Biopharmaceutics and pharmacokinetics

Lab. 4

In-vitro evaluation of Antacids

Introduction

- The Gastro-intestinal (GI) tract generates and maintains different pH environments along its length.
- pH is very important for controlling activity of digestive enzymes.

ACIDITY IN THE STOMACH

- Acidity in the stomach is normal, but excess acidity is potentially harmful.
- stomach pH range between 1-2 due to production of hydrochloric acid from structures in lining of walls.
- Acid environment kills bacteria that comes in with food, is optimum for activity of digestive enzymes

Factors that cause excess production of gastric juice (acidic secretion)

Smoking and Excess alcohol

Stress

Some anti-inflammatory drugs

- Acid indigestion(**dyspepsia)** is an illness commonly treated by self-medication.
- Antacids are drugs which **on ingestion react with the hydrochloric acid** of gastric content to **lower** the acidity.

- Antacids are **alkalis**, such as **aluminium hydroxide**, **magnesium salts** (magnesium hydroxide and magnesium trisilicate),**sodium bicarbonate**, and **calcium hydroxide**.

- They are simple ,often effective treatment for many dyspepsia's (**impairment of function of digestion**), and provide symptomatic relief in conditions such as **peptic ulcer, gastritis** (inflammation of the lining of the stomach) ,and **esophageal reflux with heartburn**.

Typical Neutralization Reaction

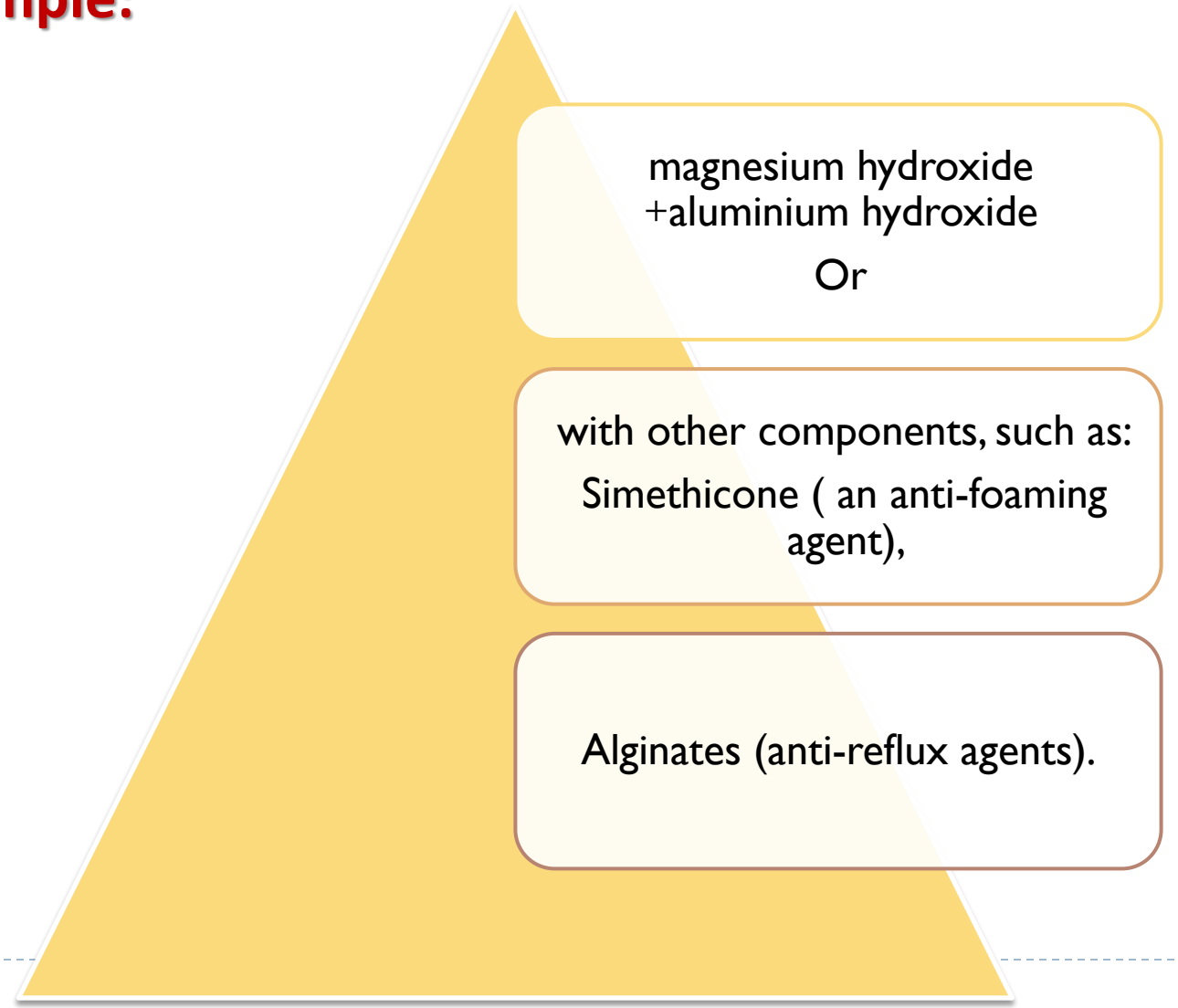
Acid + base → Salt + Water

Example Antacid Reactions:

