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REVIEW ARTICLE
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"PHARMACEUTICAL QUALITY ASSURANCE THROUGH ANALYTICAL TECHNIQUES: A REVIEW ON NIZATIDINE IDENTIFICATION"

Nishita M Mehta [1], Dr. Neha Tiwari[2*], Dr. Pragnesh Patani[3]

[1]Department of Pharmaceutical Quality Assurance, Khyati College of Pharmacy, Ahmedabad, Gujarat, India.
[2*]Department of Pharmaceutical Chemistry, Khyati College of Pharmacy,Ahmedabad, Gujarat, India.
[3]Department of Pharmacology, Khyati College of Pharmacy, Ahmedabad, Gujarat, India.

***Corresponding Author:** Dr. Neha Tiwari
*Email ID: tiwarin1707@gmail.com Khyati College of Pharmacy, Palodia, Ahmedabad, Gujarat.

ABSTARCT:
Ensuring the quality, safety, and efficacy of pharmaceutical products is essential to public health. This review focuses on the analytical techniques employed in the identification and quality assessment of Nizatidine, a histamine H2-receptor antagonist used in the treatment of gastric ulcers and gastroesophageal reflux disease (GERD). Given its structural similarity to other drugs in its class, such as ranitidine, precise and selective analytical methods are critical for accurate identification and impurity profiling. High-Performance Liquid Chromatography (HPLC) remains the most widely used technique due to its sensitivity and reliability, while advanced methods like Ultra-Performance Liquid Chromatography (UPLC) and Liquid Chromatography–Mass Spectrometry (LC-MS/MS) offer enhanced detection capabilities and reduced analysis time. Stability studies conducted under various stress conditions (heat, light, and moisture) further support shelf-life determination. All methods discussed adhere to international regulatory guidelines (USP, ICH, WHO), ensuring consistency and patient safety. Additionally, the integration of green analytical chemistry principles is emphasized to minimize environmental impact. This review underscores the pivotal role of analytical testing in pharmaceutical quality assurance, with Nizatidine serving as a representative model.

KEYWORDS: Nizatidine, Analytical Techniques, HPLC, Drug Stability, Histamine H2-Receptor Antagonist

1. INTRODUCTION

Nizatidine is a medication that belongs to a class of drugs known as **H2-receptor antagonists** (or H2 blockers). It is primarily used to **reduce the amount of acid produced by the stomach**, helping to treat and prevent certain gastrointestinal conditions.

Nizatidine is a medication that belongs to the class of H2-receptor antagonists, which work by blocking histamine receptors in the stomach to reduce acid production. It was developed as an improved version of earlier drugs like ranitidine, offering better absorption and fewer interactions with other medications. Nizatidine was introduced in the early 1990s for medical use.

It is commonly prescribed to treat conditions such as duodenal ulcers, gastric ulcers, GERD (gastroesophageal reflux disease), Zollinger-Ellison syndrome, and to prevent acid-related stomach

problems. The drug is available in oral forms and is usually taken multiple times per day based on the patient's condition.

After ingestion, Nizatidine is efficiently absorbed, reaching peak levels in the bloodstream within 1 to 2 hours, and has a half-life of around 1.5 to 2 hours. It is primarily eliminated through the kidneys. Some possible side effects include headache, diarrhea, dizziness, and nausea, with rare liver-related issues.

Compared to other H2 blockers, Nizatidine offers advantages like improved bioavailability and fewer drug interactions, making it an effective option for acid-related disorders. It's been approved by health authorities such as the FDA for clinical use.

2.NIZATIDINE THERAPEUTIC USES AND BENEFITS

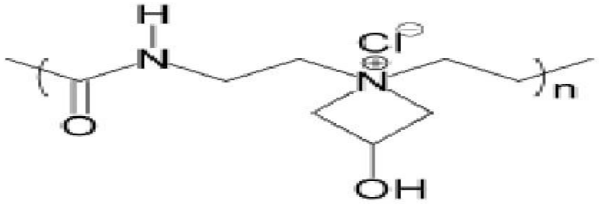
Nizatidine is an H2 receptor antagonist that plays a significant role in the management of various acid-related gastrointestinal conditions. It is commonly used in the treatment of **duodenal ulcers**, which are sores in the lining of the duodenum caused by excess stomach acid, *Helicobacter pylori* infection, or prolonged use of NSAIDs. By reducing acid secretion, Nizatidine allows these ulcers to heal and prevents further irritation. Similarly, in **gastric ulcers**, which occur due to an imbalance between stomach acid and the protective mucus layer often associated with stress, smoking, alcohol, or certain medications, Nizatidine lowers acid levels, thereby reducing pain and supporting mucosal repair.

