B. 21 Gastrointestinal pharmacology

a. Describe the mode of action and comparative pharmacology of sodium citrate and magnesium trisilicate.

sodium citrate
- non-particulate antacid
- presented as 30 ml of 0.3 mol/l solution
- raises gastric pH above 3 for 2-3 hours
- given prophylactically to reduce the incidence of pneumonitis if aspiration occurs
  - effectiveness depends on gastric volume, pH and motility
  - most effective with low volume, poor motility
- 100% bioavailable
- citrate is metabolized by the TCAC
  - represents a small alkaline load (equivalent to 27 mmol HCO₃⁻)
magnesium trisilicate
- particulate, relatively insoluble antacid
  - similar to magnesium carbonate, aluminium hydroxide, others
  - present in many proprietary preparations
  - raises gastric pH similar to citrate
  - not bioavailable, minimal absorption

b. Describe the mode of action and side effects of omeprazole.

omeprazole (and lansoprazole, pantoprazole...)
- a substituted benzimidazole
pharmacokinetics
- prodrug activated by low pH in parietal cell canaliculi
- high oral bioavailability
- plasma t¹/₂ 1-2h
- duration of effect 1-2days due to local concentration
pharmacodynamics
  - direct inhibitor of H⁺, K⁺ ATP-ase in parietal cells
adverse effects
  - complete suppression of acid secretion
  - altered bacterial flora
  - loss of barrier to infection posed by acid environment
  - upregulation of gastrin secretion (? risk of carcinoid gastrinoma)
clinical use
  - 60 mg oral daily

c. Describe the mode of action and side effects of the H₂ antagonists.

ranitidine (cimetidine, famotidine, nizatidine...)
pharmacokinetics
  - 30-90% bioavailable
  - Vₐ 1.5 l/kg
  - t¹/₂ β 2 h
  - renal elimination
pharmacodynamics
  - competitive antagonist at H₂ receptors
  - suppresses gastric acid secretion
  - high dose: ↓ cardiac output, confusion
adverse effects
  - (cimetidine inhibits p450 enzymes, competes at androgen receptors)
  - ranitidine reduces gastric alcohol dehydrogenase activity
↑ alcohol bioavailability by 40%