

Table 13.2 WATER AND ALCOHOL SOLUBILITIES OF SOME WEAK ACIDS, WEAK BASES, AND THEIR SALTS

DRUG	WATER	ALCOHOL
Atropine	455.0	2
Atropine sulfate	0.5	5
Codeine	120.0	2
Codeine sulfate	30.0	1,280
Codeine phosphate	2.5	325
Morphine	5,000.0	210
Morphine sulfate	16.0	565
Phenobarbital	1,000.0	8
Phenobarbital sodium	1.0	10
Procaine	200.0	Soluble
Procaine hydrochloride	1.0	15
Sulfadiazine	13,000.0	Sparingly soluble
Sodium sulfadiazine	2.0	Slightly soluble

Although there are no exact rules for unerringly predicting the solubility of a chemical agent in a particular liquid, experienced pharmaceutical chemists can estimate the general solubility of a chemical compound based on its molecular structure and functional groups. The information gathered on a great number of individual chemical compounds has led to the characterization of the solubilities of

groups of compounds, and though there may be an occasional inaccuracy with respect to an individual member of a group of compounds, the generalizations nonetheless are useful. As demonstrated by the data in Table 13.2 and other similar data, salts of organic compounds are more soluble in water than are the corresponding organic bases. Conversely, the organic bases are more soluble in organic solvents, including alcohol, than are the corresponding salt forms. Perhaps the most widely written guideline for the prediction of solubility is “like dissolves like,” meaning a solvent having a chemical structure most similar to that of the intended solute will be most likely to dissolve it. Thus, organic compounds are more soluble in organic solvents than in water. Organic compounds may, however, be somewhat water soluble if they contain polar groups capable of forming hydrogen bonds with water. In fact, the greater the number of polar groups present, the greater will likely be the organic compound’s solubility in water. Polar groups include OH, CHO, COH, CHOH, CH₂OH, COOH, NO₂, CO, NH₂, and SO₃H. The introduction of halogen atoms into a molecule tends to decrease water solubility because of an increase in the molecular weight of the compound without a proportionate increase in polarity. An increase in the molecular weight of an organic compound without a change in polarity reduces solubility in water. Table 13.3 demonstrates some of these generalities with specific chemical examples.

Table 13.3 SOLUBILITIES OF SELECTED ORGANIC COMPOUNDS IN WATER AS A DEMONSTRATION OF CHEMICAL STRUCTURE-SOLUBILITY RELATIONSHIP

COMPOUND	FORMULA	MILLILITERS OF WATER REQUIRED TO DISSOLVE 1 G OF COMPOUND
Benzene	C ₆ H ₆	1,430.0
Benzoic acid	C ₆ H ₅ COOH	275.0
Benzyl alcohol	C ₆ H ₅ CH ₂ OH	25.0
Phenol	C ₆ H ₅ OH	15.0
Pyrocatechol	C ₆ H ₄ (OH) ₂	2.3
Pyrogallol	C ₆ H ₃ (OH) ₃	1.7
Carbon tetrachloride	CCl ₄	2,000.0
Chloroform	CHCl ₃	200.0
Methylene chloride	CH ₂ Cl ₂	50.0