$$Al(OH)_3(s) + 3HCL(aq) \rightarrow AlCl_3(aq) + 3H_20(l)$$

$$Mg(OH)_2(s) + 2HCL(aq) \rightarrow MgCl_2(aq) + 2H_20(l)$$

They are generally formulated in combinations ,for example:



Antacids may be divided into two main groups according to their water solubility:

Water insoluble and have slow onset and prolonged action

- e.g.aluminium hydroxide,magnesium trisilicate.

Water soluble and act quickly but its effect is transient.

prolonged use may cause systemic alkalosis and renal damage

- e.g. sodium bicarbonate and sodium citrate

Antacids, by altering gastric pH, may interfere with drug absorption in number of ways:

Altered drug ionization

- :e.g. carbenoxolone (an ulcer healing drug),its absorption is completely inhibited above pH 2 and therefore ,it should not be given with antacids.

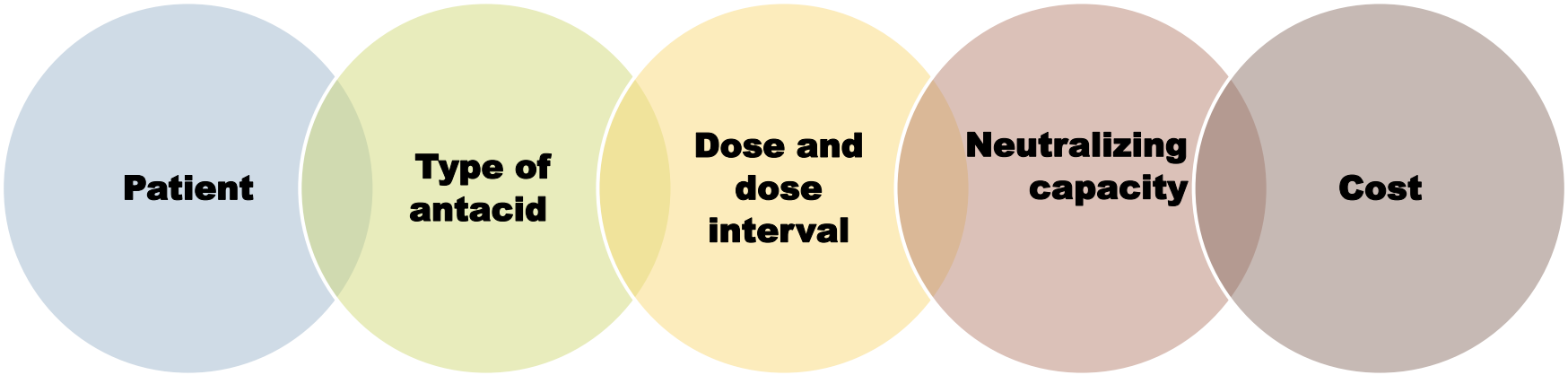
Alteration of gastric emptying

- :The stomach empties more readily when pH increases.

Drug dissolution	• may be affected by pH changes
Drug interaction	• calcium , aluminium and magnesium decrease the gastric absorption of tetracyclines due to complex formation with it
Systemic effect	• Systemic antacids may accelerate the excretion of drugs(salicylates) and inhibit the urinary excretion of basic drugs ,e.g. amphetamines.

It seems advisable to administer other drugs at least one half to one hour before antacids ingestion in order to assure consistent absorption and effect.

Several factors must be considered when selecting an antacid product



The patient : Whether he has impaired renal function ,edema , high blood pressure , allergic to milk or milk products.

Type of antacid (systemic or non-systemic): A systemic antacid, such as sodium bicarbonate is soluble, readily absorbed, and capable of producing systemic electrolyte disturbance

