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Lansoprazole Effective Against Gastric Diseases

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ABSTRACT

A benzimidazole derivative, lansoprazole is prescribed to treat a variety of peptic diseases. It is primarily metabolized in the liver, and the two primary active metabolites found in plasma are lansoprazole and lansoprazole sulfone. Limited information is available regarding the pharmacokinetic characteristics of lansoprazole, lansoprazole sulfone, and 5′-hydroxy lansoprazole, which can be utilized to quantify cytochrome P450 (CYP) 2C19 activity.. The purpose of this study was to evaluate the effects of CYP2C19 on the pharmacokinetics of lansoprazole and its metabolites in healthy Chinese male volunteers, as well as to look into the clinical plasma pharmacokinetic features of the medication.

Keywords: Lansoprazole, Ethylcellulose, Nanosponges, Fickian release.

Introduction

Drugs have undoubtedly gained new interest thanks to drug delivery technology, which gives them a second lease on life through their therapeutic targets. These days, the main issue facing researchers is focusing on medication delivery. The most important developments in the field of therapeutics will be target-oriented drug administration with increases in therapeutic efficacy, decreases in side effects, and optimized dosage regimens. In order to minimize toxic effects and maximize the therapeutic index of the drug. Proton pump inhibitors (PPI) such as lansoprazole and omeprazole are prescribed to treat GORD, acid-related dyspepsia, duodenal and benign gastric ulcers, including those that worsen after NSAID therapy, and fat malabsorption in cystic fibrosis patients despite pancreatic enzyme replacement therapy. Additionally, omeprazole has a license to treat Zollinger-Ellison syndrome and H Pylori. The enteric-coated beads used in the formulation of lansoprazole and omeprazole are supplied in the form of capsules or orodispersible tablets. Since the enteric-coated beads are made to not dissolve in water, it is not possible to dissolve the tablets and provide a proportion because doing so would result in incorrect dosing.

Physio-Chemical Properties

Weight	Average: 369.361
Chemical Formula	$C_{16}H_{14}F_3N_3O_2S$
Oral Bioavailability	80-90%
Apparent volume of distribution	0.4 L/kg
Protein binding	97%
Half-life	0.9 - 1.6 hours

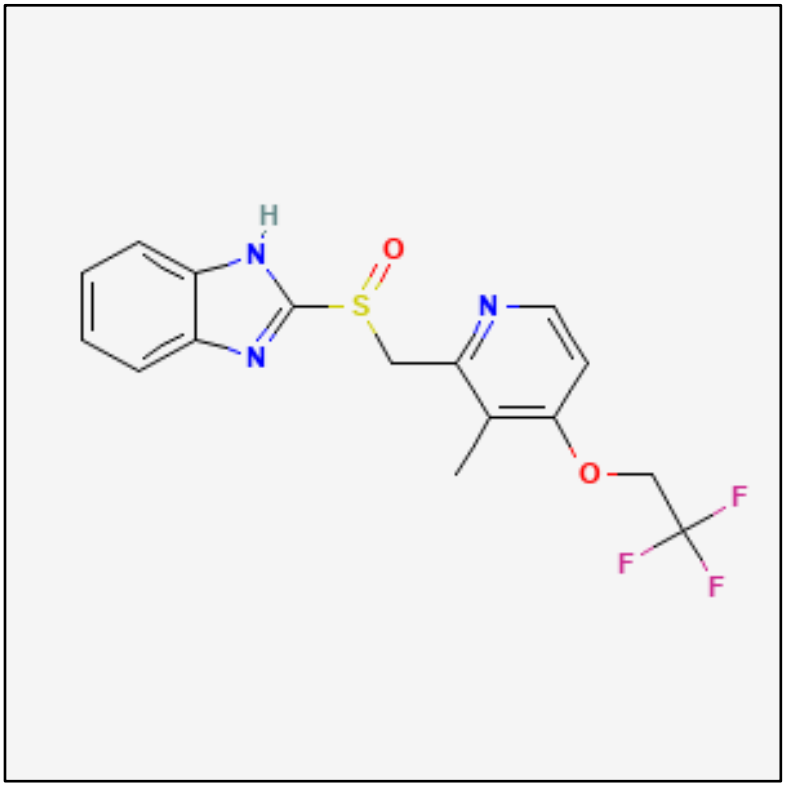

Figure 1: Structure of Lansoprazole

Delayed Drug Release

Drugs can be delivered to the distal human gut either temporally or spatially using delayed-release dosage forms The main goals of using delayed-release products are to shield the medication from stomach fluids, lessen the discomfort that certain medications cause the stomach, or make it easier for medications that are better absorbed from the intestine to pass through the digestive tract.

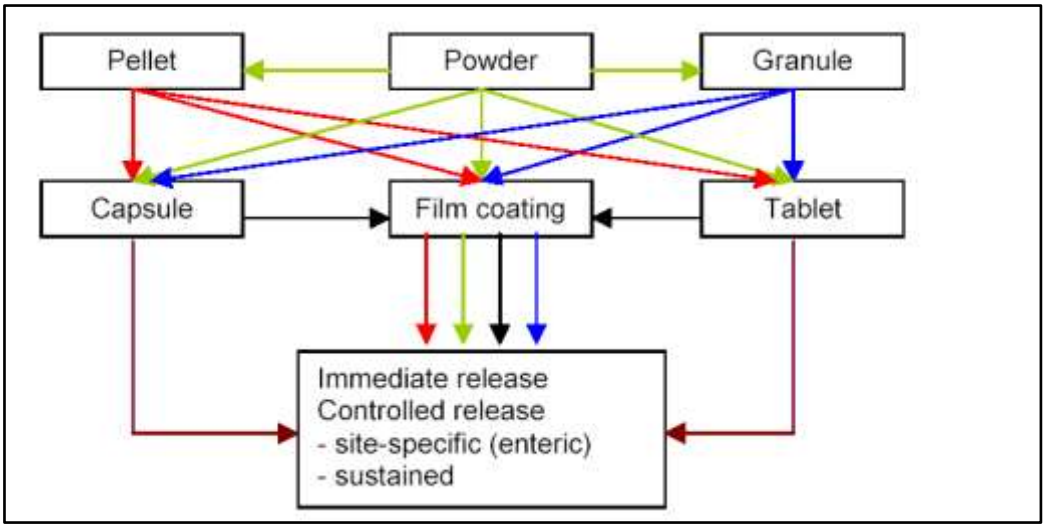

Figure 2: Delayed dosage release schematic diagram

Mechanism of Action

Lansoprazole is a prodrug, meaning that it needs to be protonated in an acidic environment in order to work as a PPI. 3. After being protonated, lansoprazole can react with parietal H+,K+-ATPase cysteine residues, namely Cys813 and Cys321, to produce stable disulfides.PPIs generally have the capacity to bind covalently to their targets, which allows them to provide prolonged inhibition of acid secretion.

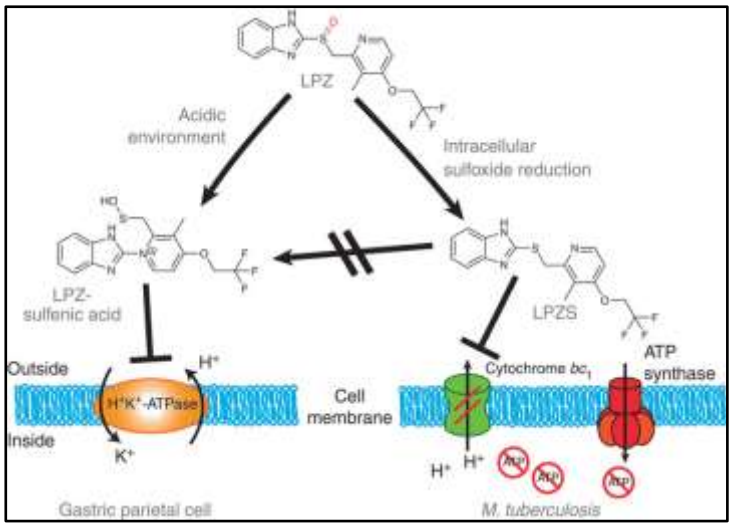

Figure 3: Mechanism of action of Lansoprazole

Synthesis of Lansoprazole

Experimental

General

Uncorrected melting points in degrees Celsius were measured using apparatus. IR spectra were recorded on a Shimadzu-435 spectrophotometer using KBr pellets, and H'-NMR spectra were obtained in DMSO-d6 using a Varian Gemini 200 MHz spectrometer. A 600-watt output was used for microwave irradiation in BPL-Sanyo, BMO, and 700T home microwave ovens.

Experimental procedure

A 600-watt microwave oven was used to microwave pyridine hydrochloride (1, 1 g), 2-mercaptobenzimidazole (2, 0.697 g), and anhydrous sodium carbonate (0.445 g) for two to ten minutes in a Pyrex conical flask. Following the reaction period, the melt was allowed to cool to room temperature, then it was dissolved in methanol, adsorbed on 60–120 mesh silica gel, and chromatographed over the same silica gel. A 7:3 solvent mixture containing benzene.

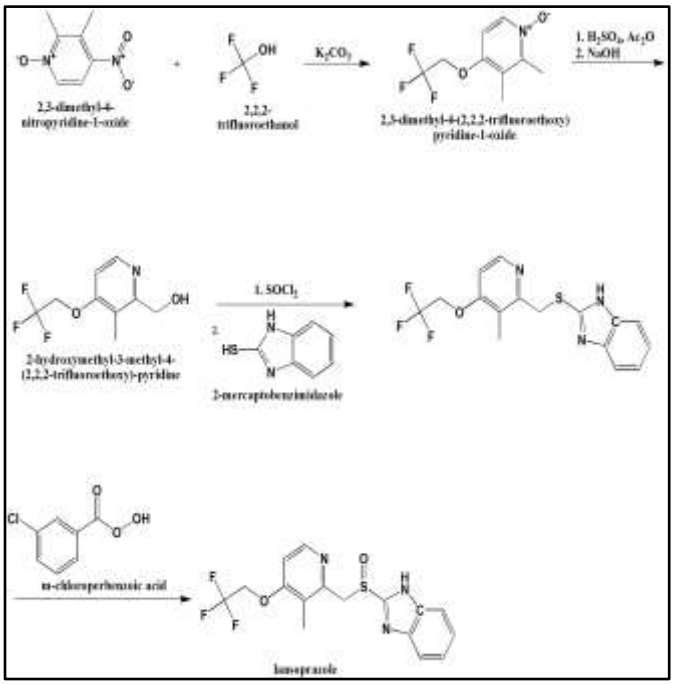

Figure 4: Synthesis of lansoprazole

Medicinal Use

Proton pump inhibitor lansoprazole is the active component of Lansoprazole.

The following conditions may require a prescription for Lansoprazole from your doctor:

- Management of stomach and duodenal ulcers

Treating heartburn and acid regurgitation; treating infections brought on by the bacteria Helicobacter pylori when combined with antibiotic therapy; treating reflux oesophagitis; preventing reflux oesophagitis;

- The management or avoidance of duodenal or stomach ulcers in individuals who need ongoing nonsteroidal anti-inflammatory drug (NSAID) treatment.

- Zollinger-Ellison syndrome treatment.

