Biopharmaceutics

Lab.2 *In-vitro* evaluation of antacids

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Lab Aim: ***in-vitro*** **assessment for over-the-counter antacids.**

Key topics:

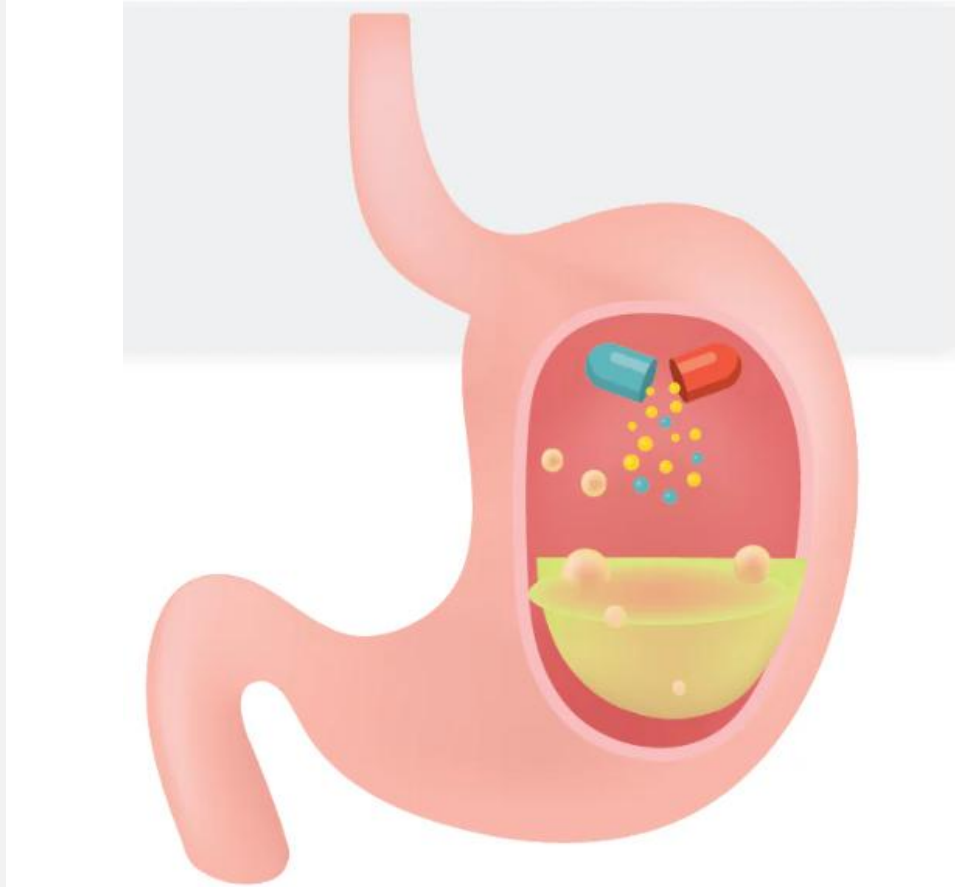
1. Physiological basis of gastric acidity.
2. Factors for excess acids.
3. Chemistry of antacids.
4. Evaluating antiacid efficacy.

THE *IN VITRO* EVALUATION OF ANTACIDS:

INTRODUCTION TO GASTRIC PH REGULATION

- The gastrointestinal (GI) tract maintains distinct pH levels in each segment to optimize digestion and nutrient absorption.

- pH regulation ensures that digestive enzymes function efficiently—**pepsin** acts in the acidic stomach, while enzymes such as **trypsin and amylase** work best in the neutral to slightly alkaline environment of the small intestine.



Role of Stomach Acidity:

- Normal stomach pH is very acidic (1-2), due to hydrochloric acid (HCl) from parietal cells.

Acidity serves three critical functions:

- **Bacterial Defense**: Kills ingested pathogens.
- **Enzyme Activation**: Activates **pepsin** for protein digestion.
- **Food Breakdown**: Denatures proteins and breaks down food particles.

- A balance is crucial, as excess acid causes discomfort and damage.