In **gastroesophageal reflux disease (GERD)**, where weakened lower esophageal sphincter muscles allow stomach acid to flow back into the esophagus, Nizatidine helps by suppressing acid production, relieving symptoms such as heartburn, chest pain, and irritation, while also preventing long-term esophageal damage. It is also beneficial in **Zollinger–Ellison syndrome**, a rare disorder characterized by gastrin-producing tumors that stimulate excessive acid secretion. In such cases, Nizatidine helps control acid levels, reducing ulcer formation and alleviating severe gastrointestinal symptoms. Additionally, Nizatidine is effective against **stress ulcers**, which develop under conditions of severe physical stress such as surgery, trauma, or critical illness, by decreasing acid secretion and promoting mucosal protection.

The **mechanism of action** of Nizatidine involves the selective blockade of H2 histamine receptors in the stomach, thereby preventing histamine-induced gastric acid secretion. This reduction in gastric acidity not only relieves symptoms but also facilitates healing of ulcers and mucosal damage. **Additional benefits** of Nizatidine include faster relief from acid-related discomfort, effective support in the healing of ulcers, and a favorable safety profile with fewer side effects compared to older H2 receptor blockers.

3.DRUG PROFILE:

Table 1 Drug Profile :

IUPAC Name	(E)-1-N'-[2-[[2-[(dimethylamino)methyl]-1,3-thiazol-4-yl]methylsulfanyl]ethyl]-1-N-methyl-2-nitroethene-1,1-diamine
Molecular Formula	$C_{12}H_{21}N_5O_2S_2$.
Chemical Structure	
Molecular Mass	331.46 g/mol.
Description	It is used to treat or prevent occasional heartburn, acid indigestion, or sour stomach. It decreases the amount of acid made in the stomach

Solubility	1 mg/ml
pH and pKa Value	1% solution of nizatidine in water is 9 pKa is −0.82, 1.95, and 6.67
Melting Point	132-136°C
CAS number	76963-41-2
Mechanism of Action	Nizatidine works by selectively blocking H2 histamine receptors in the stomach, which prevents histamine from stimulating acid production. This leads to a significant reduction in gastric acid secretion, relieving symptoms and promoting healing.

4.LITERATURE SURVEY:

Several analytical methods have been developed over time for the identification, quantification, impurity profiling, and stability testing of Nizatidine, using UV/spectrophotometric, HPLC, UPLC, HPTLC, etc. Below is a summary of selected studies, their features, and how they meet typical acceptance criteria (e.g. linearity, precision, specificity, LOD/LOQ, forced degradation for stability-indicating methods, etc).

3.1 Reported Methods of Nizatidine (Alone):

Table 2 Reported Methods of Nizatidine

No.	Journal & Year	Analytical Method	Chromatographic Conditions
1	Bulletin of Faculty of Pharmacy, Cairo University, 2011	HPLC-DAD (Stability-Indicating)	• Detection: **320 nm**• Mobile Phase: 0.05 M phosphoric acid: acetonitrile (50:50, v/v) • pH: Not stated (acidic buffer)
2	Journal of Analytical Chemistry, 2013	UV & 2nd Derivative Spectrophotometry	• Detection: **325 nm** (UV), **328/356.5 nm** (2nd derivative) • Mobile Phase: Not applicable (spectrophotometric method) • pH: –
3	J Chromatogr B (Elsevier), 2015	LC-MS/MS (Bioanalytical)	• Detection: MS/MS (MRM), no UV• Mobile Phase: Methanol: Water (95:5) with 5 mM ammonium formate• pH: Not stated (buffer near neutral)
4	Journal of Analytical Chemistry, ~2007	HPLC-UV (Plasma Assay)	• Detection: **320 nm**• Mobile Phase: Disodium hydrogen phosphate: acetonitrile: methanol: triethylamine (80:10:10:0.05 v/v/v/v) • pH: Not stated (phosphate buffer; likely ~7)
5	Journal of Food and Drug Analysis, 2019	HILIC (Nitrosation Product Study)	• Detection: **325 nm**• Mobile Phase: Acetonitrile: 0.04 M acetate buffer (92:8, v/v)• pH: **6.0**