Dosage

Weight	Drug Choice	Dose	Administration	Notes
>30kg	Lansoprazole	15mg-30mg daily	See section 3.1.	
15-30kg	Lansoprazole	15mg-30mg daily	See section 3.1.	
7.5-15kg	Lansoprazole	7.5mg-15mg daily	See section 3.1.	Use half a 15mg tablet or a whole 15mg tablet
3.5-7.5kg	Lansoprazole	3.75mg-7.5mg daily	See section 3.1.	Use quarter of a 15mg tablet or half a 15mg tablet
2-3.5kg	Omeprazole	2.5mg daily	See section 3.2.	Use quarter of a 10mg tablet Dose can be doubled in 1-2 weeks if no response.
<2kg	Omeprazole	0.7mg/kg daily	See section 3.2.	Open 10mg capsule and add contents to 10ml sodium bicarbonate 8.4%. Allow to dissolve for 20 minutes. Draw up proportion of resulting solution into oral syringe and administer. Dose can be doubled in 1-2 weeks if no response.

Figure 5: Dosage form of lansoprazole

Methodology

Preparation of lansoprazole nanosponges

Using an emulsion solvent diffusion technique, lansoprazole nanosponges were created using varying ratios of ethyl cellulose, polyvinyl alcohol, and Pluronic F68. The disperse phase was gradually added to a predetermined amount of PVA in 100 mL of aqueous continuous phase. dissolved in 30 mL of dichloromethane. The lansoprazole nanosponges that had formed were gathered using vacuum filtration and dried for twenty-four hours at 40°C in an oven.

Entrapment efficiency

To calculate the lansoprazole nanosponges' entrapment efficiency, a UV spectrophotometric technique was employed. Plotting a calibration curve for lansoprazole in methanolic HCl at 293 nm, the drug was found to be within Beer's Lambert's range of 3–18 µg/. Centrifuging lansoprazole at 1000 rpm for 30 minutes extracted the drug, which was then filtered and the concentration was determined using calibration curve data after any required dilution. This is how the percentage of entrapment was determined:

The real drug content in the nanosponge×100 compared to theoretical drug content is the % entrapment efficiency.

Particle size measurement

The average particle size of lansoprazole nanosponges were determined by photon correlation spectroscopy (PCS) using a Nano ZS-90 (Malvern Instruments limited, UK) at a fixed angle at 25º. Sample was diluted 10 times with distilled water and then it was analyzed for particle size.