FACTORS CONTRIBUTING TO EXCESS GASTRIC ACID PRODUCTION

- 1- Excess Alcohol Consumption
- 2- Smoking
- 3- Chronic Stress
- 4- Certain Anti-inflammatory Drugs (NSAIDs)
- 5- Other contributing factors can include dietary choices (e.g., spicy, fatty foods, caffeine), H. pylori infection, and certain medical conditions.

ANTACIDS: THE FIRST LINE OF DEFENSE

Common Ingredients:

- **Aluminum Hydroxide/$Al(OH)_3$**: Slow-acting (slightly soluble), can cause constipation (reduce intestinal motility by inhibiting smooth muscle contraction in GIT).
- **Magnesium Salts/$Mg(OH)_2$**: Fast-acting (neutralize pH), can cause diarrhea (exhibit **osmotic effects** in intestine: unabsorbed magnesium draws water into intestinal lumen, increasing fluid content and stool softness).
- **Sodium Bicarbonate/$NaHCO_3$**: Very fast-acting (dissociate quickly), but systemic (can cause alkalosis due to increase blood pH).
- **Calcium Carbonate/$CaCO_3$**: Rapid and potent (reacts with (HCl) to form $CaCl_2$, CO_2, and H_2O, neutralizing stomach acid. So rapid reduction in gastric acidity) but can cause constipation (slowdown bowel movement) and "rebound" acid.

Acid indigestion (**dyspepsia**) is a common condition often treated through self-medication with antacids, which neutralize excess stomach acid to relieve heartburn and discomfort.

Mechanism of Action

Antacids are fundamentally **alkaline compounds** that work by directly neutralizing stomach acid, reducing its corrosive effect on the esophageal and gastric lining.

Therapeutic Applications of Antacids

1- Peptic Ulcer Disease

2- Gastritis

3- Esophageal Reflux with Heartburn (GERD)

They provide quick, symptomatic relief for dyspepsia (bloating, nausea, heartburn) but offer only temporary relief; persistent cases require medical evaluation.

