

# eye on excipients

John Lawrence

**Bulk Solids Innovation Center, Kansas State University**

*This column covers some excipient basics and discusses how moisture content affects excipient properties and behavior.*

The moisture content of excipients plays an important role in the physical and chemical properties of pharmaceutical products. The characteristics of the excipients for a particular dosage of a formulation depend on their moisture sorption behavior, flowability, and stability during manufacturing and storage. Defined as any substance other than the API that has been appropriately evaluated for safety, excipients are included in a drug delivery system for the following reasons:

- To aid processing of the system during its manufacture;
- To protect and support stability, bioavailability, and patient acceptability;

- To assist in product identification;
- To enhance any other attribute that promotes the overall safety and efficacy of the API during storage or use [1].

Manufacturers classify excipients according to their function, such as sweetener, preservative, binder, lubricant, flow enhancer, film former, filler, disintegrant, or diluent.

According to a study by Dave in 2008, the most common excipients are lactose; microcrystalline cellulose (MCC), a diluent; sodium starch glycolate; croscarmellose sodium, a disintegrant; colloidal silicon-dioxide, a glidant; hydroxypropyl methylcellulose (HPMC); polyvidone (PVP); lactose hydrous; starch, a binder; magnesium stearate, a lubricant; and titanium dioxide, an opacifier [2].

The presence of water in an excipient is very critical in terms of stabil-

ity, flow, dissolution, compaction, and storage. The hygroscopicity of an excipient is its ability to interact with moisture from the surrounding atmosphere, and the mechanisms of moisture sorption are different for various excipients. Therefore, formulators must understand the moisture-sorption characteristics of potential excipients before working on any API formulation.

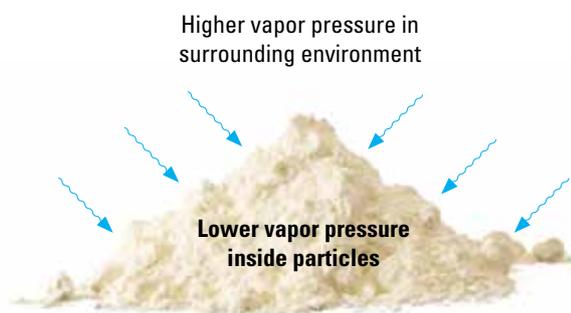
Pharmaceutical scientists refer to the equilibrium relative humidity (ERH) of an excipient (the vapor pressure inside and outside the material) as the *water activity* ( $a_w$ ). The  $a_w$  is a measure of free moisture in the material and influences a combination of water-solute and water-surface interactions and capillary forces. Generally, the  $a_w$  increases as the temperature increases.

Depending on the temperature, relative humidity (RH), and compo-

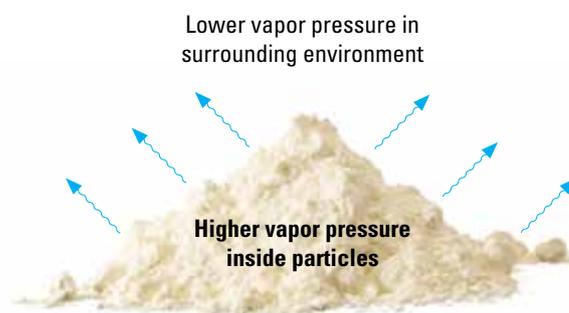
**FIGURE 1**

## Influence of vapor pressure on adsorption and desorption

**a. Adsorption: Moisture moves to material from environment to maintain equilibrium**



**b. Desorption: Moisture moves from material to environment to maintain equilibrium**



sition of a material, either adsorption or desorption will occur. Adsorption refers to moisture adhering to the material; desorption refers to the removal of moisture from the material. The moisture content of an excipient at ERH is called the equilibrium moisture content (EMC). At EMC, the material adsorbs or desorbs no moisture at a particular temperature and RH. The microbial stability, chemical stability, flow properties, hardness, compaction, and dissolution rate of a formulation depend on the  $a_w$  of its excipients.

Figures 1a and 1b show how differences in vapor pressure influence the mechanisms of adsorption and desorption. Moisture adsorbs from a surrounding environment with a higher vapor pressure into material with a lower vapor pressure, whereas moisture desorbs from material with a higher vapor pressure into a surrounding environment with a lower vapor pressure.

Two types of moisture adsorption occur, physical and chemical. Physical adsorption, or physisorption, uses van der Waals interactions and is reversible. In chemical adsorption, or chemisorption, material adsorbs molecules by chemical bonding, and the process is irreversible [3]. Different forms of adsorption and desorption exist. The most common form can be represented by a sigmoidal curve with the x-axis representing the  $a_w$  and the y-axis representing the moisture content in the material, as shown in Figure 2. The difference between the adsorption and desorption curves in

the figure is called hysteresis.

The RH of the surrounding environment at a particular temperature, from which an excipient could adsorb moisture from the atmosphere, limits the critical relative humidity (CRH) of the excipient. For example, the CRH of the excipient sodium bicarbonate powder lies between 76 percent and 88 percent RH at 25°C and between 48 percent and 75 percent RH at 40°C. This means that sodium bicarbonate powder is stable below 76 percent RH at 25°C and below 48 percent RH at 40°C [4]. Exposing an excipient to RH above the critical RH creates a liquid state that accelerates chemical and physical changes.

Pharmaceutical scientists commonly model the moisture sorption characteristics of excipients using the Guggenheim, Anderson, and de Boer (GAB) equation, as follows:

$$MC = \frac{w_m C K a_w}{(1 - K a_w) \times (1 - K a_w + K C a_w)}$$

where MC is the moisture content of the excipient (dry basis, decimal);  $w_m$  is the moisture content adsorbed or desorbed, corresponding to the monomolecular layer;  $a_w$  is the water activity; and K and C are constant parameters.

The sorption parameters for the excipients MCC, carboxymethyl cellulose (CMC), HPMC, and polyvinylpyrrolidone (PVP) are found in Crouter and Briens' article "The effects of moisture on the flowability of pharmaceutical excipients" [5]. Based on the moisture-sorption characteristics, you can identify the range of moisture content for an excipient that falls under the CRH at a particular environmental condition. As the temperature of the environment changes, those characteristics change, as does the material's behavior. The best practice is to identify the right environment, understand the material's behavior, and modify the conditions of the work environment to suit the material's requirements for processing.

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## References

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John Lawrence is research director at the Bulk Solids Innovation Center, Kansas State University (<https://bulk-solids.k-state.edu/index.html>).

**FIGURE 2**

### Sigmoidal adsorption and desorption curves

