where separate solutions for moisture management and oxygen scavenging failed, Aptar CSP's combination solution delivered a precision microclimate in the headspace of the patch that provided drastically superior results.

With the combination Activ-Film™ integrated into the patch's foil pouch, the drug was able to meet the 18 month stability requirement. The following data review outlines the processes by which the active material science solution for the TTP was developed to meet all of the customer's requirements.

Data Review: Moisture Adsorption Formulation Development

The main objective in developing Aptar CSP's Activ-Film™ combination solution for this customer was to ensure the formulation had enough capacity to meet the 18 month stability target for protecting against both oxygen and moisture. The first step was to develop the moisture-specific functionality of the final solution before incorporating the oxygen scavenging active materials.

Figure 1 illustrates how the integration of moisture adsorbing Activ-Film™ material reduces moisture in the system and maintains the appropriate level of adsorption after a few days. Since the customer was already using a superior barrier foil packaging, ingress into the system was negligible once the residual RH was adsorbed.

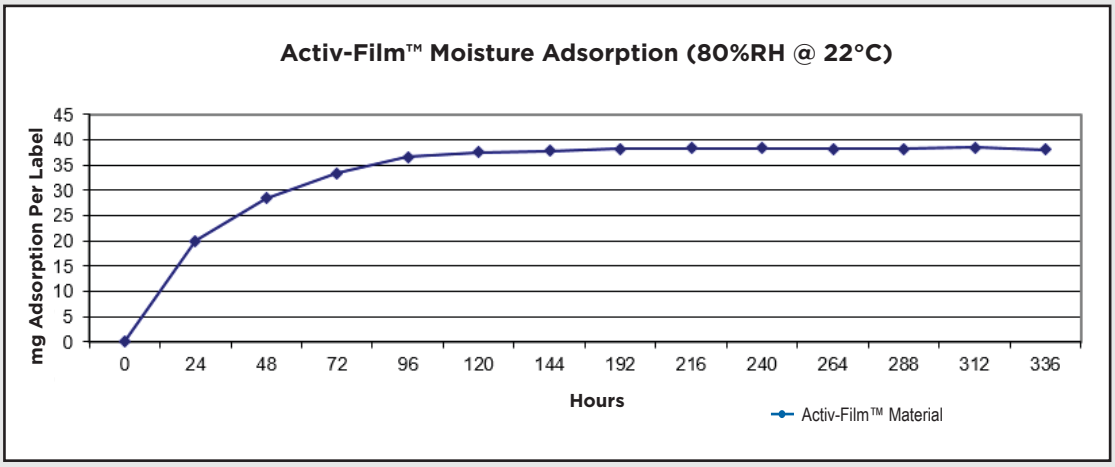


Figure 1: Moisture adsorption of Activ-Film™ at 80% RH and 22°C over time

Data Review: Oxygen Scavenging Integration Study

Once the moisture targeting formulation was finalized, additional development was needed to ensure the oxygen scavenging active materials could perform properly without impacting the moisture adsorption performance. Figure 2 shows the moisture adsorption performance of the combination Activ-Film™ formulation and confirms the integration of oxygen scavenging functionality did not impact the moisture adsorption performance.

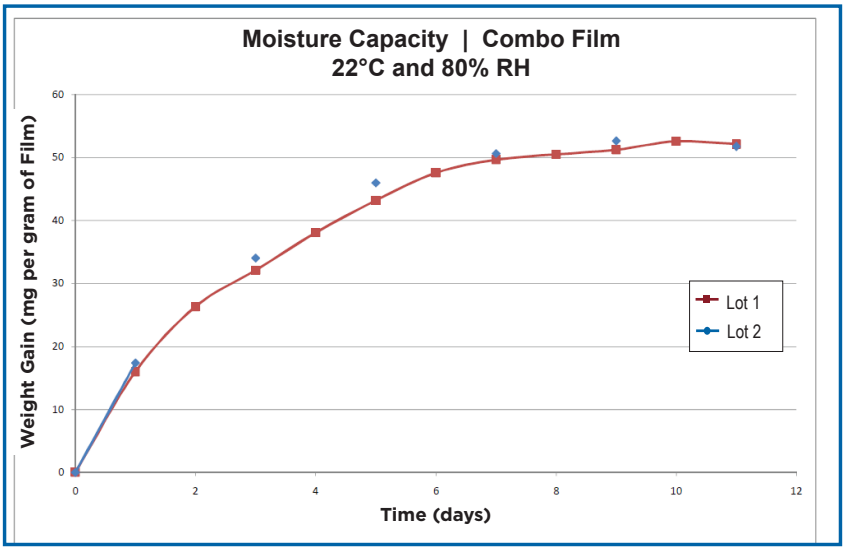


Figure 2: Moisture Adsorption Performance of Combination Activ-Film™ Solution

Data Review: Determining Ideal Activ-Film™ Thickness

In order to develop a solution that provided the best oxygen scavenging results, Aptar CSP needed to determine what film thickness would deliver the best results. The performance of oxygen scavenging Activ-Film™ solutions is dependent on surface area of the film and not volume, and therefore, thickness does not always lead to superior oxygen scavenging performance.

