pKa values

Table G.9 lists the pKa values of some compounds of pharmaceutical interest. A compound that dissociates by releasing a proton is termed an acid, and the dissociation constant is given in the left-hand column of the table. If the compound is a base, the pKa of the corresponding protonated form is listed in the right-hand column. A low value in the left-hand column indicates a strong acid. A low value in the right-hand column indicates a weak base.

The values are taken from published data and should be regarded as approximate only. Unless otherwise indicated, the values given are at 25 °C and represent the thermodynamic values.

If the compound is a weak acid, it will demonstrate increasing aqueous solubility at pH values above its pKa. Solubility will be essentially unchanged as a function of pH when solutions are at low pH values—i.e. up to one or two pH units below its pKa. The converse is true if the compound is a base. Compounds that are zwitterions normally have at least one acid group and one basic group. Such compounds normally have a U- or V-shaped curve when solubility is plotted as a function of pH, depending on how different the pKa values are from each other.

The curves for partition coefficient will be the inverse of those observed for solubility. For example, a plot of partition coefficient as a function of pH for a zwitterion will appear as an inverted U or V.

For some drugs, passive reabsorption in renal tubules, and therefore renal clearance, may be influenced by physicochemical properties such as polarity, as well as the degree of ionisation. The pKa values of ionisable groups will influence the degree of ionisation and hence polarity of drugs at any specific pH. Reabsorption also depends on physiological variables such as urine flow rate and pH.

Urine pH may vary in the range of 4.5 to 7.5 under forced acidification and alkalinisation respectively. Dietary changes, drugs and the clinical state of a patient can alter urine pH within this range.

Variation in urinary pH or flow rate can cause marked variation of renal clearance of acidic drugs with pKa values of about 3.0 to 7.5. Increasing urinary pH will increase renal clearance of susceptible acidic drugs by reducing tubular reabsorption. Basic drugs which have pKas of their conjugate acids in the range of about 7.5 to 10.5 can have highly variable renal clearance. Increasing urinary pH will cause a decrease of renal clearance for susceptible basic drugs. Such drugs may have a highly variable fraction of drug excreted in urine and total body clearance. Hence, half-life, area under the plasma drug concentration versus time curve, efficacy and toxic effects may also be highly variable.

Conversely, drugs which are highly polar in their non-ionised state or whose total body clearance is not highly dependent on renal clearance are unlikely to demonstrate significant changes in elimination when urinary pH or flow rate are altered.[1]

Table G.9 pKa values[2–6]

	Acid	Base
Acebutolol		9.4
Acetazolamide	7.2	
Acetic acid	4.8	
Acetylcysteine	3.2	
Acitretin	5.0	
Adefovir dipivoxil		4.6
Adrenaline	10.2; 12.0 (20 °C)	8.7
Alclofenac	4.6	
Alfentanil		6.5
Allopurinol		9.4
Alprazolam		2.4
Alprenolol		9.5 (20 °C)
Amantadine		10.4
Amiloride		8.7
Aminacrine		9.5
Aminocaproic acid	4.4	10.8
Aminophylline		5.0
Aminosalicylic acid	3.6	1.8
Amiodarone		6.6
Amitriptyline		9.4
Ammonia		9.3
Amoxycillin	2.4; 9.6	7.4
Amphetamine		9.9 (20 °C)
Amphotericin B	5.5	10.0
Ampicillin	2.7	7.2
Amylobarbitone	7.9	
Antazoline		2.5; 10.1
Aprepitant		4.2
Ascorbic acid	4.2; 11.6	
Aspirin	3.5	
Atazanavir	11.1	4.8
Atenolol		9.6 (24 °C)