



## Itopride Hydrochloride: A Comprehensive Review on its Role in Managing Functional Dyspepsia

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### Abstract:

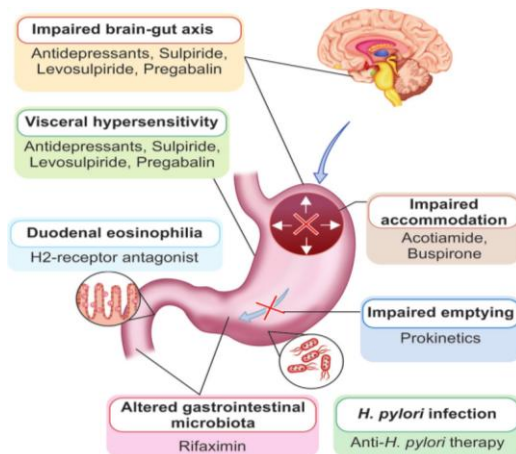
Itopride HCl is a prokinetic medication used to treat gastrointestinal problems such as functional dyspepsia and gastroesophageal reflux disease (GERD). It works by blocking dopamine D2 receptors and acetylcholinesterase, which increases gastrointestinal motility and speeds up stomach emptying. This dual process causes greater acetylcholine release while decreasing dopamine-mediated regulation of gastric motility, enabling stomach emptying and alleviating symptoms including bloating, nausea, and abdominal discomfort. The medicine efficiently treats symptoms like dyspepsia, bloating, upper abdominal pain, heartburn, nausea, and vomiting. The medicine had great tolerability, with no major side effects on the QT interval, hematological markers, or hepatic and renal functions. A part from other benzamides, itopride increases colonic peristalsis and propels luminal contents, which may assist functional bowel problems.

**Keywords:** Itopride Hydrochloride, Gastric motility, Prokinetic medication, Functional dyspepsia, Acetylcholinesterase inhibitor.

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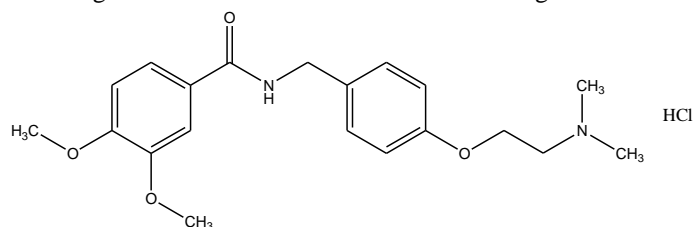
### 1. Introduction:

Functional dyspepsia is a common digestive illness marked by persistent discomfort and pain in the upper abdomen<sup>1,2</sup>. It is classified as a functional gastrointestinal illness, which means there is no obvious structural or metabolic defect to explain the symptoms; squashing early repletion (feeling full after a little meal), nausea, and upper abdominal discomfort are common symptoms. It is unclear what causes functional dyspepsia, however it could be a combination of variables such as irregular gastric motility, increased stomach sensitivity, or stress<sup>3,4,5</sup>. It is frequently identified after other illnesses have been ruled out, and therapy is usually centered on symptom management by dietary changes, drugs (such as antacids or prokinetics), and lifestyle adjustments<sup>6,7,8</sup>. Gastroesophageal reflux disease (GERD) is a chronic digestive ailment in which stomach bile irritates the esophageal lining this happens when the lower esophageal sphincter (LES), a muscle that ordinarily keeps acid from leaking backward into the esophagus, weakens or relaxes abnormally as a result, acid reflux develops, causing symptoms like heartburn, regurgitation, chest pain, difficulty swallowing, and a sour taste in the mouth<sup>9, 10,11</sup>. Obesity, pregnancy, smoking, alcohol usage, and certain medications are among the leading causes of GERD. Large meals, reclining down after eating, ingesting acidic, spicy foods can all induce and worsen it as well untreated GERD can eventually lead to consequences such as esophagitis, esophageal strictures, and an increased risk of esophageal cancer<sup>12,13,14</sup>.



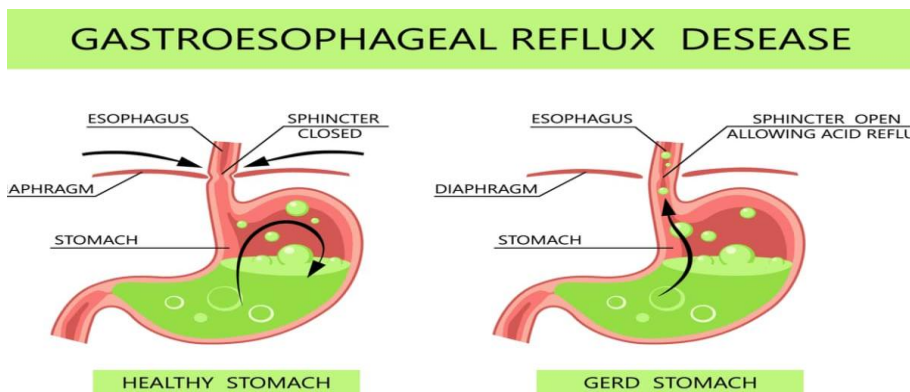
**Fig 1. Pathophysiology of Functional dyspepsia**

Itopride hydrochloride is a gastrointestinal prokinetic, motility activator medication that preferentially improves acetylcholine absorption while blocking dopamine D2 receptor antagonists and inhibiting acetylcholinesterase, making it useful in the treatment of GI disorders<sup>15</sup>. Increased acetylcholine levels enhance gastro-duodenal harmony by increasing GI peristalsis, expanding the minor esophageal sphincter pressure, stimulating gastric motility, and hastening gastric drainage<sup>16</sup>. Itopride hydrochloride (Ito.HCl) is a hydrochloride of N-p-[2(dimethylamino)ethoxy] benzylveratramide, a replaced benzamide with antiemetic and prokinetic properties<sup>17</sup>, its empirical formula is  $C_{20}H_{27}ClN_2O_4$  with molecular weight 394.9 and the structure is shown in Fig. 2.



**Fig 2. N-(4-(2-(dimethylamino)ethoxy)benzyl)-3,4-dimethoxybenzamide hydrochloride**

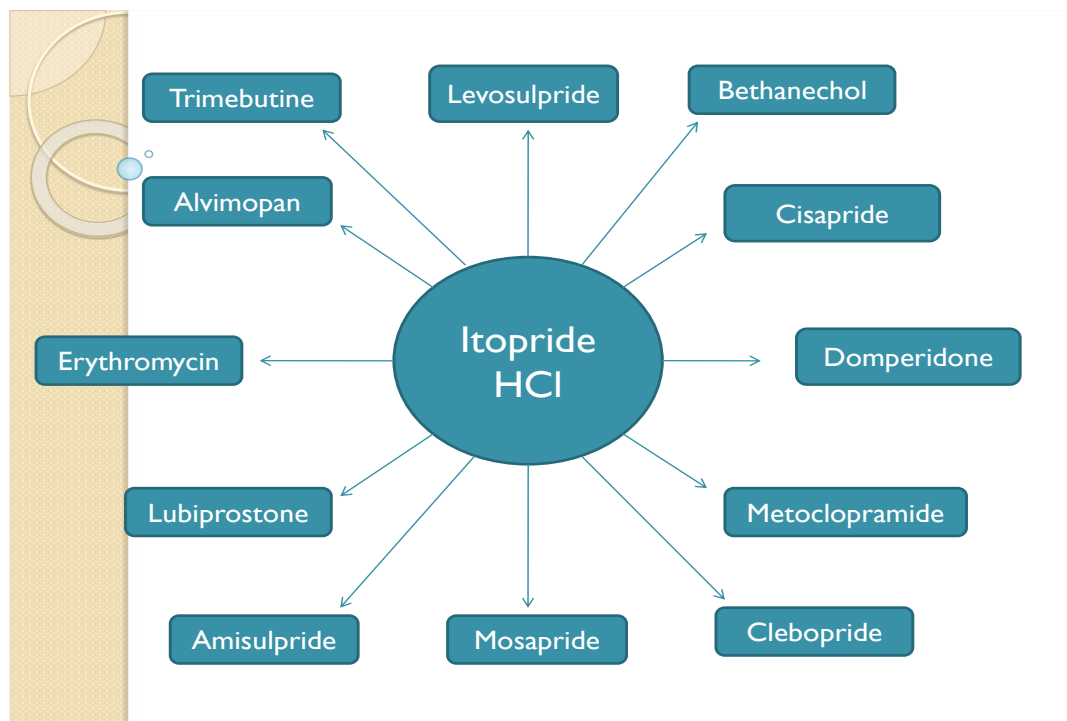
A recently developed prokinetic medication itopride is used to treat the symptoms of gastrointestinal disorders like persistent indigestion, gastroesophageal reflux disease, and non-ulcer dyspepsia it's have a special dual type mode of action utilized by itopride hydrochloride, effect by reducing the activity of acetylcholinesterase (AChE) and blocking the dopamine-2 (D2) receptor by inhibiting the release of acetylcholine and gastrointestinal stimulant with a distinct mode of action than other medications, offering a novel option for treating the abnormalities of gastrointestinal motility<sup>18,19</sup>.



