**Drug Screening Practical**

**Aim**

A major part of the drug research and development process is lead candidate selection. During this stage, the biochemical characteristics of drugs are analysed and the drug with the most favourable profile is taken forward to the next stage of the drug discovery process.

In this experiment, students will learn to analyse the physical and chemical properties of drugs. Using the data collected, students will be able to advise which drug should be taken forward to the next step as a novel antacid.

**Materials**

* Powdered Antacid tablets: ***For teachers - obscure the name of the tablet beforehand but keep active ingredient list visible. Number drugs 1 to 4 and note which tablet is labelled with which number.*** (1 set of 4 drugs per group)
* Alka-Seltzer tablet (aspirin, sodium hydrogen carbonate, citric acid)
* Rennie spearmint (calcium carbonate, magnesium carbonate)
* Setlers (Calcium carbonate)
* Gaviscon (Sodium alginate, sodium hydrogen carbonate, calcium carbonate)
* Distilled or deionized water (one beaker per group)
* 100% Ethanol, C2H5OH, can use specially denatured ethanol (small beaker per group)
* 0.5M Hydrochloric acid solution, HCl (small beaker per group)
* pH indicator papers
* Universal indicator solution, with colour chart
* Thin stem plastic (Beral) pipettes (6 pipettes per group)
* 48-well reaction plate (one per group)
* Toothpicks (for stirring)
* Small spoons for scooping powders into wells
* Test tube (for keeping excess powder, 4 per group)

**Method**

1. Add a few granules of the powdered tablet to the top 6 well wells of one row. ***NOTE:*** Use only a small amount of the powder. Label the row and transfer the rest of the powder into a test tube to be kept in case any test needs to be repeated.
2. Repeat the procedure using the three other drugs, placing a small amount of powder in 6 wells of the second row.
3. Continue to repeat the procedure for each remaining drug.
4. Note the name of each powdered drug, its active ingredients and record the appearance of the powder including the colour and any odour.

*Determine the water solubility of each drug*

1. Using a thin stem dropper, add 5 to 10 drops of distilled water to each of the powders down the first column of the well plate.
2. Stir each well with a toothpick, then observe any physical or chemical changes that occur (fizzing or dissolving).

If the resulting solution is **clear**, then the drug is **soluble**.

If the resulting solution is **cloudy**, then the drug is **slightly soluble**.

If the powder remains **unchanged**, then the drug is **insoluble**.

*Determine the solubility in ethanol of each drug*

1. Using a thin stem dropper, add 5 to 10 drops of 100% ethanol to each of the powders down the second column of the well plate.
2. Stir each well with a toothpick, then observe any physical or chemical changes that occur (fizzing or dissolving).

*Determine the pH of each drug*

1. Using a thin stem dropper, add 5 to 10 drops of distilled water to each of the powders down the fourth column of the well plate. Stir with a toothpick.
2. Add 1 or 2 drops of universal indicator solution to each of the wells. Record the colour of each solution and determine the approximate pH of each solution by comparing the colour to the universal indicator chart. Record your results.
3. For a second measurement of pH, dip one end of a pH strip into the well of powdered drug and using the colour chart on the pH paper container determine the pH. Record your results.

*Determine the reaction of each drug with simulated stomach acid*

1. Using a thin stem dropper, add 10 drops of 0.5M hydrochloric acid to each of the powders down the fifth column of the well plate and stir each well with a toothpick.
2. Observe and record any physical or chemical changes that occur (fizzing or dissolving).
3. Add 1 or 2 drops of universal indicator solution to each of the wells. Record the colour of each solution and determine the approximate pH of each solution by comparing the colour to the universal indicator chart.
4. For a second measurement of pH, dip one end of a pH strip into the well of powdered drug and using the colour chart on the pH paper container determine the pH. Record your results.

