PHYSICAL PHARMACY CAPSULE 4.11

Hydrates and Solvates

When a substance is a hydrate and water is present in the molecule, more of the chemical must be weighed to obtain the actual active drug. As a drug example that is available with different amounts of water, let us look at different forms of dexamethasone.

- Dexamethasone contains less than 0.5% of its weight in water.
- Dexamethasone acetate has one molecule of water of hydration and contains between 3.5% and 4.5% of water; the anhydrous form contains less than 0.4% water.
- Dexamethasone sodium phosphate contains a sum of water and alcohol that may be up to 16%

Another example is lidocaine hydrochloride. Lidocaine hydrochloride occurs as a monohydrate and as the anhydrous form. The water content may be between 5% and 7%

CALCULATIONS

How much adjustment should be made if using lidocaine hydrochloride monohydrate in place of lidocaine hydrochloride anhydrous for a compounded prescription?

Lidocaine HCl monohydrate $C_{14}H_{22}N_2O \cdot HCl.H_2O$ MW 288.81

Lidocaine HCl anhydrous $C_{14}H_{22}N_2O \cdot HCl$ MW 270.80

A comparison of the molecular weights reveals a factor of 1.066 can be used for the adjustment:

$$(288.81) / (270.80) = 1.066$$

EXAMPLE:

If a prescription for lidocaine hydrochloride 2% gel (100 g) is to be made, then 2 g of anhydrous lidocaine HCl could be used, OR:

2 g × 1.066 = 2.132 g of lidocaine HCl monohydrate.

Also, a direct comparison of the molecular weights and the physical quantity required can be used, as follows:

$$\frac{\text{MW hydrate}}{\text{MW anhydrous}} = \frac{\text{weight of hydrated form}}{\text{weight of anhydrous form}}$$

$$\frac{288.81}{270.80} = \frac{X}{2g}$$

$$X = 2.133\,g$$

Further, the USP monograph for lidocaine hydrochloride Jelly, USP states "It contains not less than 95% and not more than 105.09% of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$)." Note that this is the anhydrous form. It is important to also check the C of A for the lidocaine hydrochloride being used to determine the water content. Fortunately, most pure powders (anhydrous) generally only contain 0.2% to 0.5% moisture, which can be insignificant but need to be checked, nevertheless.

made quickly after opening the bulk chemical containers and then resealing them.

Solvates and hydrates must be packaged in "tight" containers to prevent the loss or gain of moisture. In fact, it is best to have all chemicals stored in "tight" containers and to keep them thoroughly closed at all times except for the short time when a weighing step is involved. Storage at the indicated temperatures is also important and to minimize any exposure to very high humidity levels. More on hydrates and solvates is presented in Physical Pharmacy Capsule 4.11, Hydrates and Solvates.