TRICORBRAUN®

CHOOSING IN-WALL DESICCANTS

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CHOOSING IN-WALL DESICCANTS FOR SOLID TABLETS AND CAPSULES

History of Desiccant Technology

Traditionally solid tablets and capsules sensitive to moisture have been processed under low humidity and packaged in USP tight containers with a separate loose desiccant device (typically silica or clay) inserted in the package. The purpose of this unit-desiccant is to remove the moisture in the headspace of the bottle present at the time of packaging when the heat seal is applied. The degree with which the desiccant can protect the product is limited by the weight of the desiccant, opening size of the bottle or container and its capacity to absorb moisture, as well as the storage conditions for the package. It is not designed for long-term use over the shelf life of the product, and usually not designed to give any protection past the point that the heat seal is broken.

Most tablet and capsule products need to be protected from moisture in order to function properly and maintain stability, efficacy, appearance and customer experience. The containers in which they are packaged are generally required to provide adequate protection in storage and use throughout the expiration dating period. This protection usually comes in the form of a resin that has better barrier properties than others and a heat seal.

The solution for products that require more than standard barrier is most often to package under lower humidity and use a desiccant. Desiccants used with pharmaceuticals, nutraceuticals and foods have traditionally been desiccant sachets or canisters inserted into the bottle, on top of the product, during product filling. When moisture is trapped inside a bottle, it can condense as the temperature drops and vaporize as temperatures rise leading to a cycle that can even with the presence of traditional desiccants. This cycling can cause degradants to form at an increased rate, leading to changes in all aspects of the products functionality appearance and customer experience.

Ever since the movement away from glass containers for pharmaceutical and nutraceutical products, packaging managers have had to manage the needs of the medication along with the limitations of the polymers they use to package products. Even plastics with strong moisture barrier properties, namely HDPE, still allow for moisture ingress into the bottle that, though slow, has to be accounted for in products with high sensitivity to moisture. This is especially necessary for regions of high heat and humidity and in cases where a long shelf life is desired.

This has traditionally been done by adding extra desiccant to account for the potential ingress over the time frame prior to opening, but is not effective once the bottle is opened.

These canister and sachet desiccant options have been the overwhelming choice since their addition to the marketplace for good reason; they are a relatively inexpensive product compared to the other alternatives and they were an improvement over barrier protection alone. The silica and clay materials are quick to absorb the initial available moisture to protect the product. To some degree, this desiccant protection can help to extend shelf life by attracting moisture that has migrated through the bottle wall into the bottle if there is remaining capacity after the headspace is cleared. Once the customer has the product and the seal is broken, this desiccant is typically discarded. Even if left in the bottle, the desiccant has either already reached saturation or soon will and the effective life is over.

Yet for the many positives of the sachet or canister desiccants, they do have limitations. First, every gram of silica or clay only absorbs one third of its weight. This means that to protect bottles with large internal volume or with products that are very hydroscopic in nature, many grams of this desiccant would be needed, leading to multiple sachets or very large canisters whose size are restricted by the opening of the bottle or the remaining available head space after insertion of the product.

Silica and clays work by trapping water molecules and physically holding them. This binding is like water in a straw, with the water molecules filling the many holes in the silica or clay. The fact that the water is not chemically bound, only physically held, means that there is always a chance for release of some or all the trapped moisture under varying environmental conditions during shipping, storage or after purchase. This high thirst and loose hold makes it very easy for a cycle of releases and absorption and an ever changing internal humidity in the package to be created as temperature rises and falls with changing ambient conditions.

Additional limitations can occur with the handling of fast absorbing material in canisters or sachets. Protection during filling, insertion and inspection is necessary to insure that the product has the necessary capacity when the bottle is finally sealed. Another aspect is the liability that can occur from ingestion of the desiccant. And lastly, the rapid absorption characteristics do not allow for long term control of the environment within the bottle before or after the customer has received it leading to shorter than necessary shelf life or increased product loadings.

