

pKa and Ka (Acid dissociation constant)

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Definition

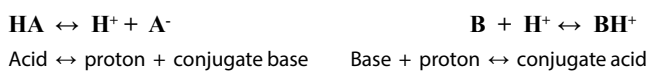
pK_a of a drug is the pH at which 50% of the drug is ionised and 50% is not ionised/unionised.^{1,2}

The pK_a is specific for each drug and these properties determine how a drug can be administered, the speed of absorption as well as speed of excretion by the kidneys.²

Keywords: pKa, Ka, acid dissociation constant

Back to basics: acids and bases

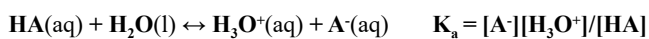
In an aqueous solution:



pH = -log [H⁺]: where [H⁺] is the concentration of free protons in the solution.

Therefore, a low pH = acidic where [H⁺] is high and a high pH = basic/alkaline where [H⁺] is low. The pH scale ranges from 0–14. An acid has a pH less than 7 and a base has a pH greater than 7.

K_a: Acid dissociation constant



In a reversible acid-base reaction, you can determine its K_{eq} (equilibrium constant) or K_a. The K_a is constant and only changes with temperature.³

The difference between a strong acid and a weak acid is the strong acid's ability to completely dissociate in an aqueous solution. If the acid base reaction favoured the left (higher [HA]) then you would have smaller concentrations of both [A⁻] and [H₃O⁺], which would result in a lower K_a value. Therefore, the higher the K_a, the stronger the acid. The lower the K_a, the weaker the acid.

$$\text{pK}_a = -\log[\text{K}_a]$$

Therefore, the lower the pK_a, the stronger the acid. The higher the pK_a, the weaker the acid.

Most drugs are weak acids or bases. Weak acids and weak bases switch between their ionised and deionised states depending on the pH of the surrounding environment.^{1,2}

Henderson Hasselbach equation: $\text{pH} = \text{pK}_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$
(remember your maths where log[1] = 0)

Based on the above, when the amount of acid (HA) = amount of conjugate base (A⁻): $\text{pH} = \text{pK}_a$ ⁴

Back to the beginning: The pK_a of a drug is the pH at which 50% of the drug is ionised and 50% is unionised.^{1,2}

An ionised/charged molecule is water soluble and cannot cross a cell membrane¹ (which is made of lipid), therefore it is dissolved inside cells, in the blood stream or urine.

An unionised molecule is lipid soluble and can cross cell membranes,¹ therefore it easily passes through/is absorbed by cells and tissues.

Example: aspirin

Aspirin has a pK_a of 3.5. Taken orally, it enters the stomach which is an acidic environment due to hydrochloric acid. Based on the information we have above, the aspirin will mostly be in the unionised form and thus lipid soluble. This means that it will be easily absorbed through the cells of the stomach and into the bloodstream. The pH of the blood stream is higher (7.4), thus the aspirin molecule will lose its [H⁺] and become ionised. The ionised form is then carried to its site of action, binds to other receptors, or is excreted in the urine.²

Conflict of interest

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