Document Title: Description, AN, Pharmaceutical App of Aw		Part # and Rev. 13431-00	
		Release Date:	
Rev.	Description	Revision By	Date

Production Filename: 13431 (In Product Library)

Path to Working Files: DecaDoc\Application Notes\Master

Dimensions: 8.5 inch wide, 11 inch tall

Material: Paper, 92 Bright White or better, 75g/m² or heavier

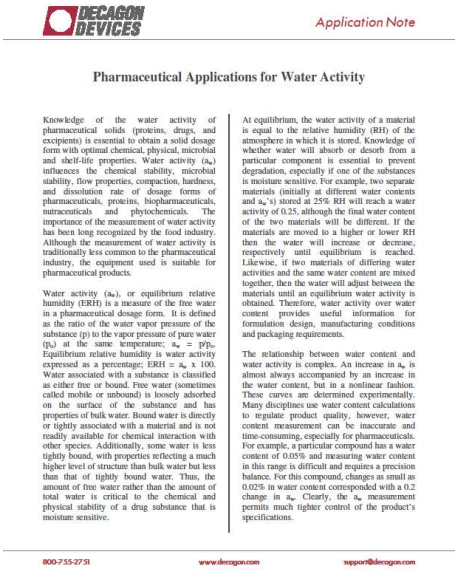
Colors: Color Print on White

Printer: HP Color LaserJet 8550-PS

Finish: None

Adhesive: None

Special Notes: Illustrations are Ref Only ** Not to Scale ** (Shown page 1 of 2)



DECAGON DEVICES Application Note

Pharmaceutical Applications for Water Activity

Knowledge of the water activity of pharmaceutical solids (proteins, drugs, and excipients) is essential to obtain a solid dosage form with optimal chemical, physical, microbial and shelf-life properties. Water activity (a_w) influences the chemical stability, microbial stability, flow properties, compaction, hardness, and dissolution rate of dosage forms of pharmaceuticals, proteins, biopharmaceuticals, nutraceuticals and phytochemicals. The importance of the measurement of water activity has been long recognized by the food industry. Although the measurement of water activity is traditionally less common to the pharmaceutical industry, the equipment used is suitable for pharmaceutical products.

Water activity (a_w), or equilibrium relative humidity (ERH) is a measure of the free water in a pharmaceutical dosage form. It is defined as the ratio of the water vapor pressure of the substance (p) to the vapor pressure of pure water (p_o) at the same temperature; $a_w = p/p_o$. Equilibrium relative humidity is water activity expressed as a percentage; ERH = a_w x 100. Water associated with a substance is classified as either free or bound. Free water (sometimes called mobile or unbound) is loosely adsorbed on the surface of the substance and has properties of bulk water. Bound water is directly or tightly associated with a material and is not readily available for chemical interaction with other species. Additionally, some water is less tightly bound, with properties reflecting a much higher level of structure than bulk water but less than that of tightly bound water. Thus, the amount of free water rather than the amount of total water is critical to the chemical and physical stability of a drug substance that is moisture sensitive.

At equilibrium, the water activity of a material is equal to the relative humidity (RH) of the atmosphere in which it is stored. 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, two separate materials (initially at different water contents and a_w's) stored at 25% RH will reach a water activity of 0.25, although the final water content of the two materials will be different. If the materials are moved to a higher or lower RH then the water will increase or decrease, respectively until equilibrium is reached. Likewise, if two materials of differing water activities and the same water content are mixed together, then the water will adjust between the materials until an equilibrium water activity is obtained. Therefore, water activity over water content provides useful information for formulation design, manufacturing conditions and packaging requirements.

The relationship between water content and water activity is complex. An increase in a_w is almost always accompanied by an increase in the water content, but in a nonlinear fashion. These curves are determined experimentally. Many disciplines use water content calculations to regulate product quality, however, water content measurement can be inaccurate and time-consuming, especially for pharmaceuticals. For example, a particular compound has a water content of 0.05% and measuring water content in this range is difficult and requires a precision balance. For this compound, changes as small as 0.02% in water content corresponded with a 0.2 change in a_w. Clearly, the a_w measurement permits much tighter control of the product's specifications.