3. Water solubility decreases with an increase in molecular weight.
4. Increased structural similarity between solute and solvent is accompanied by increased solubility.

It is the pharmacist's knowledge of the chemical characteristics of drugs that permits the selection of the proper solvent for a particular solute. However, in addition to the factors of solubility, the selection is based on such additional characteristics as clarity, low toxicity, viscosity, compatibility with other formulative ingredients, chemical inertness, palatability, odor, color, and economy. In most instances, especially for solutions to be taken orally, used intranasally, used ophthalmically, or injected, water is the preferred solvent because it comes closer to meeting these criteria than other solvents. When water is used as the primary solvent, commonly an auxiliary solvent is also employed to augment the solvent action of water or to contribute to a product's chemical or physical stability. Alcohol, glycerin, and propylene glycol, perhaps the most widely used auxiliary solvents, have been quite effective in contributing to the desired characteristics of pharmaceutical solutions and in maintaining their stability.

Other solvents, such as acetone, ethyl oxide, and isopropyl alcohol, are too toxic to be permitted in pharmaceutical preparations to be taken internally, but they are useful as reagent solvents in organic chemistry and in the preparatory stages of drug development, as in the extraction or removal of active constituents from medicinal plants. For purposes such as this, certain solvents are officially recognized in the compendia. A number of fixed oils, such as corn oil, cottonseed oil, peanut oil, and sesame oil, are useful solvents, particularly in the preparation of oleaginous injections, and are recognized in the official compendia for this purpose.

SOME SOLVENTS FOR LIQUID PREPARATIONS

The following agents find use as solvents in the preparation of solutions.

Alcohol, USP: Ethyl Alcohol, Ethanol, C_2H_5OH

Next to water, alcohol is the most useful solvent in pharmacy. It is used as a primary solvent for many organic compounds. Together with water, it forms a hydroalcoholic mixture that dissolves both alcohol-soluble and water-soluble substances, a feature especially useful in the extraction of active constituents from crude drugs. By varying the proportion of the two agents, the active constituents may be selectively dissolved and extracted or allowed to remain behind, according to their particular solubility characteristics in the menstruum. Alcohol, USP, is 94.9% to 96.0% C_2H_5OH by volume (i.e., v/v) when determined at 15.56°C, the US government's standard temperature for alcohol determinations. Dehydrated Alcohol, USP, also called absolute alcohol, contains not less than 99.5% C_2H_5OH by volume and is used when an essentially water-free alcohol is desired.

Alcohol has been well recognized as a solvent and excipient in the formulation of oral pharmaceutical products. Certain drugs are insoluble in water and must be dissolved in an alternative vehicle. Alcohol is often preferred because of its miscibility with water and its ability to dissolve many water-insoluble ingredients, including drug substances, flavorants, and antimicrobial preservatives. Alcohol is frequently used with other solvents, such as glycols and glycerin, to reduce the amount of alcohol required. It is also used in liquid products as an antimicrobial preservative alone or with parabens, benzoates, sorbates, and other agents.

However, aside from its pharmaceutical advantages as a solvent and a preservative, concern has been expressed over the undesired pharmacologic and potential toxic effects of alcohol when ingested in pharmaceutical products, particularly by children. Thus, the U.S. Food and Drug Administration (FDA) has proposed that insofar as possible manufacturers of over-the-counter (OTC) oral drug products restrict the use of alcohol and include appropriate warnings in the labeling. For OTC oral products intended for children under 6 years of age,