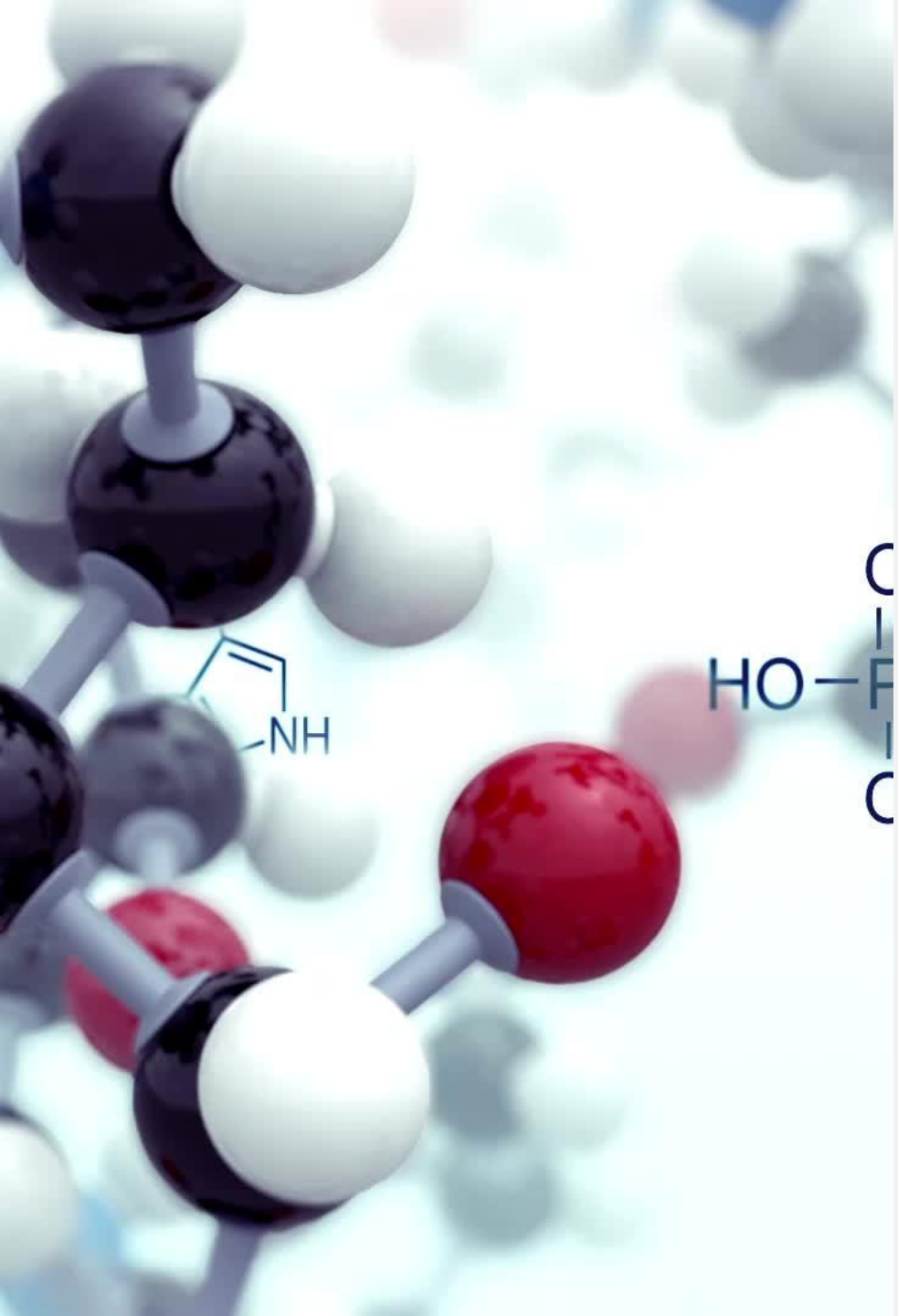
Typical Neutralization Reaction

Acid + base → Salt + Water

Example Antacid Reactions:

