

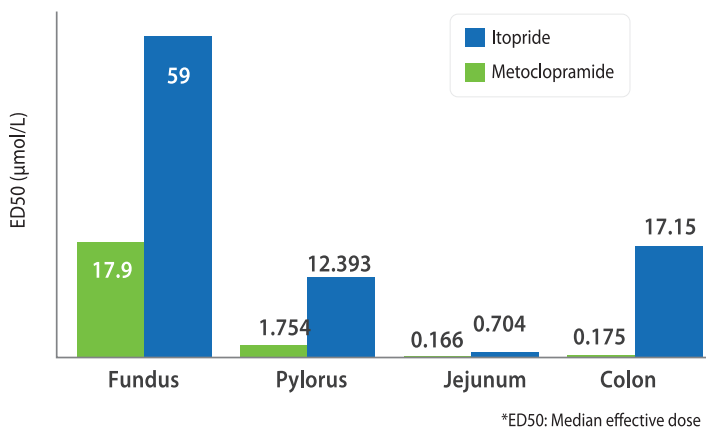
The prokinetic effect of itopride, a comparative study with metoclopramide

- Functional dyspepsia is a common GI disorder characterized by chronic/recurrent upper abdominal discomfort such as pain, fullness, bloating, belching, nausea, and heartburn, often linked with impaired gastric motility and delayed gastric emptying.
- Many available prokinetics have limitations in long-term use, including safety concerns (especially CNS-related adverse effects with D2 blockers that cross the blood–brain barrier) and restricted action mainly in the upper GIT, creating need for a safer and more effective prokinetic that supports both upper and lower GI motility.
- The aim of this study was to investigate the prokinetic effect of both itopride and metoclopramide on the different parts of GIT isolated from experimental animals in a trial to identify if there is any difference between their effects.

Study design: In-vitro comparative dose-response study

| Isolated tissues | Center | Intervention | Comparator | Key outcome |
|---|---------------------------|------------------------|----------------|--|
| Rat fundus + Rabbit pylorus/jejunum/colon tissues | Zagazig University, Egypt | Itopride hydrochloride | Metoclopramide | Itopride produced stronger prokinetic activity and increased motility in GIT vs metoclopramide |

ED50 comparison by GIT segment



Conclusion

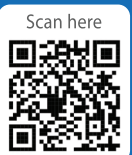
- Itopride showed higher potency than metoclopramide, demonstrated by consistently lower ED50 values.
- Itopride and metoclopramide both enhanced GIT motility, producing significant, concentration-dependent increases in contraction amplitude across tested GI segments.
- Compared to metoclopramide, itopride is safer because it does not cross the blood–brain barrier, so it has a lower risk of CNS/extrapyramidal side effects.
- Overall, itopride is the preferred prokinetic option due to its stronger effect on both upper and lower GIT motility, supporting its role in functional motility disorders.

Ref: Kamel EM, Shabayek HA, Aly FA, Elgarhi RI. The Prokinetic Effect of Itopride, A Comparative Study with Metoclopramide. Az. J. Pharm Sci. 2015; 51 (March): 18–30.

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Drug Review

Gastric motility disorder^{1,2,3,4}

- Gastrointestinal (GI) motility disorders encompass a wide array of signs and symptoms and functional dyspepsia (FD) and gastroparesis are the main associated syndromes.
- FD diagnosed based on the Rome IV criteria- The presence of one or more of the following symptoms: epigastric pain or burning, early satiety, and postprandial fullness in the absence of structural disease.
- Prokinetic agents are the mainstay therapy for FD and gastroparesis, to improve gastric emptying and relieve symptoms.
- Conventional prokinetics (e.g. domperidone, metoclopramide) only block dopamine D2 receptors (DD2R) but have no effect on acetylcholinesterase. Thereby, complete relief of functional dyspepsia symptoms can not be achieved.

