

The Purple Pill

by

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Part I – Heart Attack?

Kimberly had enjoyed eating dinner out with her classmates to celebrate finishing her midterms, but in the middle of the night she woke up with chest pains. “Aisha!” she shouted to her roommate, “I think I need to go to the hospital!”

“Oh no,” said Aisha. Kimberly was her best friend. She really hoped this was nothing serious. Aisha grabbed a pair of shoes and ran out the door to get her car. Kimberly was coughing and her voice was hoarse.

When they arrived at the emergency room, a nurse helped Kimberly out of the vehicle. “My name is Andrew. What are your symptoms?”

“Well, I woke up having chest pains. My throat is burning, and I feel like I have a lump in my throat that I can’t swallow.”

“Come with me. We’re going to get you in for an EKG right away. We’ll get your paperwork processed later,” said Andrew. They walked down the hallway to an exam room where Kimberly sat down. “I’m going to attach these electrodes to your arms, legs, and chest. The test will only take a few minutes.”

As Kimberly lay on the table, she felt worried. Did otherwise healthy 19-year-olds really have heart attacks? She didn’t have time for this! She had art class in the afternoon and a review session for her math class later in the evening.

“Try to relax,” said Andrew.

Kimberly took a deep breath. Andrew attached ten electrodes to her body, and a graph appeared on the computer screen. “That’s it,” said Andrew. “I’m going to take the EKG to Dr. Santiago, the physician on call. He’ll be down to see you in just a few minutes.”

Andrew reappeared a few minutes later with some medicine. “What is this?” Kimberly asked. “It’s a mixture of Maalox, lidocaine, and Donnatal. It will make you feel better while you’re waiting,” said Andrew.

Kimberly swallowed the medicine and lay back down on the table. A few minutes later, a man in a white coat walked into her room. “Hi Kimberly,” he said, “my name is Dr. Santiago, and I’ll be taking care of you today.”

Dr. Santiago had read Kimberly’s EKG and told her that she was not having a heart attack. After speaking with her about her condition, he sent her home with a prescription for omeprazole. Kimberly was feeling better that afternoon and even made it to class.

Questions

1. Dr. Santiago used a process called *differential diagnosis* to determine what condition Kimberly was suffering from. Explain the process of differential diagnosis.
2. What is the purpose of taking Maalox, lidocaine, and Donnatal together?
3. Draw the chemical structure of omeprazole.
4. What is the brand name of omeprazole?
5. What condition does omeprazole treat?

Part II – Proton Pump Inhibitors

As Kimberly took her first dose of omeprazole that evening, she recalled learning in her chemistry class that most drugs are organic molecules. “I wonder what the structure of omeprazole is?” she thought. She did a Google search and found the structure (Figure 1).

Kimberly also learned that omeprazole is sold by the drug company AstraZeneca under the brand name Prilosec. It is used to treat gastrointestinal reflux disorder (GERD). Prilosec was approved by the FDA in 1989 and heavily marketed as “the Purple Pill” due to its appearance.

The mechanism of action of Prilosec is proton pump inhibition. Prilosec binds to and disables the protein in your stomach that pumps protons (H^+ ions) into gastric juices. When it originally came out it was hailed as a wonder drug, as previous drugs such as cimetidine or ranitidine would only change the pH of the stomach from 1 to 2. Omeprazole, on the other hand, can increase the pH of the stomach from 1 to 5.

The pH scale indicates the acidity or basicity of a solution (Figure 2). Pure water is neither acidic nor basic; its pH is 7, and it is considered neutral. Acidic solutions have a pH less than 7, and basic (alkaline) solutions have a pH greater than 7. pH is a logarithmic scale, meaning that a solution with a pH of 1 is ten times more acidic than a solution with a pH of 2 and 100 times more acidic than a solution with a pH of 3.