IN-WALL DESICCANT TECHNOLOGIES

Recently there have been two new additions to the moisture protection choices available to anyone protecting solid tablets and capsules. Both of these new choices fall into a new category, called In-Wall Desiccants. These are so named because the desiccant materials are built directly into the wall of the bottles as outlined in Figures 1 & 2. These new pill packers are available in both multi-layer (Fig. 1) and mono-layer (Fig. 2), and are able to utilize the same HDPE resins that have been used in these types of containers for years. They also eliminate the use of a loose canister or sachet and the need to have the desiccant mixed in with the pills.

FIGURE 1

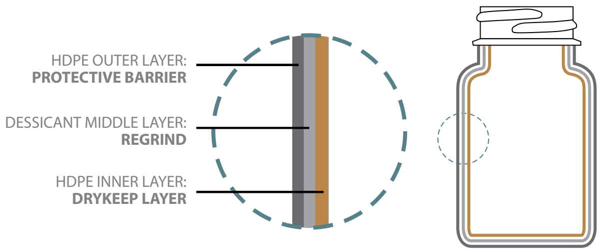
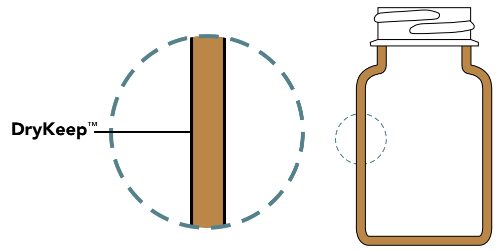


FIGURE 2



Though both the technologies are contained within the bottle wall and both have been introduced to the market at approximately the same time, there are significant differences in how they work and the results gained. The two technologies are DryKeep™ and calcium oxide. These two products differ in how they absorb moisture and the transformations they go through during absorption. In order to best describe these differences we need to look at each one individually.

CALCIUM OXIDE

Calcium oxide is the first of the in-wall desiccants we will discuss, it is a compound in the public domain that can be manufactured by anyone that has the ability to deal with its volatile nature. Calcium oxide binds with water through a chemical reaction forming calcium hydroxide. This reaction is strong enough that it will not release the water under any conditions that the package would survive. This solves the issue of moisture release from traditional desiccants that has been a concern since their introduction.

Yet with the above stated advantages of calcium oxide over loose desiccants there are also a lot of similarities to traditional desiccants. Foremost would be that they both react quickly with any available moisture that they drive the relative humidity as low as possible (seeking an RH of between 0-10%). This fast absorption of moisture means that these products must be closely monitored in the filling process to ensure they do not use a lot of their moisture absorbing capacity. However, unlike silica gels or clay any moisture absorbed by the calcium oxide bottles cannot be driven off making them useless. Another similarity is both a silica/clay and calcium oxide material will only absorb approximately 1/3 of their weight in moisture. And lastly, neither is safe for ingestion; raising concerns about putting them in such close proximity with oral medications.

The calcium oxide also has other processing and handling concerns. The chemical reaction to form a hydroxide from an oxide causes a release of heat, odor and a cubic expansion which forces the middle layer to swell, leading to delamination and distortion of the bottle. The resulting high pH can also lead to potential resin degradation. Because of the quick uptake of this product and the inability to drive moisture out with heat, very special care must be taken in filling this product. Calcium hydroxide, the reacted version of calcium oxide is alkaline or has a high pH. This pH level probably leads to an MSDS statement that it is toxic to fish. Therefore calcium hydroxide appears difficult to manage in filling and storage and is an environmental concern.

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DRYKEEP™

The other new option for In-Wall Desiccants is a compound called DryKeep™ patented by Sasaki Chemical and under exclusive license in the United States by TricorBraun. Of all the desiccant options this would seem to be the most versatile. DryKeep™ is a compounded masterbatch of desiccant encapsulated in medical grade HDPE. This desiccant compound is molded into the middle layer of the multilayer bottle. It also absorbs through chemical bonding; not allowing for the release of the captured moisture back into the environment. However, this is where the similarities with calcium oxide end.

DryKeep™ is composed of a natural occurring salt, with hundreds of years of history and is safe for ingestion. This compound of DryKeep™ and medical grade HDPE is then used as a molding resin in the middle layer of the bottle in its dried form. Stociometricly DryKeep™ absorbs moisture on a one to one weight ratio. The result is a desiccant material that absorbs three times the amount of the aforementioned materials because DryKeep™ absorbs 100% of its weight in moisture. This high gain means less material needed to obtain the same protection, or the ability to give more protection with the same amount of desiccant material.

