TREATING ASPIRIN OVERDOSE WITH PH

Aspirin is one of the most commonly used drugs in the world, and at some point you’ve probably had it to deal with that headache or overcome the battle with the common cold. And although rarely lethal alone, aspirin overdose is a real concern, so do you know how it’s treated?

Drugs and pH

All drugs are either weak bases or weak acids, and for them to take effect, they must be absorbed into cells from the extracellular fluid (ECF). However, the lipid-based cell membrane stands in its way, deciding what goes in and out. Due to the chemical makeup of the membrane, only lipid soluble molecules are let through, where as the rest bounce off and remain in the ECF.

Whether the drug is lipid-soluble or not based on whether its ionised. If the drug ionises, it becomes water-soluble meaning it has poor absorption through the stomach, placenta and Blood-Brain Barrier (BBB), whereas that which remains non-ionised are absorbed well by lipids, such as the cell membranes. [1]

So What Is Ionisation?

Ionisation is the process by which atoms gain or lose electrons during chemical reactions, causing it to become positively or negatively charged. It occurs when a particle has an odd number of electrons, as they are more stable when all electrons are paired. [2]

The two factors that determine whether a drug will ionise are the pKa of the drug, and the pH of the solution it’s in. You’ve probably heard of pH before, it’s the measure of how basic or acidic a solution is on a scale of 1-14, with 1 being most acidic. The pKa of a drug is the pH of the solution when 50% is ionised, and 50% remains unionised. This is calculated using the Henderson-Hasselbalch equation

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pH = pK + \log \left( \frac{[A^-]}{[HA]} \right)
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Henderson-Hasselbalch Equation
The amount of ionisation of a drug (%) is calculated by the following formula.

$$\frac{100}{1+10^{x(pH - Pka)}}$$

where $x = -1$ if acid drug or $1$ if basic.

The pH value will differ significantly depending on the fluid the drug is in. For example, the pH of blood is kept between 7.35-7.45 [3], whereas the pH of gastric acid is between 1.5-3.5 [4]. This means the same drug will ionise at different rates depending on how it is administered, and what fluids it therefore travels through.

Aspirin is a weak acid with a 3.5 pKa [5]. It is an orally administered drug, meaning it will be primarily reacting with gastric acid, which as shown earlier has a pH of 1.5-3.5. The lower the pH of the gastric acid, the less ionised the drug will be, and therefore more effective. Using a pH value of 2.5 for gastric acid (average of 1.5-3.5), the amount of Aspirin that is ionised is 9.1%, leaving about 91% unionised and free to do its job.

**Absorption and Excretion**

Once the drug is absorbed it begins the 'mechanism of action' (MOA), the process by which the drug changes the body to cause its desired effect. For Aspirin, the MOA involves the inhibition of the enzyme cyclooxygenase effectively reducing pain and inflammation. [Toth et Al.]

Removing the drug from the body is very important, as it can otherwise cause a build up of concentration with each dose. The kidney is primarily responsible for excreting drugs. One important part of the renal filtration process is the unionised drugs being reabsorbed into the body alongside other important nutrients, and the ionised drugs and other waste are excreted as urine.

**Increasing Elimination, Increasing pH**

Changing the uric pH can have a significant impact on how much of the drug is excreted, such as in aspirin overdose where alkaline urine might eliminate more than 30% of ingested aspirin as free salicylate whereas in acidic urine it might be as low as 2% (Zahid et Al.) Since the pKa of the drug can’t be changed once in the body, increasing the pH of urine can cause more ionisation forcing more aspirin to be excreted as waste. The uric pH is increased by intaking Sodium bicarbonate until it reaches between 7.5-8 pH [6]. In cases of aspirin overdose this is one of the most effective forms of treatment.
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3. Galardy, P et Al. 2007, Comprehensive Pediatric Hospital Medicine, Moseby, Philadelphia


