expected from Raoult's Law and the thermodynamic activities of the components are greater than their mole fractions, i.e. $a_1 > x_1$ and $a_2 > x_2$. This type of system is said to show a *positive deviation* from Raoult's Law and the extent of the deviation increases as the miscibility of the components decreases. For example, a mixture of alcohol and benzene shows a smaller deviation than the less miscible mixture of water + diethyl ether whilst the virtually immiscible mixture of benzene + water exhibits a very large positive deviation.

Conversely, if the solute and solvent molecules have a strong mutual affinity (that sometimes may result in the formation of a complex or compound), then a negative deviation from Raoult's Law occurs. Thus, p_1, p_2 and therefore P are lower than expected and $a_1 < x_1$ and $a_2 < x_2$. Examples of systems that show this type of behaviour include chloroform + acetone, pyridine + acetic acid and water + nitric acid.

Although most systems are non-ideal and deviate either positively or negatively from Raoult's Law, such deviations are small when a solution is dilute. This is because the effect that a small amount of solute has on interactions between solvent molecules is minimal. Thus, dilute solutions tend to exhibit ideal behaviour and the activities of their components approximate to their mole fractions, i.e. a_1 approximately equals x_1 and a_2 approximately equals x_2. Conversely, large deviations may be observed when the concentration of a solution is high.

Knowledge of the consequences of such marked deviations is particularly important in relation to the distillation of liquid mixtures. For example, the complete separation of the components of a mixture by fractional distillation may not be achievable if large positive or negative deviations from Raoult's Law give rise to the formation of so-called azeotropic mixtures with minimum and maximum boiling points, respectively.

Ionization of solutes

Many solutes dissociate into ions if the dielectric constant of the solvent is high enough to cause sufficient separation of the attractive forces between the oppositely charged ions. Such solutes are termed *electrolytes* and their ionization (or dissociation) has several consequences that are often important in pharmaceutical practice. Some of these consequences are indicated below.

Hydrogen ion concentration and pH

The dissociation of water can be represented by Equation 3.5:

$$H_2O \leftrightarrow H^+ + OH^- \tag{3.5}$$

It should be realized that this is a simplified representation because the hydrogen and hydroxyl ions do not exist in a free state but combine with undissociated water molecules to yield more complex ions such as H_3O^+ and $H_7O_4^-$.

In pure water the concentrations of H^+ and OH^- ions are equal and at 25 °C both have the values of 1×10^{-7} mol L^{-1}. The Lowry–Brönsted theory of acids and bases defines an acid as a substance which donates a proton (or hydrogen ion) so it follows that the addition of an acidic solute to water will result in a hydrogen ion concentration that exceeds that of pure water. Conversely, the addition of a base, which is defined as a substance that accepts protons, will decrease the concentration of hydrogen ions in solution. The hydrogen ion concentration range decreases from 1 mol L^{-1} for a strong acid down to 1×10^{-14} mol L^{-1} for a strong base.

In order to avoid the frequent use of inconvenient numbers that arise from this very wide range, the concept of pH has been introduced as a more convenient measure of hydrogen ion concentration. pH is defined as the negative logarithm of the hydrogen ion concentration $[H^+]$ as shown by Equation 3.6:

$$\mathrm{pH} = -\log_{10}[H^+] \tag{3.6}$$

so that the pH of a neutral solution like pure water is 7. This is because, as mentioned above, the concentration of H^+ ions (and thus OH^- ions) in pure water is 1×10^{-7} mol L^{-1}. The pH of acidic solutions is less than 7 and the pH of alkaline solutions is greater than 7.

pH has several important implications in pharmaceutical practice. It has an effect on:

- the degree of ionization of drugs that are weak acids or bases
- the solubility of drugs that are weak acids or bases
- the ease of absorption of drugs from the gastrointestinal tract into the blood. For