**Fig 3. Symptoms of GERD**

Various research methods, are employed by the scientist such as spectrophotometry, TLC, liquid chromatography with ultraviolet detection, fluorescence detection, electrochemical method, tandem-mass spectrometry, chemiluminescence detection, and ion selective electrode, have been documented for itopride in its therapeutic

fluids, such as human plasma by improving stomach motility, accelerating gastric emptying, and decreasing gastric reflux, pro-kinetic medications help to alleviate symptoms. There are various medication are available in recent such as domperidone, cisapride, and metoclopramide are common effective GERD therapies, but they are showing resistance so there is a need for new medication for effectiveness<sup>20,21</sup>.



**Fig 3. Drugs homogeneous to Itopride hydrochloride**

## 2. Pharmacological activity of Itopride hydrochloride:

**a. Prokinetic Action:** Prokinetic action refers to the ability of certain medications to enhance the motility of the gastrointestinal (GI) tract, thereby improving the movement of food and waste through the digestive system, prokinetic agents work by stimulating the muscles of the GI tract, enhancing the coordinated contractions<sup>22,23</sup>. Itopride increases the motility of the gastrointestinal system this leads to faster gastric emptying, improved peristalsis, and alleviation of symptoms such as bloating, nausea, and discomfort commonly associated with gastrointestinal disorders<sup>24,21</sup>.

**b. Anti-emetic Effect:** The anti-emetic effect refers to the ability of certain substances to alleviate nausea and vomiting this effect is particularly beneficial in medical scenarios such as chemotherapy, where nausea is a common side effect, or in the treatment of motion sickness. Anti-emetic drugs work by blocking specific receptors in the brain, such as serotonin or dopamine receptors, which are involved in the vomiting reflex<sup>25,26</sup>. Itopride may also have an anti-emetic (anti-nausea) effect, due to its action on the central nervous system (CNS) via D2 receptor antagonism these effects makes it useful in the treatment of nausea and vomiting related to gastrointestinal dysmotility<sup>27,28</sup>.

**c. Improved Gastric Emptying:** Improved gastric emptying refers to the enhanced rate at which the stomach contents are passed into the small intestine this is a physiological process crucial for efficient digestion and absorption of nutrients there are many factors contributing to improved gastric emptying include dietary modifications, physical activity, and the management of underlying conditions like diabetes or gastroparesis<sup>29,30</sup>. Itopride can enhance gastric emptying, because it is prokinetics which useful for patients who experience delayed gastric emptying (gastroparesis), a common feature in conditions like functional dyspepsia and other digestive issues<sup>31</sup>.

