Physical

Pharmacy

ALFRED MARTIN

Physical Pharmacy

PHYSICAL CHEMICAL PRINCIPLES IN THE PHARMACEUTICAL SCIENCES

Alfred Martin, Ph.D.
Emeritus Coulter R. Sublett Professor
Drug Dynamics Institute,
College of Pharmacy,
University of Texas

with the participation of
PILAR BUSTAMANTE, Ph.D.
Titular Professor
Department of Pharmacy
and Pharmaceutical Technology,
University Alcala de Henares,
Madrid, Spain

and with illustrations by
A. H. C. CHUN, Ph.D.
Associate Research Fellow
Pharmaceutical Products Division,
Abbott Laboratories

B. I. Waverly Pvt Ltd
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States of Matter

BINDING FORCES BETWEEN MOLECULES

In order for molecules to exist in aggregates in gases, liquids, and solids, *inter*molecular forces must exist. An understanding of intermolecular forces is important in the study of pharmaceutical systems and follows logically from the previous discussion of *intra*molecular bonding energies. Cohesion, or the attraction of like molecules, and adhesion, or the attraction of unlike molecules, are manifestations of intermolecular forces. A knowledge of these forces is important for an understanding not only of the properties of gases, liquids, and solids, but also of interfacial phenomena, flocculation in suspensions, stabilization of emulsions, compaction of powders in capsules, and the compression of granules to form tablets.

Repulsive and Attractive Forces. When molecules interact, both repulsive and attractive forces operate. As two molecules are brought close together, the opposite charges in the two molecules are closer together than the like charges and cause the molecules to attract one another. When the molecules are brought so close that the outer charge clouds touch, the molecules repel each other like rigid elastic bodies.

Thus attractive forces are necessary in order that molecules cohere; repulsive forces are necessary in order that the molecules do not interpenetrate and annihilate one another. Moelwyn-Hughes[1] points to the analogy between human behavior and molecular phenomenon. Just as the actions of humans are often influenced by a conflict of loyalties, so molecular behavior is governed by attractive and repulsive forces.

Repulsion is due to the interpenetration of the electronic clouds of molecules and increases exponentially with a decrease in distance between the molecules. At a certain equilibrium distance, about 3 or 4 $\times$ 10^{-8} cm (3 or 4 angstroms), the repulsive and attractive forces are equal. At this position, the potential energy of the two molecules is a minimum and the system is most stable (Fig. 2–1). This principle of minimum potential energy applies not only to molecules but to atoms and to large objects as well.

Under the following headings are discussed the various types of *attractive* intermolecular forces.

Van der Waals Forces. Dipolar molecules frequently tend to align themselves with their neighbors, so that the negative pole of one molecule points toward the positive pole of the next. Thus, large groups of molecules may be associated through weak attractions known as *dipole–dipole* or Keesom forces. Permanent dipoles are capable of inducing an electric dipole in nonpolar molecules (which are easily polarizable) in order to produce *dipole–induced dipole*, or Debye, interactions, and nonpolar molecules can induce polar-
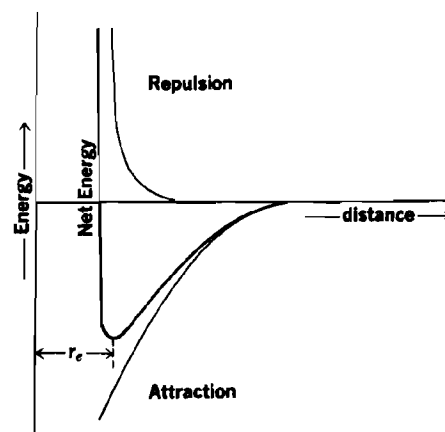

Fig. 2–1. Repulsive and attractive energies and net energy as a function of the distance between molecules. Note that a minimum occurs in the net energy because of the different character of the attraction and repulsion curves.

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Solutions of Nonelectrolytes

Concentration Expressions
Equivalent Weights
Solutions of Nonelectrolytes

Ideal and Real Solutions
Colligative Properties
Molecular Weight Determination

Materials may be mixed together to form a true solution, a colloidal solution, or a coarse dispersion. A *true solution* is defined as a mixture of two or more components that form a homogeneous molecular dispersion, in other words, a one-phase system, the composition of which can vary over a wide range. The terms in this definition warrant further comment, and an attempt at clarification is made in the following paragraphs.

A *system* is a bounded space or a definite quantity of substance that is under observation and experimentation. Under some circumstances, the system may consist only of radiant energy or an electric field, containing no material substances. The term *phase* has already been defined in Chapter 2 as a distinct homogeneous part of a system separated by definite boundaries from other parts of the system. Each phase may be consolidated into a contiguous mass or region, such as a single piece of ice floating in water, or it may be distributed as small particles throughout the system, such as oil droplets in an emulsion or solid particles in a pharmaceutical suspension.

These latter two are examples of *coarse dispersions*, the diameter of the particles in emulsions and suspensions for the most part being larger than 0.1 μm (100 Å or 10^{-5} cm). A *colloidal dispersion* represents a system having a particle size intermediate between that of a true solution and a coarse dispersion, roughly 10 to 5000 Å. A colloidal dispersion may be considered as a two-phase system (heterogeneous) under certain circumstances and as a one-phase system (homogeneous) under others. A colloidal dispersion of silver proteinate in water is heterogeneous since it consists of distinct particles constituting a separate phase. A colloidal dispersion of acacia or sodium carboxymethylcellulose in water, on the other hand, is homogeneous. It does not differ significantly from a solution of sucrose and

may be considered as a single-phase system or true solution.[1]

A solution composed of only two substances is known as a *binary solution*, and the components or constituents are referred to as the *solvent* and the *solute*. We use the terms *component* and *constituent* interchangeably here, as do other authors, to represent the pure chemical substances that make up a solution. The *number of components* has a definite significance in the phase rule, as explained on p. 37. The constituent present in the greater amount in a binary solution is arbitrarily designated as the solvent and the constituent in the lesser amount as the solute. When a solid is dissolved in a liquid, however, the liquid is usually taken as the solvent and the solid as the solute, irrespective of the relative amounts of the constituents.

When water is one of the constituents of a liquid mixture, it is usually considered the solvent. When dealing with mixtures of liquids that are miscible in all proportions, such as alcohol and water, it is less meaningful to classify the constituents as solute and solvent.

Properties of Solutions. The physical properties of substances may be classified as *colligative, additive,* and *constitutive.* Some of the constitutive and additive properties of molecules were considered in Chapter 4. In the field of thermodynamics, physical properties of systems are classified as *extensive* properties, depending on the quantity of the matter in the system (e.g., mass and volume) and *intensive* properties, which are independent of the amount of the substances in the system (e.g., temperature, pressure, density, surface tension, and viscosity of a pure liquid).

Colligative properties depend mainly on the number of particles in a solution. The colligative properties of solutions are osmotic pressure, vapor pressure lowering, freezing point depression, and boiling point eleva-

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