properties of the solvent or vehicle must be considered, evaluated, and determined to be suitable for the task at hand. Among the many considerations are the solvent's physical and chemical stability at various pH levels, viscosity, which must be such as to allow ease of injection (suitable for use in syringes); fluidity, which must be maintained over a fairly wide temperature range; boiling point, which should be sufficiently high to permit heat sterilization; miscibility with body fluids; low vapor pressure to avoid problems during heat sterilization; and constant purity or ease of purification and standardization. No single solvent is free of limitations; hence, cross-consideration and assessment of each solvent's advantages and disadvantages help the formulator determine the most appropriate solvent for a given preparation. Among the nonaqueous solvents employed in parenteral products are fixed vegetable oils, glycerin, polyethylene glycols, propylene glycol, alcohol, and a number of less often used agents, including ethyl oleate, isopropyl myristate, and dimethylacetamide. These and other nonaqueous vehicles may be used provided they are safe in the amounts administered and do not interfere with the therapeutic efficacy of the preparation or with its response to prescribed assays and tests.

The USP specifies restrictions on the fixed vegetable oils in parenteral products. For one thing, they must remain clear when cooled to 10°C (50°F) to ensure the stability and clarity of the injectable product during refrigeration. The oils must not contain mineral oil or paraffin, as these materials are not absorbed by body tissues. The fluidity of a vegetable oil generally depends on the proportion of unsaturated fatty acids, such as oleic acid, to saturated acids, such as stearic acid. Oils to be employed in injections must meet officially stated requirements of iodine number and saponification number.

Although the toxicity of vegetable oils is generally considered to be relatively low, some patients exhibit allergic reactions to specific oils. Thus, when vegetable oils are employed in parenteral products, the label must state the specific oil. The most commonly used fixed oils in injections are corn oil, cottonseed oil, peanut oil, and sesame oil. Castor oil and olive oil have been used on occasion (Physical Pharmacy Capsule 15.1).

PHYSICAL PHARMACY CAPSULE 15.1

Colligative Properties of Drugs

Drug molecules have properties that are often divided into additive, constitutive, or colligative.

Additive properties depend on the total contribution of the atoms in the molecule or on the sum of the properties of the constituents of the solution. An example is molecular weight.

Constitutive properties depend on the arrangement and, to a lesser extent, the number and kind of atoms in a molecule. Examples are refraction of light, electrical properties, and surface and interfacial properties.

Colligative properties depend primarily on the number of particles in solution. Example properties include changes in vapor pressure, boiling point, freezing point, and osmotic pressure. These values should be approximately equal for equimolar concentrations of drugs.

LOWERING OF VAPOR PRESSURE

A vapor in equilibrium with its pure liquid at a constant temperature will exert *vapor pressure*. When a solute is added to the pure liquid, it will alter the tendency of the molecules to escape the original liquid. In an ideal solution or one that is very dilute, the partial vapor pressure of one component (p_1) is proportional to the mole fraction of molecules (N_1) of that component in the mixture: