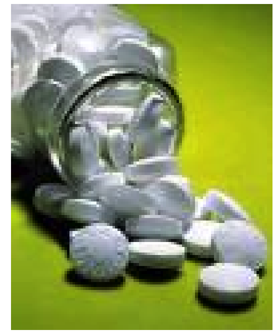
Model Case Study #1: An Unfortunate Overdose
BC 362, Medical Biochemistry

Case Background:



Susan, a 26-year-old female, was brought to your ED by her housemate Ann, who found Susan disoriented and incoherent at home. Upon examination, you note that Susan is hyperventilating and has tachycardia (rapid heart rate). Ann tells you that Susan had been suffering from depression and had admitted taking an entire bottle of aspirin a couple of hours earlier.

Susan's stomach is rinsed (a "lavage") with saline, and she is given a dose of activated charcoal to absorb the aspirin. Eight hours later, nausea and vomiting become severe, her respiratory rate is increased, and further treatment is required. You order a second gastric lavage with a sodium bicarbonate solution (pH 8.5) and more activated charcoal. Over the next several hours, Susan's breathing stabilizes and her blood pH slowly drops.

Lab Findings:

	Upon Admission	8 hrs later	Normal Values
P_{CO_2}	26 mm Hg	19 mm Hg	35-45 mm Hg
$[HCO_3^-]$	18 mM	21 mM	22-26 mM
pH	7.45	7.75	7.35-7.45

Biochemistry:

Blood pH is normally tightly maintained at 7.4. If the pH drops below 7.0 or rises above 7.5, death may occur. Regulation of acid-base balance in the bloodstream is achieved by use of the carbonic acid-bicarbonate buffer system as follows:

- Added base reacts with carbonic acid to form bicarbonate and water.
- Added acid reacts with bicarbonate to form carbonic acid.

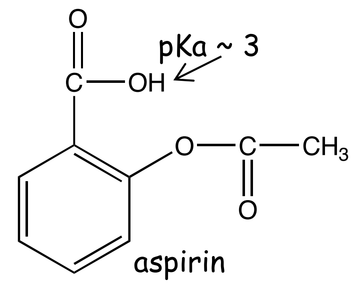
The carbonic acid–bicarbonate system can be restored to balance by eliminating excess carbonic acid as CO_2 in the breath or bicarbonate in the urine. Therefore, both the lungs and the kidneys are essential in maintaining acid-base balance.

Vocabulary:

Tachycardia, lavage

Analysis:

1. At the time of admission, you suspect that Susan's stomach might still contain aspirin tablets that are slowly dissolving. The fact that Susan's symptoms worsen confirms your suspicions.



Given the structure of aspirin shown here, consider how the pH of the stomach affects aspirin solubility. Note that activated charcoal can only absorb dissolved aspirin in solution.

Aspirin is more soluble under which situation? (Pick one.)

A. Normal stomach pH (~2.5) B. After bicarbonate lavage (pH ~8)

(Hint: which species is more water soluble…the protonated carboxylic acid or the deprotonated carboxylate? How do the ratios of the two species compare in stomach acid vs. in sodium bicarbonate?)

2. Aspirin acts directly on the central nervous system to stimulate heart and respiratory rate. What effect does hyperventilation have on Susan's blood chemistry? Would blood pH go up or down? Explain.

3. Using the lab value for pH, calculate the ratio of HCO_3^- to H_2CO_3 in Susan's blood 8 hours after admission. (Assume that $pK_a = 6.1$ for the first dissociable proton of H_2CO_3.) At normal blood pH, this ratio is 20:1. Why is the blood buffering system less effective than normal in this patient?

Patient Outcome:

Forty-eight hours after aspirin ingestion, Susan's blood pH has returned to normal. She is discharged with a referral to a mental health professional, and you have saved another patient!

Reference:

Cornely, K. (1999) Cases in Biochemistry, Wiley & Sons.

Solutions:

1. In the highly acidic environment of the stomach, the pH is below the pKa of the carboxylic acid, so that group is protonated. The aspirin is uncharged and not very soluble.
   When the pH is brought up by the gastric lavage (pH 8.5), the carboxylic acid, deprotonates. The aspirin is now charged and much more soluble. Therefore, it can be removed by the charcoal.

2. Hyperventilation would increase the exchange rate of CO_2 and O_2, thereby decreasing the partial pressure of CO_2 and increasing the partial pressure of O_2 in the bloodstream. Decreased CO_2 could result in alkalosis. CO_2 is proportional to the amount of carbonic acid in the bloodstream. In other words, during hyperventilation, CO_2 is blown off, so the amount of acid in the bloodstream decreases, leading to an increase in pH.

3 a) $pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$ $\qquad 7.75 = 6.1 + \log \frac{[HCO_3^-]}{[H_2CO_3]}$

$$\frac{[HCO_3^-]}{[H_2CO_3]} = 44.7$$

b) $pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$ $\qquad 7.40 = 6.1 + \log \frac{[HCO_3^-]}{[H_2CO_3]}$

$$\frac{[HCO_3^-]}{[H_2CO_3]} = 20.0$$

Thus, the ratio of conjugate base to conjugate acid is much higher than normal in the patient. The patient has too much bicarb; thus, the blood cannot effectively buffer against the addition of a base because there is not enough of the acid.