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

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



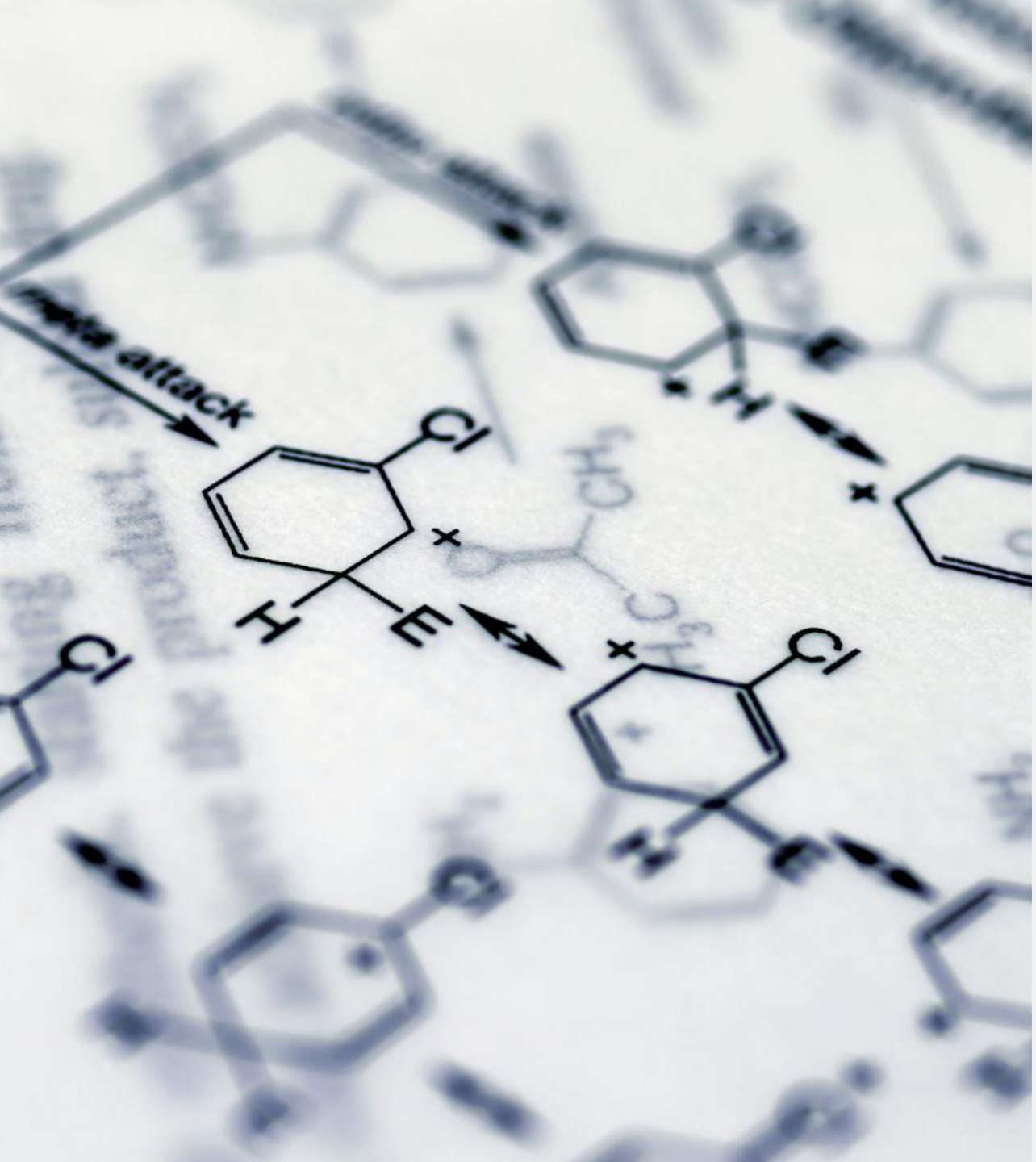
Modern Antacid Formulations

- Modern antacids combine agents for enhanced efficacy:

1. **$Mg(OH)_2$ + $Al(OH)_3$**: Balances diarrhea (Mg) and constipation (Al) side effects.

2. **Simeticone:** An anti-foaming agent that relieves bloating and gas.

3. **Alginates:** Form a viscous "raft" on stomach contents to physically prevent acid reflux.



Antacid Classification by Solubility:

- **Water-Soluble Antacids** (e.g., $NaHCO_3$): Absorbed systemically, leading to potential systemic effects.

- **Water-Insoluble Antacids** (e.g., Al, Mg, Ca compounds): Act locally in the GI tract, generally not absorbed.

Drug Interactions - Part 1

Antacids can significantly alter the absorption of other drugs by:

- **Altered Drug Ionization:** Changing gastric pH can alter a drug's ionization state, impacting its absorption (e.g., Carbenoxolone).
- **Alteration of Gastric Emptying:** Increased pH can accelerate stomach emptying, affecting drug dissolution and absorption rates.

Drug Interactions - Part 2

Further mechanisms of interaction:

- **Drug Dissolution Affected by pH:** Bioavailability depends on dissolution rate, which is pH-dependent.
- **Complex Formation:** Ca, Al, and Mg ions can form insoluble complexes with drugs like tetracyclines, reducing their absorption.
- **Systemic Effects:** Systemic antacids can alter urinary pH, thereby accelerate the excretion of acidic drugs (increase polarity then less absorb) (like salicylates) and inhibit the excretion of basic drugs (like amphetamines) (reverse).
- **Recommendation: Administer other drugs 30-60 minutes before the antacid.**

Factors in Antacid Selection

Choosing the right antacid involves balancing therapeutic needs with potential side effects and drug interactions. Pharmacists must consider a range of factors for optimal patient outcomes.

Buffering Capacity

How effectively and for how long an antacid can neutralize stomach acid.

Onset and Duration

How quickly the antacid starts working and how long its effects last.

Drug Interactions

Potential for interference with other medications the patient is taking.

Patient-Specific Factors

Underlying health conditions (e.g., renal impairment, heart failure) and dietary restrictions.

Onset of Action for Common Antacids

The speed at which an antacid begins to neutralize stomach acid is a critical factor in patient comfort and therapeutic effectiveness. Different active ingredients exhibit varying onset times.

