pKa and pH — What’s their interaction with the body and drugs?

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Deconstructing the meaning of pKa

pKa is the acid-base ionisation constant of a drug. The pKa of a drug influences multiple determinants such as lipophilicity (ability to dissolve in fats; known as pH partitioning), solubility and permeability of the drug and the interaction capability it has within the body.

These factors also work with pharmacokinetics of the body; known as absorption, distribution, metabolism and excretion (ADME).

pKa values of drugs and the pH of the surrounding body environment, ultimately control the absorption and excretion.

These two things affect the rate in which a specific drug can diffuse across membranes, the Central nervous system (CNS) and the blood brain barrier. The BBB is a group of blood vessels that regulate the movement of molecules and cells between, what you may have already guessed, the blood and the brain.

Essentially pKa and the pH of an aqueous solution determines the percentage of ionisation (positive charge) and unionisation (negative charge) of a drug. To help you figure out the % of ionisation, there is an equation called the Henderson-Hasselbalch equation.

Henderson-Hasselbalch equation

\[ \text{pH} = \text{pKa} + \log \left( \frac{[A^-]}{[HA]} \right) \]

The pH partition theory, suggests that; acids with pKa values below 3 and bases with pKa values above 8 were poorly absorbed.

Influencing drug absorption and excretion

pKa of a drug influences absorption as it determines whether the drug will be ionized or not, in conjunction with the bodies pH.

If the drug is a weak acid or base, they are deemed as being unionized and have greater lipid-solubility. This means these drugs will find it easier to cross membranes and be absorbed faster by the body, rather than drugs in ionised states.

In easy terms, a weak acidic drug will be better absorbed in a pH environment which is lower than its pKa value. Alternatively, a weak base is better absorbed in a pH environment higher than its pKa value.
pKa also plays an important role on the excretion of a drug. If a drug is ionized then its chances of being excreted through the kidneys is high, as there is a higher attraction for water verses lipids. If the drug is non-ionized then it will be lipid soluble and reabsorbed into the blood.

Alteration of urine pH affects the ratio of the ionised or unionised state of a drug, affecting the drugs excretion. To increase elimination, acidic drugs are placed in alkaline urine pH and basic drugs in acidic urine pH – in turn shifting the equilibrium Henderson-Hasselbalch equation, increasing ionization states and making them more water soluble. 

**How can an overdose be reversed?**

Accelerating drug excretion after overdose is key. One drug is Amphetamine. Amphetamine is classed as a weak base and readily lipid soluble and non-ionized in alkaline urine pH.

When urine pH is acidified, Amphetamine is then pushed toward an ionized and therefore charge and water soluble form.

In the case of overdose, Ascorbic Acid (Vitamin C) may be used to acidify the urine and in turn increase the renal excretion of the weak base, as it has kept it in a charged form which ensures it water soluble.

**Why should we care about pKa?**

Through the discovery of the influence that pKa has on drug performance, many new forms of technology have developed drugs with closer specification for its tailored success. future technology construction including computer software is needed for future investigation.

This enables a more specific route of administration and a controlled, safe amount of drug administered, which ensures that overdose is avoided and only peak therapeutic amount is prescribed.

By taking pKa into account ADME can be accounted for and the parameter of solubility is an extremely important physicochemical parameter that is routinely investigated in the pharmaceutical industry.
Reference List


