Drug Disposition

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Clinical Pharmacokinetics of Drugs Used in the Treatment of Gastrointestinal Diseases (Part I)

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Summary

Drug treatment of gastrointestinal diseases, which was previously limited to the use of antacids, anticholinergics, antispasmodics, cathartics and laxatives, has changed markedly over the past decade. Histamine H₂-receptor antagonists (e.g. cimetidine, ranitidine and more recently famotidine and nizatidine) have revolutionised the treatment of peptic acid disorders, but their role is currently challenged by muscarinic-M₁-receptor antagonists (e.g. pirenzepine), proton pump inhibitors (e.g. omeprazole), prostaglandin analogues

1 A complete reference list will appear in Part II of this article in the next issue of the Journal.
and site-protective drugs (e.g. colloidal bismuth subcitrate and sucralfate). Newer antiemetics with prokinetic properties (e.g. metoclopramide, domperidone and cisapride) have also been introduced in the management of gastrointestinal motility disturbances, and new anti-inflammatory salicylates (e.g. olsalazine and mesalazine) have been developed for the treatment of chronic inflammatory bowel diseases. Finally, diphenoxylate and loperamide have gained wide clinical application as nonspecific antidiarrhoeal agents. The basic pharmacokinetic properties of the above agents are briefly reviewed with the main emphasis on the newer and more important drugs in current use. Furthermore, the effects of age and disease on pharmacokinetics, in addition to drug interaction potentials and pharmacokinetic-pharmacodynamic relationships, are discussed.

The anti-inflammatory salicylates, nonspecific antidiarrhoeal agents, laxatives and cathartics will be dealt with in Part II.

Few areas of therapeutics have expanded so rapidly as that of drugs for the treatment of gastrointestinal disorders. The drugs may best be grouped according to their therapeutic indications (Table I). In particular, numerous novel agents have proved to be of benefit for patients with peptic ulcer disease, e.g. histamine H2-receptor antagonists, muscarinic M1-receptor antagonists, proton pump inhibitors, prostaglandin analogues and various so-called site-protective drugs. Moreover, newer antiemetics with prokinetic properties have been introduced in the management of gastrointestinal motility disturbances, and a number of anti-inflammatory salicylates have been shown to be of clinical value in the treatment of chronic inflammatory bowel diseases. Finally, diphenoxylate and loperamide have gained wide clinical application as nonspecific antidiarrhoeal agents. The purpose of this review is to outline the basic pharmacokinetic properties of drugs in current use for the treatment of gastrointestinal diseases. The effects of age and disease on pharmacokinetics, drug interaction potential and pharmacokinetic-pharmacodynamic relations are also described. The major emphasis is put on the newer and more important drugs. Agents used in the treatment of disorders of the liver, biliary tract and pancreas are not discussed.

### 1. Histamine H2-Receptor Antagonists

Histamine H2-receptor antagonists have often been regarded as drugs of first choice in the treatment of peptic ulcer. Reflecting this practice, ranitidine and cimetidine are the most widely sold drugs in the world (Russell & McWhirter 1987) and they are the standards against which any new anti-