Water Activity as an Alternative to Karl Fischer Moisture Testing

Water has long been recognized as important in determining product safety and stability. Karl Fischer titration is a widely used analytical method for quantifying water content in a variety of pharmaceutical products. Simply knowing the total amount of water by Karl Fischer may not be the most effective method for understanding the effects of water on safety and stability. Water activity (a_w) is an alternative water measurement that provides essential information about the energy or availability of water in a product. Numerous scientific investigations demonstrate that water activity is a better predictor of product safety and stability than total amount of water. Water activity has long been used in the food industry as an effective tool and with the publication of USP Method <1112>, it is now considered a viable option in the pharmaceutical industry as well.

Not All Water Is Equal

Water in a system may be thought of as present in three general forms: bulk or "free", absorbed, and "bound" or monolayer water. Bulk or "free" water has the same energy and properties as pure water. Absorbed water is held less tightly, but still has reduced energy and different properties than pure water. "Bound" water has reduced energy as the result of direct physical binding of water to the matrix by hydrogen or ionic bonding. In reality, water molecules readily move between each of the forms and it is impossible to quantify the amount of water in any one form. Rather, the overall energy status of water is determined by the relative contributions of each of these water layers. A reduction in the energy of the water, (i.e. lower water activity), results in less available water for influencing biological and chemical reactions. Moisture content analysis provides the total amount of water, but does not differentiate the type of water.

Karl Fischer titrations are effective at quantifying even the tightly "bound", and are often considered a better moisture analysis method than loss on drying. In fact, this extra water that is measured using Karl Fischer is often referred to as the "bound" water. Although a Karl Fischer analysis may provide a more complete determination of total water content, it still only provides the amount of water and not the energy status of the water. Water activity measures the energy or "availability" of water and is not dependent on the amount of water, but the relative contributions of each type of water. Consequently, water activity provides better correlations to biological and chemical reaction rates than Karl Fischer analysis.

What is Water Activity?

Water activity describes the thermodynamic energy status of the water in a system. Though not scientifically correct, it may help to picture water activity as the amount of "available" water in a system. It is not determined by how much water is present in a product, but is a comparison of how much the water in the product resembles and behaves like pure water. Water activity values range from 0 (bone dry) to 1.0 (pure water). As water activity decreases, the water in a product decreases in energy, is less "available" as a solvent, for microbial growth, chemical reactivity, or for moisture migration. For example, water in a product that has a water activity of 0.80 has enough energy to support mold growth while the water in a product with a water activity less than 0.60 cannot support the growth of any microorganism. Water also becomes more mobile as water activity increases, which influences molecular mobility as well as chemical and enzymatic reaction rates.

More scientifically, water activity is defined as the vapor pressure of water (p) over a sample divided by the vapor pressure of pure water (p_o) at a given temperature. By measuring this vapor pressure relative to the vapor pressure over pure water at the same temperature, it is possible to determine the energy of water in the sample. This is reasonable since water that is associated chemically or physically in a sample has lower energy and will not readily move into the vapor phase, thereby decreasing the vapor pressure above the sample.

Why Measure Water Activity?

Water activity is the best index for microbial growth. A product may contain a relatively large percentage of moisture, but if the water is chemically "bound" to humectants or solutes, such as salts, sugars, or polyols, the water is biologically unavailable for microbial growth. The water activity concept has served microbiologists and food technologists for decades and is the most commonly used criterion for food safety and quality. Every microorganism has a limiting a_w below which they cannot grow. No direct relationship exists for moisture content and microbial growth.

There also is a close relationship between water activity and physical stability of products. Differences in water activity levels between components or a component and the environmental humidity is a driving force for moisture migration. Knowledge of whether water will absorb or desorb from a particular component is essential to prevent degradation, especially if one of the substances is moisture sensitive. For example, if equal amounts of component 1 at 2% moisture and component 2 at 10% moisture are to be blended together, will there be moisture exchange between the components? The final moisture content of the blended material would be 6%, but did any moisture exchange between component 1 and 2? The answer depends on the water activities of the two components. If the water activities of the two components are the same, then no moisture will be exchanged.

Likewise, two ingredients at the same moisture content may not be compatible when mixed together. If two materials of differing water activities but the same water content are mixed together, the water will adjust between the materials until an equilibrium water activity is obtained. Thus, for a multi-component product, to prevent moisture migration, one should match the water activity of the two components. If one component is at a higher water activity than the other, water will migrate from high water activity to low water activity. This migration could lead to undesirable changes in the quality of both components. Therefore, water activity provides useful information for formulation design, manufacturing conditions, and packaging requirements.

Replacing Karl Fischer with Water Activity

Karl Fischer analysis can produce reliable results under controlled conditions, but is subject to many sources of variation. It also involves the use of some less than desirable chemicals and requires training to do properly. Consequently, there are several reasons for finding a viable alternative. Water activity can replace Karl Fischer analysis, not because it provides the same information, but because it provides more useful information. The results provided by a water activity analysis will not resemble Karl Fischer moisture content, but will provide better correlations to microbial safety, chemical stability, and physical properties. This is especially true for products that can experience large stability changes when only small, difficult to measure, changes in moisture content occur.

How are Karl Fischer and Water Activity Related?

There is a relationship between Karl Fischer water content and water activity, but it is complex and unique to each product. An increase in water activity is usually accompanied by an increase in the water content, but in a nonlinear fashion. This relationship between water activity and moisture content at a given temperature is called the moisture sorption isotherm. For most products, the isotherm is sigmoidal in shape, although materials that contain large amounts of crystalline molecules have a J-type isotherm curve shape. Many different equations are utilized to characterize a product's isotherm relationship. For small water activity ranges, linear regression can describe an isotherm relationship, but it rarely works for the entire water activity range. More complex equations are used to characterize the isotherm for the entire water activity range. The most common equations are the Guggenheim-Anderson-de Boer (GAB) and Brunauer-Emmett-Teller (BET) equations. Like linear regression, these equations are adjusted to find coefficients that do the best job of explaining the isotherm relationship. Data analysis software programs are used to determine these coefficients, which then can be used to predict the moisture content at any water level or vice versa.

A Complete Moisture Analysis by a Single Instrument

While water activity is a viable alternative to Karl Fischer moisture content for determining product safety and quality, it may still be necessary to know moisture content for determining purity. Water activity still may be able to replace Karl Fischer for this purpose since it is possible to determine moisture content based on water activity through the moisture sorption isotherm relationship. This would allow a water activity instrument to replace Karl Fischer by providing both moisture content and water activity measurements. If you are interested in additional information about replacing Karl Fischer with water activity, contact Decagon Devices.

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