Itopride (Itonorm) - next generation dual acting gastrointestinal prokinetic

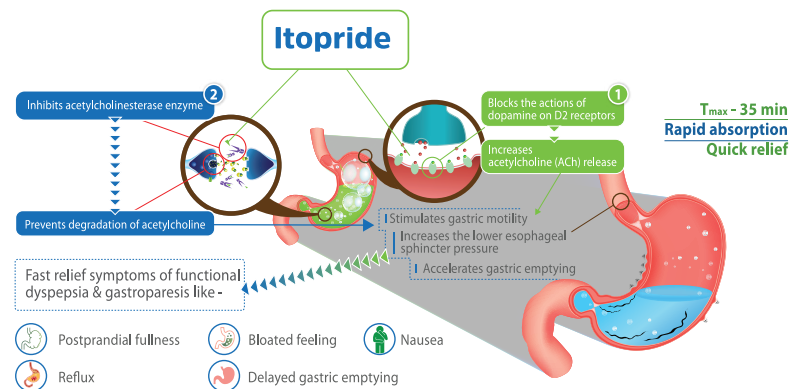


Figure: Mechanism of action of Itopride

Proven Safety and results^{6,7,8,9,10}

- Itopride does not cross the BBB hence exerts no CNS effects (e.g. headache, nausea, dyskinesia). It does not cause hyperprolactinemia and has no impact on QT interval, as a result doesn't affect heart rate.
- The drug is metabolized by flavin-containing monooxygenase 3 (FMO3) pathway hence no drug-drug interactions with CYP450 inhibitors.
- Itopride is a relatively safer molecule compared with other prokinetics, with no extrapyramidal symptoms or cardiotoxicity concerns, can be used for long-term in GI motility disorders either alone or in combination with other drugs.
- Itopride has good efficacy in terms of global patients' assessment, postprandial fullness, and early satiety in the treatment of patients with FD and shows a low rate of adverse reactions.
- Significant improvement in glycaemic indices was also evident posttreatment with itopride. Itopride showed effectiveness in addressing symptoms of reduced GI motility in patients with diabetes, with improved quality of life.
- Itopride 100 mg t.i.d is effective in decreasing pathologic reflux in patients with GERD and therefore it has the potential to be effective in the treatment of this disease.

Ref.: 1. Brian E. Lacy, Kirsten Weiser; Gastrointestinal Motility Disorders: An Update. Dig Dis 1 July 2006; 24 (3-4): 228-242.; 2. the treatment of dysmotility. EMJ Gastroenterol. 2014;3:42-7.; 3. Oshima T. Functional Dyspepsia: Current Understanding and Future Perspective. Digestion. 2024;105(1):26-33. ; 4. Camilleri M, Atieh J. New Developments in Prokinetic Therapy for Gastric Motility Disorders. Front Pharmacol. 2021 Aug 24;12:711500. ; 5-Dite, Petr & Rydlo, Martin & Dockal, Milan & Martinek, Arnost. (2014); 6-7. Huang X, Lv B, Zhang S, Fan YH, Meng LN. Itopride therapy for functional dyspepsia: a meta-analysis. World J Gastroenterol. 2012 Dec 28;18(48):7371-7. ; 8-a new prokinetic, in patients with mild GERD: a pilot study. World J Gastroenterol. 2005 Jul 21;11(27):4210-4. ; 9. Rai RR, Choubal CC, Agarwal M, Khaliq AM, Farishta FJ, Harwani YP, Kumar SY. A Prospective Multicentric Postmarketing Observational Study to Characterize the Patient Population with Reduced Gastrointestinal Motility among Indian Diabetic Patients Receiving Itopride: The Progress Study. Int J Appl Basic Med Res. 2019 Jul-Sep;9(3):148-153. ; 10. Chaudhuri, S. (2023). Role and safety of prokinetic drugs in the treatment of upper gastrointestinal motility disorders: an Indian perspective. International Journal of Research in Medical Sciences, 11(10), 3937-3944.



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