In either case, the measured IDR will clearly be affected either by the pH of the medium or the microenvironment surrounding the solid surface created by the dissolving salt. The effect of pH on IDR is easily established by selection of the dissolution media. Standard media (0.1M HCl, phosphate buffers, etc.) can be used or, in order to get a more realistic insight into dissolution *in vivo*, simulated gastrointestinal fluids (as discussed earlier) can also be employed.

If the drug is an acid or base, then the self-buffering effect as dissolution occurs should not be ignored. In particular, the saturated concentration of solute in the diffusion layer often means that the pH in the medium immediately surrounding the dissolving solid differs significantly from that of the bulk solvent and will lead to deviations from the ideal behaviour predicted by Equations 23.26 and 23.27. A schematic representation of the buffering effect of salicylic acid is shown diagrammatically in Figure 23.11.

IDR and the common ion effect

The common ion effect (discussed in Chapter 2) should not be ignored, especially for hydrochloride salts, as the chloride ion is often present in reasonably high concentrations in body fluids (0.1 M in gastric fluid and 0.13 M in intestinal fluid). For this reason, fed and fasted simulated intestinal fluids should contain 0.1 and 0.2 M Cl^- respectively.

Hence, when the concentration of Cl^- in solution is high, the solubility advantage of choosing a hydrochloride salt is diminished. Li et al (2005) demonstrated the effect of chloride concentration on the IDR of haloperidol salts and showed that dissolution of the hydrochloride salt was slower than that of a either the phosphate or mesylate salt.

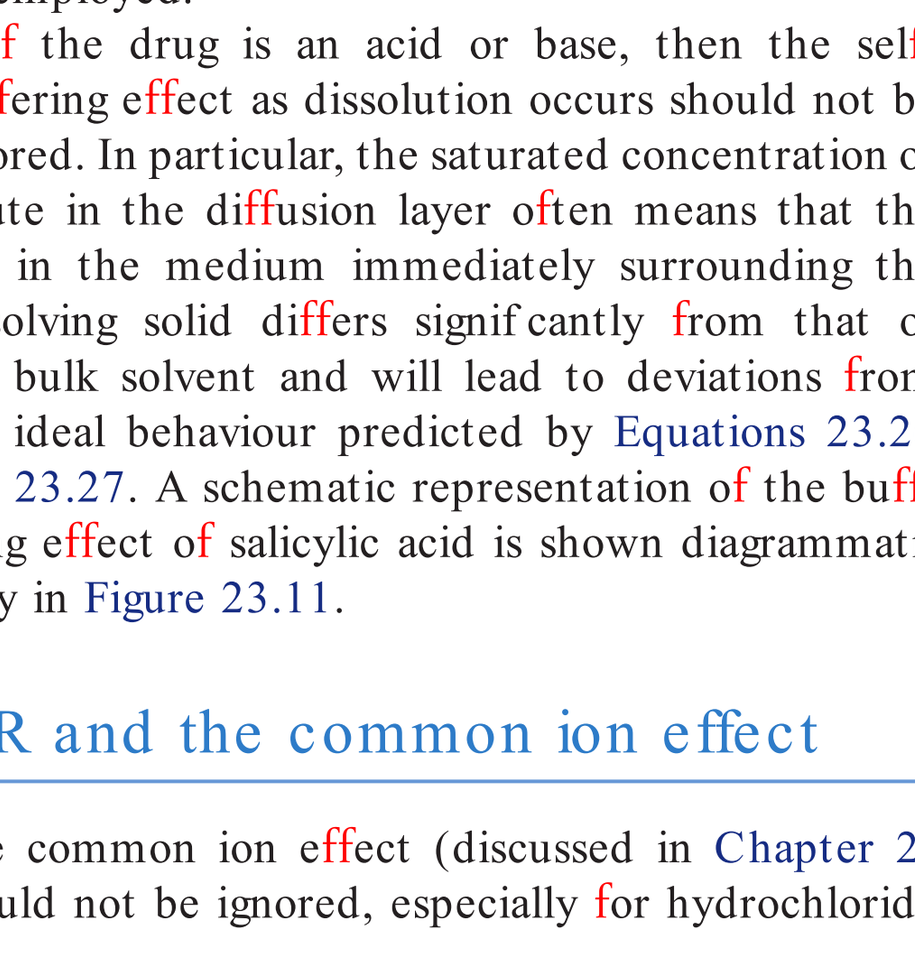

Fig. 23.11 • pH across the diffusion layer as a function of dissolution medium for salicylic acid. Redrawn from Serajuddin and Jarowski, 1985.

Salt selection

If a drug candidate has poor aqueous solubility or is difficult to isolate or purify, but is a weak acid or base, then conversion to a salt form may be beneficial. A number of physicochemical properties may change upon formation of a salt (Table 23.7). Any such changes may be beneficial or detrimental and so a decision must be made early during preformulation as to which salt form (if any) is to be taken into

Table 23.7 Possible advantages and disadvantages of salt formation

Advantages	Disadvantages
Enhanced solubility	Decreased percentage of active
Increased dissolution rate	Increased hygroscopicity
Higher melting point	Decreased chemical stability
Lower hygroscopicity	Increased number of polymorphs
Improved photostability	Reduced dissolution in gastric media
Better taste	No change in solubility in buffers
Higher bioavailability	Corrosiveness
Better processability	Possible disproportionation
Easier synthesis or purification	Additional manufacturing step
Potential for controlled release	Increased toxicity