BMOL2201/6201 Case Study

1. Acute Aspirin Overdose: Relationship to the Blood Buffering System

Focus concept: The carbonic acid-bicarbonate buffering system responds to an overdose of aspirin.

Topics to revise
- Principles of acids and bases, including pK_a and the Henderson-Hasselbalch equation.
- Buffering and how this maintains the blood pH.

The Blood Buffering System

Bicarbonate is the most significant buffer compound in human blood; other buffering agents, including proteins and organic acids, are present at much lower concentrations. The buffering capacity of blood depends primarily on two equilibria:

(1) between gaseous CO_2 dissolved in the blood and carbonic acid formed by the reaction:

$$CO_2 + H_2O \leftrightarrow H_2CO_3$$

and

(2) between carbonic acid and bicarbonate formed by the dissociation of H^+

$$H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The overall pK for these two sequential reactions is 6.35. (The further dissociation of bicarbonate to carbonate with pK = 10.33, is not significant at physiological pH)

When the pH of the blood falls due to metabolic production of H^+, the bicarbonate-carbonic acid equilibrium shifts toward more carbonic acid. At the same time, carbonic acid loses water to become CO_2, which is then expired in the lungs as gaseous CO_2. Conversely, when the blood pH rises, relatively more bicarbonate forms. Breathing is adjusted so that increased amounts of CO_2 in the lungs can be reintroduced into the blood for conversion to carbonic acid. In this manner, a near-constant hydrogen ion concentration can be maintained.

Disturbances in the blood buffer system can lead to conditions known as acidosis, with a pH as low as 7.1, or alkalosis, with a pH as high as 7.6. (Deviations of less than 0.05 pH unit from the "normal" value of 7.4 are not significant.) For example, obstructive lung diseases that prevent efficient expiration of CO_2 can cause respiratory acidosis. Hyperventilation accelerates the loss of CO_2 and causes respiratory alkalosis. Overproduction of organic acids from dietary precursors or sudden surges in lactic acid levels during exercise can lead to metabolic acidosis.

Acid-base imbalances are best alleviated by correcting the underlying physiological problem. In the short term, acidosis is commonly treated by administering $NaHCO_3$ intravenously. Alkalosis is more difficult to treat. Metabolic alkalosis sometimes responds to KCl or NaCl (the additional Cl^- helps minimize the secretion of H^+ by the kidneys), and respiratory alkalosis can be ameliorated by breathing an atmosphere enriched in CO_2.

Case Study

A patient has just been admitted to the emergency room around 9 pm. The patient was disoriented, had trouble speaking, and was suffering from nausea and vomiting. She was also hyperventilating, i.e. over breathing. The patient accidentally took an entire bottle of aspirin, which contained 250 tablets, around 7 pm that evening. Blood from the patient is analysed and the analyses shown in Table 1. The patient is experiencing mild respiratory alkalosis.

Table 1: Arterial blood gas concentration in patient

	Patient, two hours after aspirin ingestion	**Patient, ten hours after aspirin ingestion**	**Normal values**
p_{CO_2}	26 mm Hg	19 mm Hg	35-45 mm Hg
HCO_3^-	18 mM	21 mM	22-26 mM
p_{O_2}	113 mm Hg	143 mm Hg	75-100 mm Hg
pH	7.44	7.55	7.35-7.45
Blood salicylate concentration, mg/dL	57	117	

In the emergency room, the patient is given a stomach lavage with saline and two doses of activated charcoal to adsorb the aspirin. Eight hours later, nausea and vomiting became severe, and her respiratory rate increased; she was in severe respiratory alkalosis, and further treatment was required. A gastric lavage at pH = 8.5 and further activated charcoal treatments are administered, one every 30 minutes. A bicarbonate drip was required to prevent the blood bicarbonate concentration from dropping below 15 mM. After 12 hours, blood salicylate concentrations began to decrease. The patient's blood pH begins to drop around 24 hours after the aspirin ingestion and finally returned to normal at 60 hours after the ingestion.

Aspirin is chemically acetyl salicylic acid, which is converted to salicylic acid (a weak acidwith pK_a = 2.97) in the stomach, which can ionise to form the salicylate ion.

Q1: At pH 2.0 in the stomach, the predominant form of this weak acid is: ….

Q2: At pH 8.5, what is the predominant form of this weak acid?

It has been shown that salicylates act directly on the nervous system to stimulate respiration. Thus, the patient is hyperventilating due to her salicylate overdose.

Q3: Analyse the changes observed in O_2 and CO_2 levels, compared to normal.

Q4: What do the blood pH values indicate?

Q5: Why was the bicarbonate drip necessary?