PHYSICAL PHARMACY CAPSULE 4.12

Organic Salts

It is important to know whether or not a drug is "dosed" on the base or the salt form. Consider that the fentanyl dose is calculated on the "base" form but the "salt" is the form that is used in the dosage form. For example:

A prescription calls for 10 mL of fentanyl 50 µg/0.1 mL (as the citrate) topical gel. How much fentanyl citrate will be required?

1. 50 µg/0.1 mL = X µg/10 mL, X = 5 mg
2. Fentanyl MW = 336.47
   Fentanyl citrate MW = 528.59
3. 336.47/5 mg = 528.59/X, X = 7.85 mg
4. Each mg of fentanyl equals 528.59/336.47 = 1.57 mg fentanyl citrate

In a different example, Diphenhydramine Hydrochloride Capsules USP are based on the total molecule, that is, diphenhydramine hydrochloride. The USP states "Diphenhydramine Hydrochloride Capsules USP contain not less than 90% and not more than 110% of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$)." As one can see, the weight of the "HCl" is considered in the dose of the drug. For example:

A prescription calls for 30 capsules of diphenhydramine hydrochloride 35 mg each. How much diphenhydramine hydrochloride will be required?

1. Since the total salt molecule is part of the dose:
2. 30 × 35 mg = 1.05 g of diphenhydramine hydrochloride is required.

UXP XII (1942) lists about 20 tablet monographs that are all based on the "salt" form of the drug, for example, Morphine Sulfate Tablets USP contain not less than 93% and not more than 107% of the labeled amount of morphine sulfate [$(C_{17}H_{19}O_3N)_2 \cdot H_2SO_4 \cdot 5H_2O$]. The names of the monographed items in this time period were quite clear as the salt names were a part of the official name if it was to be used. For example, Barbital Tablets USP are based on the labeled amount of barbital ($C_8H_{12}N_2O_3$), but Barbital Sodium Tablets were based on the labeled amount of barbital sodium ($C_8H_{11}N_2O_3Na$).

USP XVI (1960) monograph for Amodiaquine Hydrochloride Tablets USP states "Amodiaquine Hydrochloride Tablets contain an amount of amodiaquine hydrochloride ($C_{20}H_{22}ClN_3O \cdot 2HCl \cdot 2H_2O$) equivalent to not less than 93% and not more than 107% of the labeled amount of amodiaquine base ($C_{20}H_{22}ClN_3O$)." It is evident in this monograph that the dose is calculated on the "base" form of the drug.

It is the responsibility of the formulator to determine whether or not the base/acid of the salt form of the drug is to be used in the calculations for the amount of API to actually be used.

with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance without regard to the actual charged state of the molecule in vivo.

For example, the active moiety of a hydrochloride salt of a base will be the free base and not the protonated form of the base. The active moiety of a metal acid salt will be the free acid.

This Policy is followed by USP in naming drug products and compounded preparations that are newly recognized in the USP. Revising existing monographs to conform to this Policy is not intended, except where the USP Council of Experts determines that, for reasons such as safety, a nomenclature change is warranted."

See example organic salt considerations in Physical Pharmacy Capsule 4.12, Organic Salts.