## 3. Pharmacokinetics properties of Itopride:

**a. Absorption:** Itopride absorption in the body is a vital phase in pharmacokinetics, as the medication moves from the site of delivery into the bloodstream. This process can occur through many methods,

including as passive diffusion, assisted diffusion, active transport, and endocytosis. Depending on the chemical qualities of the drug and the physiology of the absorption site, factors such as the drug's solubility, pH, and the presence of food in the gastrointestinal tract can all have a substantial impact on absorption rates. Oral drugs must pass via the stomach and intestines, where they may undergo first-pass metabolism in the liver before entering the bloodstream<sup>32</sup>.

**b. Distribution:** Itopride is transported from the bloodstream to numerous tissues and organs, and its distribution is affected by a number of factors, including blood flow to tissues, capillary membrane permeability, the drug's lipophilicity, and binding affinity to plasma proteins. Drugs are often delivered faster to organs with high blood flow, such as the liver and kidneys, than to tissues with low perfusion rates, such as muscles and fat. Itopride is broadly distributed in bodily tissues, but it does not pass through the blood-brain barrier<sup>18</sup>.

**c. Metabolism:** Itopride metabolism in the body takes place predominantly in the liver, where cytochrome P450 play an important role in turning medicines into metabolites. This process is divided into two stages: Phase I and Phase II reactions<sup>33</sup>.

**d. Excretion:** The excretion of Itopride metabolites are eliminated from the body, primarily through the kidneys via urine the renal excretion involves filtration, reabsorption, and secretion within the nephrons, other pathways include biliary excretion through feces, and minor routes such as sweat and saliva<sup>34</sup>.

#### **4. Clinical uses of Itopride hydrochloride:**

**a. Functional Dyspepsia:** Functional dyspepsia (FD) is a common gastrointestinal disorder characterized by persistent or recurring upper abdominal discomfort and pain such as an ulcer.

**b. Gastroesophageal Reflux Disease (GERD):** Itopride can help improve gastric motility and prevent reflux in some patients.

**c. Gastroparesis:** A condition where the stomach takes too long to empty its contents<sup>35,36</sup>.

#### **5. Side Effects and Safety Profile of Itopride HCl:**

**a.** Gastrointestinal issues such as diarrhea, abdominal cramps, bloating, or constipation.

**b. Headache** or dizziness, likely due to its central nervous system effects.

**c. Fatigue** or drowsiness, especially if the medication is taken at higher doses.

**d. Extrapyramidal Symptoms (EPS):** Though rare, there is a risk of movement disorders, such as tremors, rigidity, or tardive dyskinesia, because of its dopamine receptor antagonism. However, these side effects are less common than with other dopamine antagonists<sup>37</sup>.

**e. CYP450 Interactions:** Itopride can interact with other medications that are metabolized by the liver enzymes (CYP450), especially those that induce or inhibit these enzymes. Caution should be taken when combining Itopride with other drugs, such as warfarin or certain anticonvulsants, as they may alter the pharmacokinetics of Itopride<sup>38,39</sup>.

#### **6. Caution to be taken:**

**a. Severe Liver or Kidney Impairment:** Since Itopride is metabolized in the liver and excreted via the kidneys, patients with severe hepatic or renal impairment should use this drug with caution, as there may be an increased risk of toxicity.

**b. Pregnancy and Breastfeeding:** Although Itopride has not been shown to be teratogenic in animal studies, it should be used in pregnancy only if the potential benefits justify the potential risks. Caution should be taken when prescribing Itopride during breastfeeding, as it is not known whether the drug is excreted in breast feeding<sup>40,41</sup>.

#### **7. Conclusion:**

Itopride hydrochloride prokinetic and anti-emetic qualities make it an effective treatment for a variety of gastrointestinal motility problems its potential to improve stomach motility while also reducing nausea makes it a useful treatment option for people with functional dyspepsia, gastroparesis, and GERD. While the drug is generally well tolerated, as with all medications, it should be used with caution, especially in patients with pre-existing illnesses or those taking other medications that may interact with itopride.

#### **Credit authorship contribution statement:**

**Aslam warsi:** Conceptualization, Methodology, Investigation, Data curation, Writing- Original draft, Supervision; **Ashvani Kumar:** Writing-reviewing and editing.

**Declaration of competing interest:**

The authors assert that no competing interest exist.

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