DryKeep™ absorbs water through hydration forming chemical bonds. This type of absorption has no affect on the volume of the molecules meaning there is no cubic expansion leading to delamination or aesthetic issues caused by the swelling of the desiccant. The absorption in the form of a hydrate also means that there is no chemical reaction or change in the pH or properties of DryKeep™. This slow absorption is the effect of the DryKeep™ molecules finding their equilibrium based on the resin they are compounded into and allows for a bottle that can be designed to hold a desired RH range. This property is an advantage over other systems because a product being too dry can in many cases be as detrimental as it being too wet. Typically DryKeep™ is compounded into HDPE, a resin with low moisture vapor transfer (MVTR) maintain a relative humidity similar to most controlled filling rooms. However if it is compounded into a resin with high MVTR the relative humidity inside the bottle will be maintained at a lower level as the equilibrium humidityof the compound has been lowered. Due to the lowered moisture barrier of these resins moisture can move to the desiccant easier. All of this functionality and flexibility is available with HDPE inner and outer layers allowing products and customers to contact the exact same materials they do today.

The controlled absorption of moisture and tailored relative humidity of this product coupled with the high volume that it can absorb allows for much more flexibility, extended protection and ease of handeling. In filling no special care has to be taken with these bottles in the filling process. Early studies show that bottles can be exposed to ambient filling conditions in excess of twenty four hours without substantial loss of desiccating power. This would simply mean that hoppers on the filling line may need to be emptied before weekend shutdown, but in the normal course of the week, no special care would need to be taken. Where DryKeep™ differs from the other options on the market is that is has a slow measured and controllable uptake because of its steady movement toward a hydrate and the equilibrium humidity of the chosen resin.

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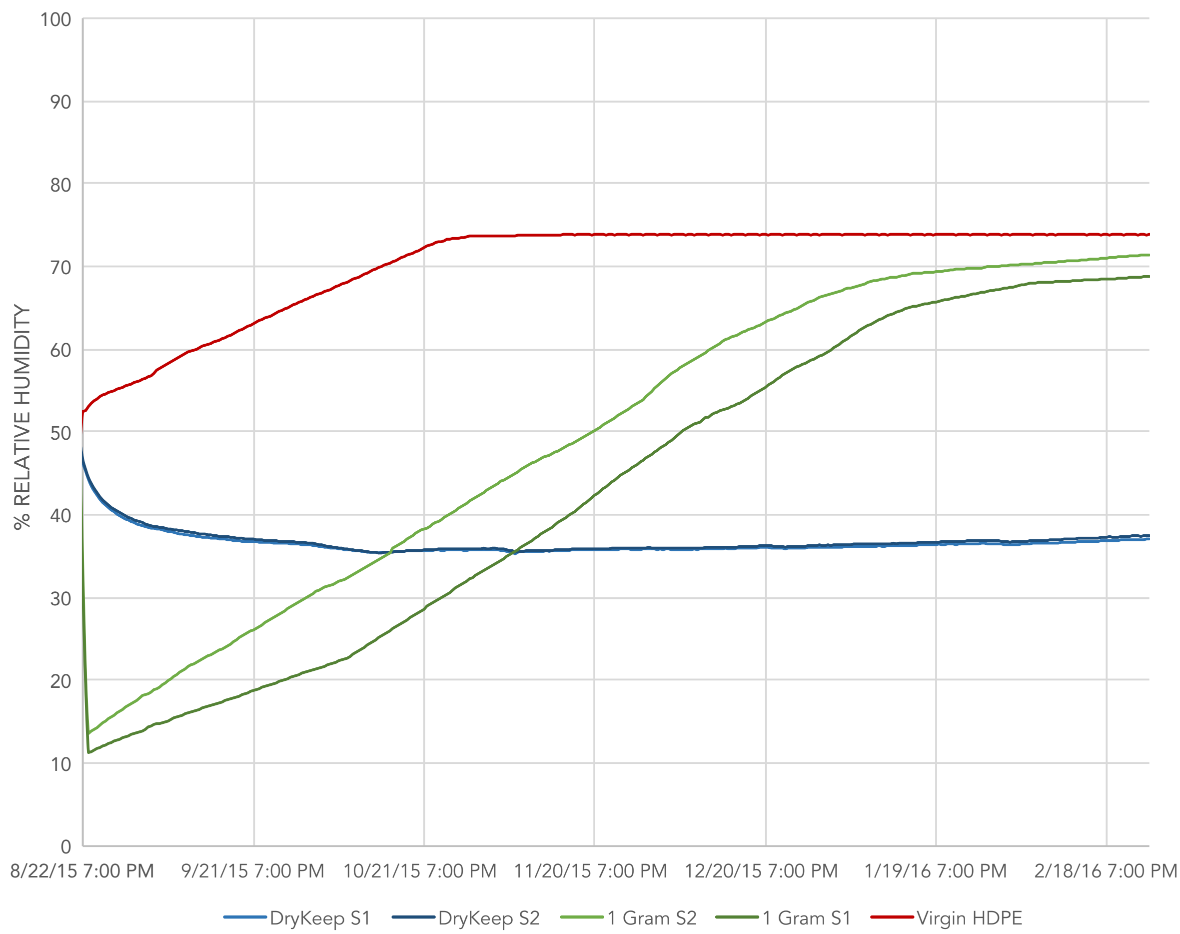
The graph below outlines performance characteristics of the standard desiccant technology curve in the market



