

solvent in the former preparation, but each has its pharmaceutical advantage because of its physical form. For instance, the pilular extract is preferred in compounding a plastic dosage form such as an ointment

or paste or one in which a pliable material facilitates compounding, whereas the powdered form is preferred in the compounding of such dosage forms as powders, capsules, and tablets.

PHARMACEUTICS



CASE STUDY

SUBJECTIVE INFORMATION

You have been given the responsibility of formulating a new oral solution containing a nasal decongestant (phenylephrine) and cough suppressant (dextromethorphan) for treating the symptoms of a cold or influenza. The oral solution should have a reasonably pleasant taste and appearance, be stable and preserved, and contain a suitable dose combination so that one or two teaspoonfuls can be used per administration to a 6- to 12-year-old child.

OBJECTIVE INFORMATION

Phenylephrine hydrochloride ($C_9H_{13}NO_2 \cdot HCl$), molecular weight 203.67, is the salt form selected for this drug. Phenylephrine hydrochloride occurs as white or nearly white odorless crystals with a bitter taste. It melts at $140^{\circ}C$ to $145^{\circ}C$ ($284^{\circ}F$ to $293^{\circ}F$). It is freely soluble in water and in alcohol. It is stable in aqueous solution below pH 7. Above pH 7, degradation occurs apparently involving the side chain, with loss of the secondary amine function; the phenolic group remains intact. The presence of heavy metals, especially copper, can catalyze the decomposition. It has two dissociation constant (pK_a) values, one at 8.77 and one at 9.84.

Dextromethorphan ($C_{18}H_{25}NO$, MW 271.40) is a practically white to slightly yellow odorless crystalline powder that melts at $109.5^{\circ}C$ to $112.5^{\circ}C$ ($229^{\circ}F$ to $234.5^{\circ}F$). It is practically insoluble in water. Dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$, MW 370.32) occurs as practically white crystals or crystalline

powder with a faint odor and a melting range of $124^{\circ}C$ to $126^{\circ}C$ ($255^{\circ}F$ to $259^{\circ}F$). It is freely soluble in alcohol. It is stable in aqueous and hydroalcoholic solutions.

ASSESSMENT

The two drugs should be soluble and stable in a slightly acidic oral solution consisting of water and alcohol. The vehicle should be slightly thickened by a viscosity-increasing additive; it also should be sweetened and flavored. These drugs are bitter, so a flavor that will help mask the bitterness must be selected. The addition of a small amount of menthol may also be considered as a flavor enhancer. An appropriate preservative must be selected.

PLAN

An aqueous solution consisting of water, alcohol (low concentration, such as 5%), and glycerin (10%) adjusted to a pH in the range of 4 to 5 should be reasonable. Sucrose can be added as a sweetener (40%) and also for its viscosity-enhancing effect. It can be further thickened with methylcellulose (0.5%) or other cellulose polymer commonly used in oral liquids. A small amount of sorbitol (10%) will help give a smooth mouth feel and minimize cap lock of the container. Several flavor combinations can work, but raspberry and marshmallow work nicely to cover the bitter tastes of drugs. A blend of 0.05% methylparaben and 0.02% propylparaben can be added as a preservative. The addition of about 0.25% menthol will further enhance the flavoring and also impart an additional aromatic effect.