Fast | **Intermediate** | **Slow**

$Mg(OH)_2$ & $CaCO_3$

Magnesium hydroxide and Calcium Carbonate

Although sparingly soluble, it dissociates rapidly into Mg^{2+} and OH^- ions that instantly neutralize acid ($H^+ \rightarrow H_2O$).

$$Mg(OH)_2 + 2HCl \rightarrow MgCl_2 + 2H_2O$$

Reacts directly with gastric HCl to form $CaCl_2$, CO_2, and H_2O — the gas release helps mixing, accelerating acid neutralization.

$$CaCO_3 + 2HCl \rightarrow CaCl_2 + CO_2 + H_2O$$

$MgCO_3$

Magnesium Carbonate

Less reactive than $Mg(OH)_2$ or $CaCO_3$; requires more time to react with acid to form $MgCl_2$ and CO_2.

$$MgCO_3 + 2HCl \rightarrow MgCl_2 + CO_2 + H_2O$$

Mg Trisilicate & Aluminum Compounds

Magnesium Trisilicate and Aluminum Hydroxide

Reacts gradually with acid; forms colloidal silica and magnesium chloride slowly, giving a sustained but delayed effect.

$$Mg_2Si_3O_8 \cdot xH_2O + 6HCl \rightarrow 2MgCl_2 + 3SiO_2 + 3H_2O$$

Dissolves and reacts slowly with gastric acid; produces a prolonged buffering action but delayed onset.

$$Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O$$

Buffering Capacity

- The core of efficacy is buffering capacity the ability to maintain a therapeutic pH over time.

- **$Mg(OH)_2$:** High capacity, can cause diarrhea.

- **$CaCO_3$:** High capacity, can cause constipation/rebound.

- **$NaHCO_3$:** Rapid but short-lived; systemic.

- **$Al(OH)_3$:** Slower onset, prolonged action.

- **Optimal therapy often uses combination products.**

- **Experiment Aim**
- **Aim:** *In-vitro* evaluation of commercial antacids to compare their buffering capacities.

- **Objectives:**
  1. Accurately assess the effectiveness of different formulations.
  2. Provide practical insights for scientific antacid selection.

Experimental Procedure: Part 1 - Initial Acid Neutralization

1

Preparation: Accurately measure **2 grams of finely ground antacid powder** (or its equivalent in formulation) and add it to 100 mL of 0.1 N HCl in a beaker. Ensure thorough mixing to facilitate the reaction.

2

Initial pH Measurement: Using a calibrated pH meter, record the pH of the mixture at precise intervals: **0.5, 2, 4, 6, 8, and 10 minutes** after adding the antacid. Stir the solution continuously during this phase.

3

Acid Replacement: After the 10-minute mark, carefully remove **20 mL of the mixture** using a pipette. Immediately replace this with **20 mL of fresh 0.1 N HCl** to simulate continuous acid secretion in the stomach.

These initial steps are critical for observing the immediate acid-neutralizing effect of the antacid and establishing a baseline for its buffering capacity under sustained acid conditions.

Experiment Principle

· The experiment simulates gastric conditions through:
· **Alternate Acid Addition**: Mimics intermittent HCl secretion.
· **Periodic Acid Removal**: Replicates stomach emptying to assess sustained buffering.

Experimental Procedure - Part 2

1· **Repeated Acid Addition**: Continue the process of removing 20 mL of the mixture and replacing it with 20 mL of fresh 0.1 N HCl **at 10-minute intervals.**
2· **pH Monitoring**: pH is recorded after each cycle.
3· **Endpoint**: The procedure continues until the pH falls below 2.75, indicating exhausted buffering capacity.
4· **Measure**: The total time until pH < 2.75 is the measure of buffering capacity.
5· **Recording**: Data is recorded in a table (Time vs. pH).

Time in minutes	pH of the mixture
0.5	
2	
4	
6	
8	
10	
20	
40	
50	

Conclusion

Practical Application

This experiment provides a practical understanding of how different antacid formulations perform under simulated gastric conditions, directly correlating to their real-world efficacy.

Data Interpretation

The buffering capacity, measured by the time it takes for the pH to drop below 2.75, is a direct indicator of an antacid's neutralizing power. Higher values signify more effective formulations.

Critical Analysis

Consider factors like particle size, active ingredient concentration, and formulation type (tablet vs. liquid) that might influence the observed buffering capacity.

Thank you for your listening