Aptar CSP tested 0.3 mm and 0.6 mm Activ-Film™ to explore how film thickness and various extrusion manufacturing process parameters impacted performance. The study showed that the thinner 0.3mm film provided slightly higher capacity and a faster rate for oxygen pull down than the 0.6 mm film (Figure 3), delivering better overall oxygen scavenging performance.

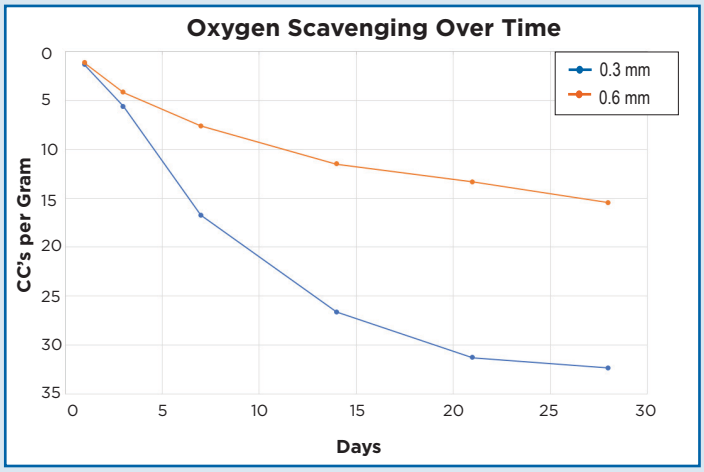


Figure 3: Oxygen Scavenging Performance of Activ-Film™ at Varying Thicknesses

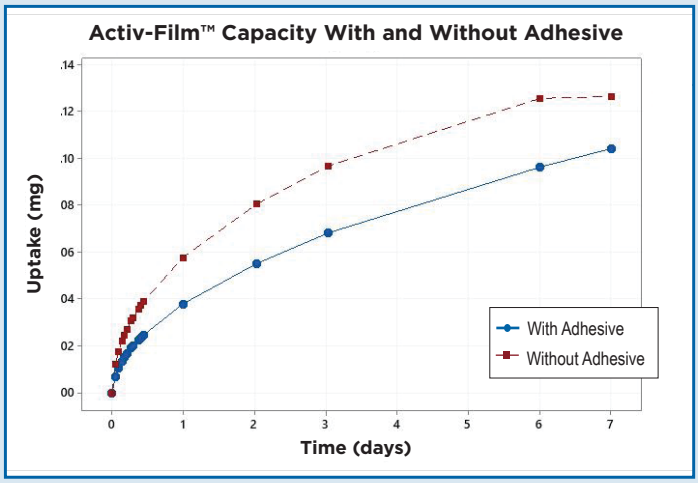


Figure 4: Assessment of Activ-Film™ Performance With and Without Adhesive

Data Review: Impact of Adhesive

The final parameter Aptar's solution needed to meet for the customer was that it needed to be provided in a label-based format. The Activ-Film™ label would be applied to the inside of an existing foil pouch with a pre-validated adhesive. However, when using an adhesive to apply Activ-Film™ material, half of the surface area of the film is restricted from scavenging in the headspace. Additionally, certain adhesives can alter the kinetics of the Activ-Film™ material and impact performance.

As illustrated in Figure 4, the final Activ-Film™ solution was tested to ensure performance both with and without an adhesive label. The graph illustrates consistent performance between the two populations with only a slight reduction in capacity, which did not impact the final Activ-Film™ formulation.

Conclusion

Innovations in active material science technologies enable the development of customized solutions to meet the diverse stability protection needs of transdermal therapeutic patches. Aptar CSP Technologies' engineered solutions, like our combination Activ-Film™ material, are able to solve a host of challenges with little to no impact on existing manufacturer processes or packaging designs. As illustrated in this case study, Aptar CSP delivers complete support services to meet the specific needs of each customer's product, helping to bring more new drugs to market and expand patient access to a growing range of dermal applications.