The chart demonstrates the MVTR performance differences between an HDPE bottle in 100% virgin material (red line), a virgin bottle with a 1 gram silica/clay desiccant (green lines) and a bottle with 75% virgin and 25% DryKeep. The interior of the virgin bottle immediately starts a trend up to 75% RH (the test chamber settings), the virgin with 1 gram desiccant quickly starts trending down to almost 10%, and once its capacity is used up, starts trending on the same trajectory as the virgin bottle up toward 75%RH. The DryKeep bottles, slowly trend down toward 35%, and remain in and around that window there for duration.

From a cost performance, since the active in DryKeep can absorb 100% of its weight in water compared with 33% for the clay/silica products, the triple performance advantage of DryKeep will be cost neutral will offering 2-3X more absorption and therefore a longer shelf life. And since the DryKeep remains with the package, it will provide superior performance to the end customer, from the first dose to the last.

The Matrix below outlines the properties of the various desiccant technologies currently available on the market.

Desiccant Type	Absorption Type	Absorption Rate	Re-Release of Moisture	Cubic Expansion	Toxicity	Requires Special Material Handling
Silica or Clay	Physical	Fast	Yes	N/A	No	Yes
Calcium Oxide	Chemical	Fast	No	Yes	Yes	Yes
DryKeep™	Chemical	Controlled	No	No	No	No

CONCLUSIONS

For years the traditional silica and clay type desiccants have been the best option on the market. They were necessary to protect product, at least until the point of purchase. Now with In-Wall Desiccants the long standing problems with these traditional products no longer need to trouble those trying to protect their products from moisture. Of the In-Wall desiccant technologies available DryKeep™ would seem to have characteristics and flexibility making it the better choice:

- Absorbs 100% of its weight in water
- Will not release moisture back into the bottle
- Slow and steady hydration (absorption)
- pH neutral
- Ease of handling during filling
- Line speeds not dependent upon insertion and inspection of loose desiccant
- Approved as a food additive (non-toxic)
- No heat generated
- No cubic expansion
- No chemical reaction

The ability of DryKeep™ to hold so much more moisture without swelling or chemical changes would be enough to swing most people to say it is the better of the desiccant technologies. If you couple this with the ease of handling in processing and lack of safety concerns, it is definitely the hands down choice. All of these advantages allow for packaging engineers to design a bottle that not only protects the pills until the heat seal is removed but allows for them to know that the product will be safe in the desired environment for the life of the bottle and product, a luxury only known in blister packs today. This increased confidence in the environment should allow many companies to extend shelf life or reduce ingredient load to get the same desired results. The combined properties should allow for a longer shelf life, the potential for lower levels of materials to meet efficacy claims, and more faith that the performance of the product is the same on the last dose as it was in the first.