**Drug Screening Table of Results**

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| --- | --- | --- | --- | --- | --- |
| **Drug ID number** | **Active ingredients** | **Solubility in H2O** | **Solubility in 100% ethanol** | **pH** | **Reaction with 0.5M hydrochloric acid** |
| Universal indicator | pH strip |
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|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

Solubility = soluble/slightly soluble/insoluble

Fizzing = no fizzing/minor fizzing/substantial fizzing

**Background**

The drugs in this experiment are being tested for their suitability as antacids. Antacids are chemicals that relieve indigestion or heartburn by neutralising excess stomach acid. Most antacids will not dissolve completely in water and are made to dissolve slowly in the acidic juices of the stomach so that carbon dioxide will be given off gradually as the antacid neutralises the excess acid.

The stomach's digestive juices (gastric acid) contain hydrochloric acid (HCl) which plays a crucial role in creating the pH required for the activity of the protein-digesting enzyme pepsin and to kill bacteria that enters the digestive system. The stomach lining of a healthy adult produces 2-3L of dilute HCl each day to aid digestion, with the gastric pH ranging from 1.0 to 3.0. While the stomach continuously produces a small amount of acid, it is stimulated to produce more acid in the presence of food. Too much food, certain types of food, or high levels of stress may cause the stomach to secrete more gastric acid, thus lowering the pH of the stomach which can result in pain or discomfort.

Most antacids contain weak bases such as sodium bicarbonate, calcium carbonate, or a combination of these. The basic compounds in the antacids neutralize excess HCI as well as affecting the function of the enzyme pepsin. An acid—base neutralization reaction occurs between the antacid base and the gastric acid in the stomach. An effective antacid does not bring the pH of the stomach fluid to complete acid—base neutrality (pH 7) as this would completely shut down digestion and promote rebound acid hypersecretion —an automatic response which floods the stomach with gastric acid. Instead, an effective antacid neutralizes some of the HCl in the gastric juices—enough to relieve the pain and discomfort, yet still allowing for the continuation of normal digestive processes.

Carbonate-containing antacids, such as sodium bicarbonate, react with stomach acid to produce a neutral salt and carbonic acid.

NaHCO3 + HCl → H2CO3 + NaCl

Sodium bicarbonate + hydrochloric acid -> carbonic acid + sodium chloride

Carbonic acid is a weaker acid than HCI and in the presence of water, rapidly catalyses into carbon dioxide and water:

H2CO3 → CO2 + H2O

carbonic acid -> carbon dioxide + water

Hydroxide-containing compounds, such as magnesium hydroxide, react with the acid to produce its neutral salt and water, as shown below:

Mg(OH)2 + 2 HCl → MgCI2 + 2 H2O

Magnesium hydroxide + hydrochloric acid → magnesium chloride + water

When antacids containing sodium bicarbonate and citric acid are mixed with water, the bicarbonate ions and citric acid react to produce a fizzing reaction from the release of carbon dioxide. Other antacids are formulated with calcium carbonate alone as individuals with high blood pressure are advised to avoid excess sodium. Antacids formulated with calcium carbonate are advertised as a calcium supplement for people with osteoporosis, however, one would be best advised to use a calcium supplement tablet that does not work as an antacid if antacids are not required by an individual. If used over long periods of time, calcium carbonate tends to cause constipation, thus the reason for antacids containing a combination of calcium carbonate and magnesium hydroxide. This combination tends to overcome the constipation as magnesium hydroxide produces an opposite laxative effect. Magnesium hydroxide, while effective in controlling ulcer pain, has a lower neutralizing capacity and can cause trouble if taken too frequently by people with kidney impairment.

**Analysis**

Using the information you have collected in the table above, consider the properties of each drug and what this biochemical information means. These drugs are being considered as antacids – chemicals that relieve indigestion by neutralising excess stomach acid.

1. Compare the pH of the antacids before adding HCl, then compare the pH of antacids after adding HCl.
2. Which antacid seems to be most effective? Which antacid seems to be least effective? Explain why.
3. Individuals with high blood pressure are advised to avoid excess sodium. Which drug(s) would be suitable and which drug(s) would not be suitable for someone with high blood pressure?
4. The company you work for wants to develop an antacid for individuals that can be used for a long period of time by the geriatric population. Which drug would you suggest as the best candidate to be taken forward into the next stage of drug development and why?