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QUESTION 22

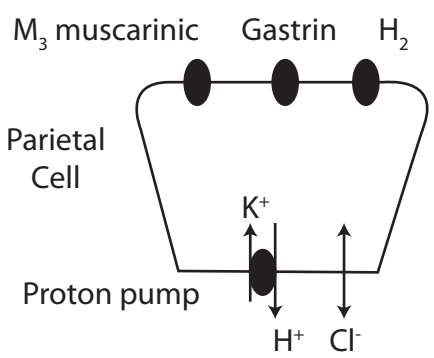
Compare and contrast the pharmacology of drugs that alter the pH of gastric fluid.

Main classes, PPI, H2 receptor antagonists, antacids (see below)

Other

muscarinic blockers - pirenzipine - act on the M3 muscarinic receptor and decrease proton pump action

prostaglandin E2 analogues - misoprostil - act via GPCR mediated inhibition of adenylyl cyclase, decreasing cAMP and reducing proton pump activity

	Proton pump inhibitors	H2 Receptor Antagonists	Antiacids
Pharmaceutical	Most commonly used Omeprazole is the prototype Available both IV and oral	Less commonly used than PPIs Ranitidine is the prototype Available both IV and oral	Available in a range of inorganic compounds Oral only
Pharmacodynamics mechanism			The basic solution neutralises acid in the gut, raising the pH by physicochemical properties
effects	↓acidity/gastric secretions no change emptying/LOS tone inhibition of cyp450	↓acidity/gastric secretions no change emptying/LOS tone arrythmias if given IV fast	Reduce acidity water soluble - faster acting insoluble - slower but less sytemic effects
side effects	increased risk of infection aspiration GIT osteoporosis	idiosyncratic thrombocytopaenia, hepatitis, leucopaenia	can cause metabolic alkolosis diarrhoea and constipation
Pharmacokinetics Absorption	rapidly absorbed variable bioavailability depending on formulation	absorbed via the gut bioavailability 50%	oral, not systemic
Distribution	highly protien bound >95% small Vd 0.3 L/kg	low protien binding 15% moderate Vd 1-2L/kg	not known
Metabolism	rapidly and completely metabolised hepatically via hydroxylation	Minimal hepatic metabolism	act as a proton acceptor
Elimination	excreted in urine, inactive half life 1-2hrs	excreted in the urine mostly unchanged half life 1-3 hours	in faeces

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