3.2 Reported Methods of Nizatidine with combination of other drugs:

Table 3 : Reported Methods of Nizatidine with combination of other drug

No.	Journal & Year	Analytical Method (Combination)	Key Result / Validation Criteria
1	Journal of Analytical Chemistry, 2013 (SpringerLink)	UV & 2nd-Derivative Spectrophotometry for **Nizatidine + Ranitidine** (SpringerLink)	• UV method: Nizatidine at 325 nm, Ranitidine at 325.5 nm; LOD ≈ 0.07 µg/mL for Nizatidine, 0.04 µg/mL for Ranitidine • 2nd derivative method: peak-to-peak amplitudes (328/356.5 nm for Nizatidine, 326/357 nm for Ranitidine); LOD ≈ 0.02 µg/mL (Nizatidine), 0.016 µg/mL (Ranitidine) • Applied to pure drug and formulations • Good accuracy & precision; no significant difference vs reference method via t- and F-tests (SpringerLink)
2	J AOAC International, 2002 (PubMed)	Spectrophotometric charge-transfer complexation with **Nizatidine + Ranitidine**	• Detection wavelengths: 515 nm (with rho-CA), 467 nm (with DDQ) • Concentration ranges: for Nizatidine ~20–200 µg/mL (with rho-CA) & 20–160 µg/mL (with DDQ); for Ranitidine ~20–240

		(using reagents p-chloranilic acid & DDQ) (PubMed)	& 20-140 µg/mL respectively • Recovery via standard addition; excipients show negligible interference • Statistical tests (t- and F-tests) show accuracy & precision acceptable at 95% confidence level (PubMed)
3	Oxford University Press – Journal "Analytical & Are Comparative Studies", 2017 (PubMed)	HPTLC stability-indicating method for **Nizatidine + Ranitidine + Famotidine** (PubMed)	• Densitometric detection: 320 nm for Nizatidine & Ranitidine; 280 nm for Famotidine • LOD: ~5.47–9.37 ng/band; LOQ: ~16.30–31.26 ng/band for all three drugs • Separation of drug peaks from their degradation products under stress (acidic, basic, oxidative, thermal) per ICH guidelines • Validation: linearity, precision, accuracy, robustness etc. • Degradation kinetics studied; half-lives & rate constants determined for comparison among the three drugs (PubMed)

3.3 Official Reported method for the Nizatidine :

Table 4: Official Reported method for the Nizatidine

Monograph / Product	Identification Test(s) / Method(s)	Key Conditions / Requirements	Acceptance / Result Criteria
USP-Nizatidine (Raw / Bulk, dried basis)	**Identification A**: Infrared (IR) Absorption Spectrum	Compare IR absorption of sample vs USP Nizatidine RS; dried basis.	The IR spectrum of sample exhibits maxima only at the same wavelengths as USP reference standard.
	Identification B: Retention time in liquid chromatography	Use Chromatographic system described under "Assay" method: Column 4.6 mm × 15-cm, 5-µm packing (L1), detector at 254 nm; mobile phase: buffer solution + methanol (76:24) (Buffer = 0.1 M ammonium acetate + diethylamine, adjusted to pH ~7.5). Flow rate ≈ 1.0 mL/min. Injection volume ~50 µL; test solution concentration etc. (	The retention time of the major peak in Assay preparation corresponds to that of the standard preparation. Tailing ≤ 2.0; column efficiency ≥ 1500 theoretical plates.
USP-Nizatidine Capsules	**Identification A**: IR (on residue after methanol extraction of capsule contents)**	Extract capsule contents with methanol, evaporate, prepare KBr pellet, record IR spectrum and compare with that of USP Nizatidine RS prepared similarly.	The IR absorption spectrum exhibits maxima only at the same wavelengths as that of the standard.
	Identification B: Chromatographic / Retention Time relative to internal standard in assay**	In Assay, chromatograph sample and standard under specified chromatographic conditions (column L1, 5-µm, 4.6×15 cm; detector 230 nm). Use internal standard (phenol), and match the retention time of the major (nizatidine) peak relative to the internal standard. Resolution between nizatidine and internal standard (phenol) not less than 3; tailing factor ≤1.6; %RSD for replicate injections ≤1.5%. (DrugFuture)	The retention time of the major peak in the Assay preparation should match that of the standard preparation (relative to internal standard). System suitability: R ≥ 3 vs phenol; tailing ≤1.6; RSD ≤1.5%.

CONCLUSION:

This review highlights the critical role of precise and validated analytical methods in ensuring the quality and identification of Nizatidine. Techniques such as HPLC, infrared spectroscopy, and LC-MS/MS are essential for verifying the drug's purity, stability, and identity, both when used alone and in combination with other medications. Conducting stability tests under various stress conditions is

vital to guarantee the safety of the product. Following official pharmacopeial guidelines and incorporating environmentally friendly analytical practices further strengthen the quality control process. Collectively, these strategies help ensure that Nizatidine meets regulatory standards and provides safe and effective treatment to patients.

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