मानवाची उत्पत्ती व विकासाचे विविध टप्पे

Human Origin and Different Steps in Its Development

संपादक
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79.
Effect of Antiulcerative drugs on Human body

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Abstract

The proton pump inhibitors (eg, omeprazole, lansoprazole, rabeprazole, pantoprazole, and esomeprazole) effectively block acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump that resides on the luminal surface of the parietal cell membrane.Anti-secretory drugs (H2 receptor antagonists and proton pump inhibitors are the mainstays of treatment for ulcer healing.

Keywords

proton pump inhibitors, ulcers, Pantpprazole, Omeprazole, benzimidazole

Introduction

The treatment of peptic ulcers has changed dramatically in the past two decades, mirroring the revolution in understanding of the etiologies of peptic ulcers. Principles of treatment include:Antibiotic therapy is indicated for ulcer disease associated with *Helicobacter pylor* (*H. pylori*) infection.Maintenance therapy, once a mainstay of treatmen for peptic ulcer disease, is no longer indicated after successful eradicatio of *H. pylori* [1]. Antacids, bismuth, and protective agents were show to heal peptic ulcers in an era before the role of *H. pylori* wa recognized, and, in retrospect, studies were performed on largely *H pylori*-positive peptic ulcer patients. H2 receptor antagonists (H2RAs inhibit acid secretion by blocking histamine H2 receptors on the parieta cell. H2RAs (eg, cimetidine, ranitidine, famotidine, and nizatidine) ar still used for treatment and maintenance therapy of peptic ulcer disease treatment of gastroesophageal reflux disease, and management o dyspepsia. However, they achieve less acid suppression than proto pump inhibitors. However, proton pump inhibitors have been shown t

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have superior healing rates for both duodenal and gastric ulcers [2]. In patients with NSAID-induced ulcers who require continued NSAID therapy while receiving treatment for ulcer disease, proton pump inhibitors are also superior to H2RAs [3]. Side effects of H2RAs include rare, severe adverse events, such as renal and hepatic toxicity. However, H2RA remain useful in some patients because of their low cost and good safety profiles. In addition, less acid inhibition may be an advantage by avoiding the consequences of profound acid inhibition. Adverse effects — H2RAs are remarkably safe drugs; in randomized trials, the frequency of adverse reactions is generally similar to placebo [4]. A number of uncommon side effects have been reported, primarily as isolated cases or in retrospective uncontrolled series. However, causality cannot be established from the temporal association between drug use and an untoward effect, particularly when the clinical situation is complicated by serious medical illness and the use of multiple drugs [5]. The proton pump inhibitors (PPIs) (eg, omeprazole, lansoprazole, dexlansoprazole, rabeprazole, pantoprazole, and esomeprazole) effectively block acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump that resides on the luminal surface of the parietal cell membrane.

PPIs all achieve a similar level of acid secretory inhibition, although small differences in efficacy have been demonstrated when comparing various agents given in standard clinical doses. For example, esomeprazole was slightly more effective than other delayed release PPIs in healing of esophagitis. Slightly superior healing has also been demonstrated with immediate release omeprazole compared with lansoprazole or pantoprazole [6]. Twice daily dosing is recommended for large gastric ulcers but is not required for duodenal ulcers. Fixed dose combinations of the PPI esomeprazole with ibuprofen have been developed for use in the prevention of NSAID-induced gastroduodenal injury [7].

On the other hand, differences in healing rates with various PPIs observed in clinical trials of esophagitis have not been demonstrated in the treatment of peptic ulcer disease. As a result, our approach is based upon clinical experience and the pharmacology of these drugs. If a standard PPI therapy fails to heal an ulcer, we proceed with twice daily dosing, and if that treatment fails, we switch to another PPI. Esomeprazole or immediate-release omeprazole may be more effective than other PPIs. Immediate release omeprazole taken at bedtime also

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appears to be superior to delayed release PPIs taken before dinner [8], this regimen may have some advantage for refractory ulcers.

Proton pump inhibitors (PPIs) are more effective and long-lasting acid inhibitors than H2 receptor antagonists (H2RAs). As a result, they are superior in healing both gastric and duodenal ulcers, although the advantage for gastric ulcers is modest [9,10].

The derivatives of benzimidazole are possessed broad spectrum of biological activities including antibacterial, antiviral,[11] antitumor, antimutagens,[13] cardiovascular,[14] anticalmodulin,[15] and many other activities are well documented.[16]

In particular, mercapto benzimidazole is used for the synthesis of the most known prazole drugs pantoprazole,[17] omeprazole, rabeprazole,[19] and lansoprazole[20] which are antiulcerous agents useful in the treatment of stomach and duodenal ulcers. By all means, benzimidazole acts as "privileged substructure" for drug design. Among these, pantoprazole is the proton pump inhibitor drug used in gastroesophageal reflux disease and as antihelicobacter agent for the treatment of gastrointestinal disorders. Pyridine and 5-difluoromethoxy-2-mercapto-1H-benzimidazole are the two key constituents of this drug. After the extensive literature search, it was observed that quinoline, 2-mercapto-1H-benzimidazole are the important pharmacophore, but till date enough efforts have not been made to combine these two moieties as a single molecular scaffold. So, our object was to synthesize and biological screening of a series of new compounds incorporating these moieties.

Origin of the research problem

Among these, Omeprazole is a proton pump inhibitor used in the treatment of dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, laryngopharyngeal reflux, and Zollinger–Ellison syndrome. Omeprazole is one of the most widely prescribed drugs internationally and is available over the counter in some countries. It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system. Omeprazole was first marketed in the United States in 1989 by AstraZeneca, under the brand names Losec and Prilosec.

Pantoprazole is also a proton pump inhibitor drug that inhibits gastric acid secretion. Pantoprazole is used for short-term treatment of erosion and ulceration of the esophagus caused by gastroesophageal reflux disease. Pantoprazole may also be used in combination with

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antibiotics to treat ulcers caused by *Helicobacter pylori*. Pantoprazole was developed by Altana and was licensed in the USA to Wyeth. It was initially marketed under the brand name Protonix by Wyeth-Ayerst Laboratories. Similarly Lansoprazole and Rabeprazole are antiulcer drugs in the class of proton pump inhibitors. For these all antiulcer drugs, Pyridine and 2-mercapto-1H-benzimidazole are the two key constituents of this drug.

Conclusion

We have synthesized quinoline containing 2-mercapto-1H-benzimidazole as a single molecular scaffold. So, our object was to synthesize and biological screening of a series of new compounds incorporating these moieties which may act as antiulcerative proton pump inhibitor.

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