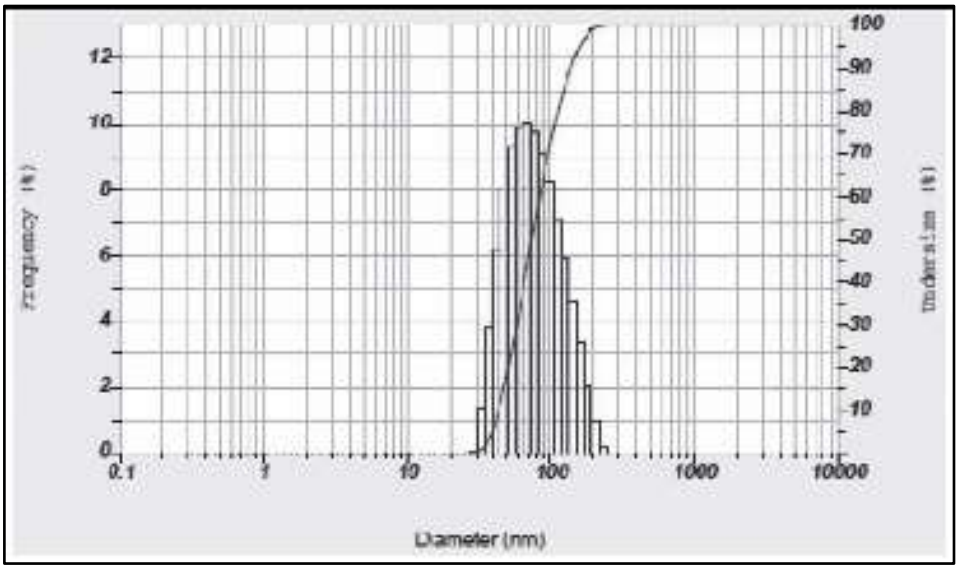

Figure 6. Lansoprazole nanosponges Particle Size

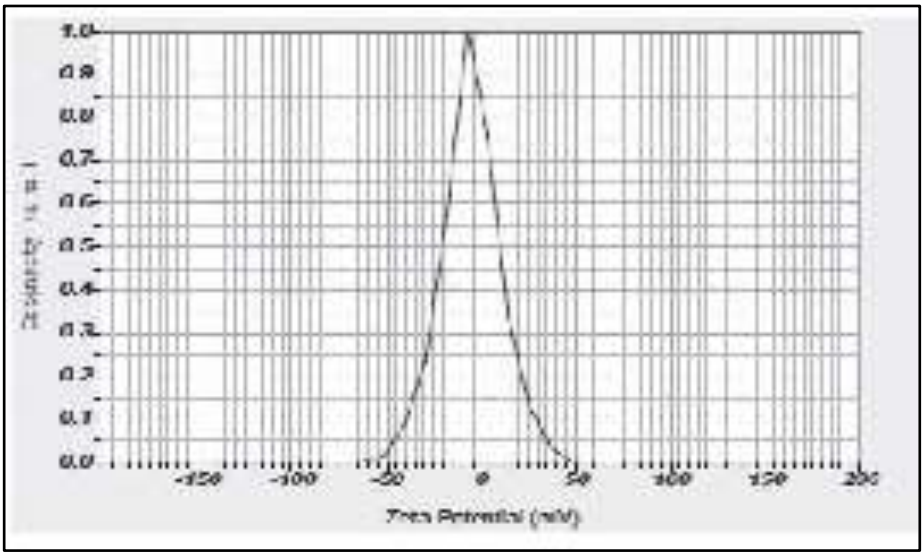

Figure 7. Zeta potential of lansoprazole nanosponges

Preparation of lansoprazole tablets

Tablets containing lansoprazole were made using the direct compression method. After combining the appropriate amount of polymers, excipients, and lansoprazole nanosponges thoroughly, the mixture was compressed into 100 mg tablets using 8 mm.

Evaluation of lansoprazole tablets

Weight variation

Twenty tablets were subjected to the weight variation test in accordance with the guidelines provided by the Indian Pharmacopoeia. A weight deviation of ±7.5% from the average is the maximum allowable limit.

Thickness

Using a vernier caliper, the thickness of 20 randomly chosen tablets from each formulation was measured in millimeters.

Hardness

A Monsanto-style hardness tester was used to randomly select twenty tablets from each formulation and measure the tablets' hardness in kg/cm2.

Friability

The Roche Friabilator was used to measure tablet friability.

Twenty pre-weighed tablets that were chosen at random were put inside the device, turned 100 times, and then the tablets were weighed again. The mass loss in percentage was used to calculate the friability using the formula F= (WA-WB/WA)×100.

Where F stands for friability, WA for initial weight (gm), and WB for final weight (gm). A weight loss of no more than 1% is considered acceptable.

Conclusion

The majority of the ideal characteristics needed for an oral controlled release dosage form were present in the lansoprazole nanosponges. It has been possible to create lower particle size (83.4 nm) nanosponges with the help of negatively charged surface charge.

Up to 12 hours of continuous controlled release were indicated by the release profile. For a full day, the enteric-coated Lansoprazole tablet exhibited controlled release behavior and no drug release in an acidic medium, which is desirable.

Because of their strong potential for prolonged drug release, nanosponge systems may be useful for lowering dosages, reducing administration frequency. Thus, it can be said that the lansoprazole nanosponges, an oral enteric-coated tablet, are thought to be the best and most efficient way to treat ulcers and associated diseases.

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