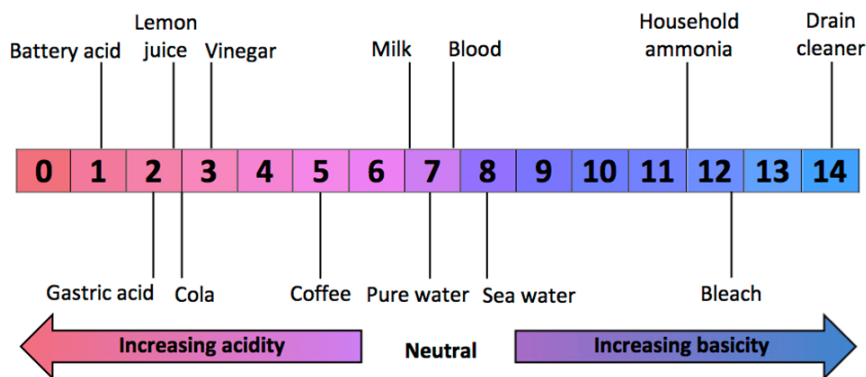


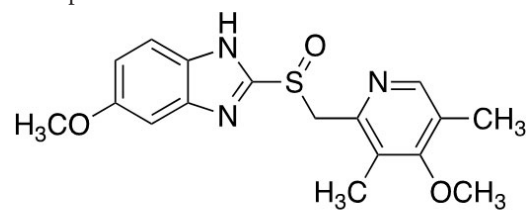
Figure 2. Approximate pH values of some common substances.

When Prilosec’s U.S. patent expired in April 2001, AstraZeneca introduced esomeprazole (Nexium) as a patented replacement drug. Prilosec became an over-the-counter medicine, while Nexium was available only by prescription until 2014. AstraZeneca encouraged their Prilosec patients to switch to Nexium, which was also marketed as “the Purple Pill.” The chemical structure of esomeprazole is shown in Figure 1.

Questions

1. What does the phrase “mechanism of action” mean in reference to a drug?
2. Briefly explain how a proton pump inhibitor works.
3. If omeprazole increases the pH of the stomach from 1 to 5, by what factor is the acidity decreased?
4. The structure of omeprazole has the symbol (\pm) under it. What does this symbol mean?
5. What is the relationship between the chemical structures of omeprazole and esomeprazole?
6. The “*es*” in esomeprazole refers to the stereochemistry of the molecule. Indicate on the structure of esomeprazole what the “*es*” refers to.

Omeprazole



(\pm)

Esomeprazole

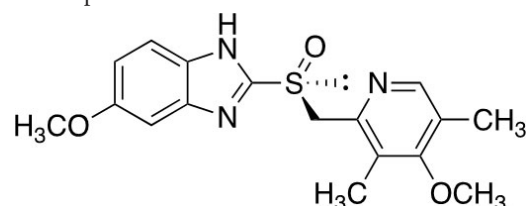


Figure 1. Chemical structures of omeprazole (top) and esomeprazole (bottom).

Part III – An Improvement?

Kimberly continued her research and learned that esomeprazole is a single enantiomer, while omeprazole is a mixture of esomeprazole and its mirror image. An equal mixture of two enantiomers is known as a *racemic mixture*. In most cases, chiral molecules contain a tetrahedral carbon atom with four different substituents. In esomeprazole, the chiral center is a sulfur atom. The lone pair of electrons (indicated as $\cdot\cdot\cdot\cdot\cdot\cdot$) is one of the four different attached groups. A sulfur atom with three different substituents and a lone pair is chiral because the groups do not freely rotate. Therefore, the mirror image is nonsuperimposable.

“I wonder how esomeprazole works differently in the body than omeprazole,” Kimberly thought. She found a column in *The Wall Street Journal* and started to read.

Assignment

Write a one- to two-page paper answering the question: “Is Nexium an improvement over Prilosec?” Give two or three specific reasons for your answer. Support your reasons with evidence from *The Wall Street Journal* column below or any other valid source. Each student should work independently and submit his or her own paper.

- Harris, G. Prilosec’s maker switches users to Nexium, thwarting generics. *The Wall Street Journal* June 6, 2002.