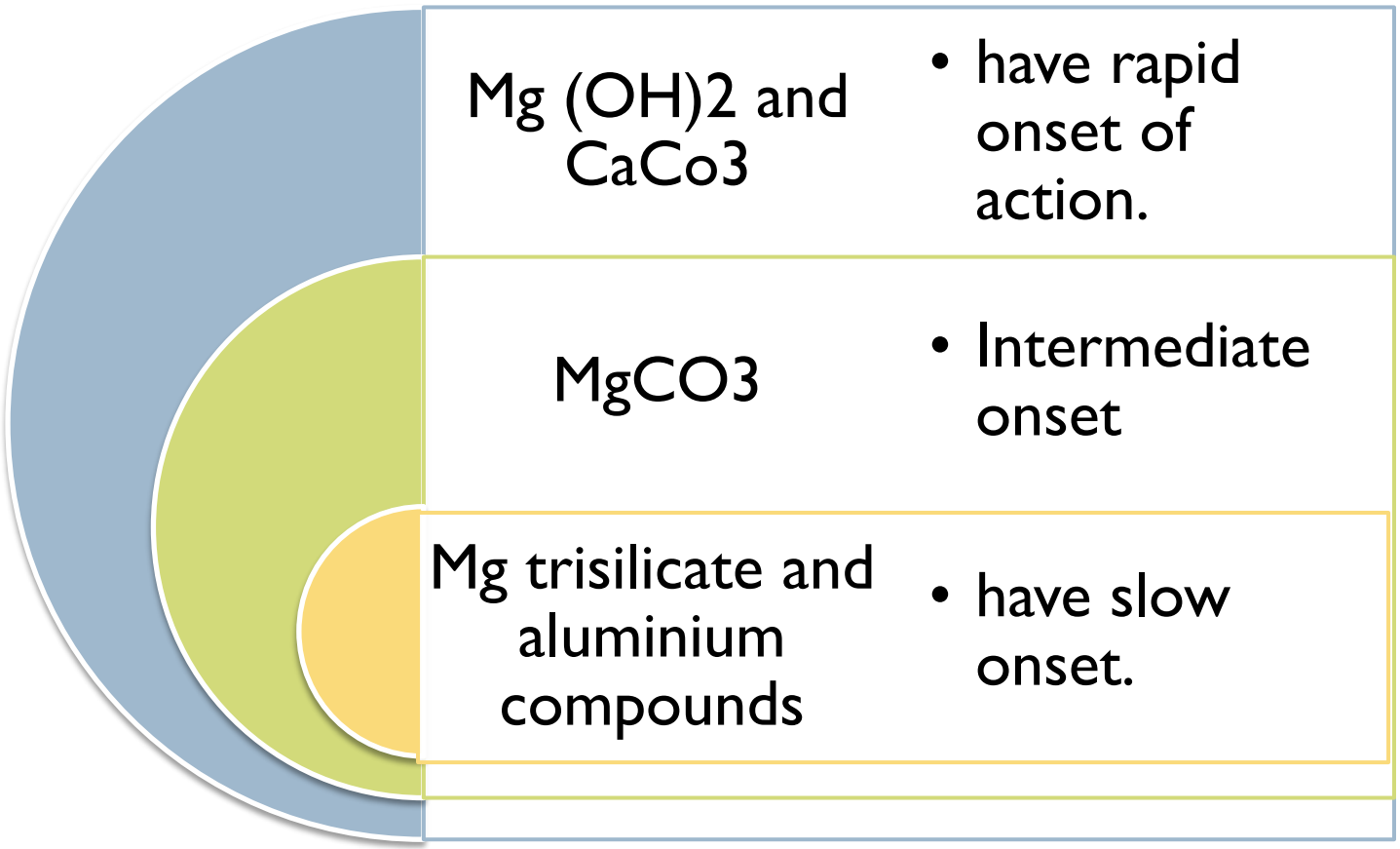
Non systemic such as calcium carbonate or basic aluminum substances ,form compounds that are not absorbed and thus do not exert any systemic effect.

Neutralizing capacity

- Antacids differ in their ability to neutralize gastric secretions

Dose and dose interval

- An ideal antacid should be rapid in onset and provide a continuous buffering action


Mg (OH)2 and CaCo3
• have rapid onset of action.
MgCO3
• Intermediate onset
Mg trisilicate and aluminium compounds
• have slow onset.

Aim of the experiment:

The objective of this experiment is to

- evaluate in vitro , a number of antacid marketed products and compare their buffering capacity .

Principle

- A simple procedure is used, to mimic the physiological conditions in the stomach . Techniques of alternate addition and removal of (0.1N HCl)solution are used to mimic the release of HCL from the lining cells and the periodic emptying of the stomach.

Experimental

1. A quantity of 2gm of finely ground powder or its equivalent of formulations was added to 100ml of 0.1N HCl.
2. The pH of the mixture was determined after the intervals of 1, 2, 4, 6, 8 and 10 minutes.
3. A quantity of 20ml of the mixture was then removed by a pipette and replaced by 20ml fresh 0.1N HCl.

4. The process was repeated at 10 minutes interval until **a pH below 2.75** was reached which shows that the buffering power of antacid was spent out.

5. the time at which pH falls below 2.75 was used as measure of buffering capacity

Enter your results in a table and plot a graph against time as you conduct the experiment.

Time in minutes	PH of the mixture
1	
2	
4	
6	
8	
10	
20	
40	
50