Blood buffer Case Base Problem

You are an emergency room physician and you have just admitted a patient, Susan year old who was brought to the emergency room around 9:00 Susan was found disoriented and had trouble speaking. At the hospital she begins to suffer from nausea and vomiting. She is also hyperventilating. Ann, Susan’s friend reveals an empty bottle of aspirin found in Susan’s car. The aspirin bottle, when full, would have contained 250 tablets. Susan admits she took the tablets around 7:00 that evening. You draw blood from her and the following analysis is shown below:  

<table>
<thead>
<tr>
<th></th>
<th>2 hrs after aspirin ingestion</th>
<th>10 hrs after aspirin ingestion</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{CO_2}$</td>
<td>26 mm Hg</td>
<td>19 mm Hg</td>
<td>35 - 45 mm Hg</td>
</tr>
<tr>
<td>$HCO_3^-$</td>
<td>18 mM</td>
<td>21 mM</td>
<td>22 - 26 mM</td>
</tr>
<tr>
<td>$P_{O_2}$</td>
<td>113 mm Hg</td>
<td>143 mm Hg</td>
<td>75 - 100 mm Hg</td>
</tr>
<tr>
<td>pH</td>
<td>7.44</td>
<td>7.55</td>
<td>7.35 - 7.45</td>
</tr>
<tr>
<td>[Blood salicylate ]</td>
<td>57 mg/dl</td>
<td>117 mg/dl</td>
<td></td>
</tr>
</tbody>
</table>

In the emergency room Susan is given a stomach lavage with saline and 2 doses of activated charcoal to adsorb the aspirin. Eight hours later she is still experiencing nausea and vomiting and her respiratory rate increased, and further treatment is required. You carry out a gastric lavage with a sodium bicarbonate solution pH 8.5 and administer further activated charcoal treatments. A bicarbonate drip was required to prevent the blood bicarbonate concentration from dropping below 15 mM. Over the next four hours, blood salicylate concentration begins to decrease. Her blood pH begins to drop around 24 hours after the ingestion and finally returns to normal at 60 hours.

a. Aspirin or acetylsalicylic acid is converted to salicylic acid and acetic acid by the acids and esterases in the stomach.
   - Draw the structure of acetylsalicylic acid and acetic acid and write the balanced equation for this transformation.
   - Write the protonization equation for salicylic acid and indicate which form will be water soluble.
   - What is a pharmacologically active form of a drug and how does it relate to aspirin?
   - What is the impact of high respiratory rate on stomach pH? Blood pH?

b. Since Susan has been brought into the hospital only two hours after the overdose, you suspect that her stomach might contain undissolved aspirin that is continuing to be absorbed. The fact that Susan is still experiencing high respiratory rates, nausea and vomiting 10 hours after the ingestion confirms your suspicion and you decide to use a gastric lavage at pH 8.5 to effectively remove the undissolved aspirin. This treatment solubilizes the aspirin so that it can easily be removed from the stomach.
   - What is the impact of high respiratory have on the blood pH?
   - Calculate the percent of protonated and unprotonated forms of salicylic acid at the pH of the stomach, which is usually around 2.0, and compare that to the percent of protonated and unprotonated forms of salicylic acid at the pH of the lavage.
   - Why does the lavage result in increased solubility of the drug? (Assume that the pK values for the carboxylic group in the salicylic acid and the acetylsalicylic acid are the same pKa=3).

c. It has been shown that salicylates act directly on the nervous system to stimulate respiration. Thus our patient is hyperventilating due to her salicylate overdose.
   - Explain how the salicylate-induced hyperventilation leads to the values of partial pressures of oxygen and carbon dioxide symptoms seen in the patient
   - Explain how the salicylate-induced hyperventilation causes the pH of the patient’s blood to increase. Illustrate your answers with the appropriate equations.
   - Why was the bicarbonate drip necessary?

e. Use the Henderson-Hasselbalch equation to determine the ration of $HCO_3^-$ to $H_2CO_3$ in the patient’s blood 10 hours post ingestion.
   - Describe how this buffer system functions to maintain blood pH. Include relevant equations.
   - How does the ratio 10 hours post ingestion compare to the ratio found in normal blood?
   - At 10 hours, post ingestion, can the $HCO_3^-$/$H_2CO_3$ system serve as an effective buffer in this patient? Explain?
   - Compare the concentration of $HCO_3^-$ in a normal person and in our patient. Then calculate the concentration of $H_2CO_3$ in the patient’s blood 10 hours after aspirin ingestion. Again, compare this value to the concentration of $H_2CO_3$ normally found, and again address the question of buffer effectiveness in the patient.