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VALIDATION OF ANALYTICAL METHODS FOR ESTIMATION OF ESOMEPRAZOLE IN PHARMACEUTICAL DOSAGE FORMS - A REVIEW

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ABSTRACT

Esomeprazole is used to treat condition where there is too much acid in the stomach. It is used to treat duodenal and gastric ulcers, erosive esophagitis, Gastro Esophageal Reflux Disease (GERD), and Zollinger-Ellison syndrome, a condition wherein the stomach produces too much acid. In the pharmaceutical industry, analytical method development gives important information of drugs potency, bioavailability and its stability. Analytical methods have been report for various studies in analysis of product. So far, around Thirty Seven analytical methods have been reported for various studies on analysis of esomeprazole in bulk, pharmaceutical formulations and biological fluids, tablets, and capsule. This review highlights different analytical methods such as chromatography, spectroscopy, and hyphenated techniques of esomeprazole. These techniques are either explored for the quantification, detection of metabolite and also for stability-studies of the esomeprazole. The present studies revealed that HPLC techniques along with spectroscopic have been most widely explored for the analysis. The brief review may provide information to the researchers who are working in the area of analytical research of esomeprazole.

KEYWORDS: Esomeprazole, Analytical methods, HPLC, HPTLC, LCMS, GCMS, UPLC, TLC, UV-Spectroscopy, Infra-red spectroscopy, NMR Spectroscopy.

INTRODUCTION

The aim of our review article is to compile all the available information on the analytical determination of Esomeprazole in different pharmaceutical dosage forms. The purpose of analytical development is to establish the identity, purity, physical characteristics, and potency of drugs, including the drug's bioavailability and stability. Analytical development helps to understand the process of showing that analytical procedures are adequate for the purpose of assessing drugs, and particularly the active pharmaceutical ingredient (API).

Steps for analytical development

1. Purpose of Analytical Method Development In the pharmaceutical industry, analytical method development gives important information on the potency of a drug, the drugs' bioavailability, the drugs stability and also its effects. In the very first step, the purpose of conducting any Analytical Method Development is established.
2. Highlighting of Steps In the second step of Analytical Method Development, the steps involved in the development are recorded in a laboratory book.
3. Characterization of the Analyte In this step, both the biological and chemical properties in addition to the physical properties of the analyte are collected. After that, the analyte is obtained and stored according to its specific requirements. The methods for analysis are then recorded with an example being the chromatography technique which employs different methods such as the High-Performance Liquid Chromatography.
4. Definition of Requirements for the method development of the analysis are done and recorded. All the materials, reagents and instruments are procured those are required for the analysis of the sample.
5. Review of Literature and Previous Methods All literature information related to the specific analyte e.g., a specific drug is assessed for any biological, chemical and chemical properties regarding the analyte. Reference is then made from journals, books and any other publications.
6. Choosing an Analytical Method From the information obtained from the literature during the literature review, a specific methodology is modified to cater for accurate output and also because methods change with the requirements of the analyte. If there are no previous methods in the literature being reviewed regarding the analyte, the procedure goes on uninterrupted.
7. Setting up of Instruments Appropriate instruments for the analytical method development are set up in the laboratory by each of the instruments standard operating procedures.

Standard Operating Procedures usually abbreviated as SOP's are a set of instructions or steps to aid in performing a specific procedure in a laboratory set up. They are usual\ly universal and standardized for ease of use in any laboratory set up.

8. Optimization of the Method in carrying out the optimization of the analytical method, parameters are changed individually depending on the arising interests. Optimization of an analytical method is done in reference to a systematic and procedural plan while making sure to critically follow all the documented steps.
9. Analytical Figures of Merit Documentation, Documentation of the analytical figures of merit decided upon is done. These analytical figures of merit include quantification limits, detection limits, analysis time frame, operational costs and sample preparation.
10. Development Method Evaluation the resultant product of analysis should give a desirable result as expected in the identification of the analyte.
11. Sample Estimation, Quantitative Demonstration and Analysis of Samples Estimation of an analyte with an example being a drug in a matrix sample containing the analyte is done here.

Analytical technique

Analytical technique is a method that is used to determine a chemical or physical property of a chemical substance, chemical element, or mixture. There are a wide variety of techniques used for analysis, from simple weighing to advanced techniques using highly specialized instrumentation.

A. Spectroscopy

- Visible Spectroscopy
- Ultraviolet Spectroscopy
- Fluorimetry
- Nephelometry
- Turbidimetry
- Atomic Absorption Spectroscopy
- Infra-Red Spectroscopy
- NMR Spectroscopy
- ESR Spectroscopy
- Mass Spectroscopy

B. Chromatography

- Column Chromatography
- Ion-Exchange Chromatography
- Gel-Permeation (Molecular Sieve) Chromatography
- Affinity Chromatography
- Paper Chromatography
- Thin-Layer Chromatography
- Gas Chromatography
- Dye-Ligand Chromatography
- Hydrophobic Interaction Chromatography
- Pseudo-affinity Chromatography
- High-Pressure Liquid Chromatography (HPLC)

C. Electrochemical methods of analysis

- Potentiometric Electrodes
- Colorimetric Methods
- Voltammetry
- Polarography
- Stripping Voltammetry
- Hydrodynamic Voltammetry
- Amperometry

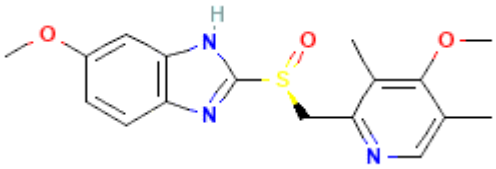
D. Electrophoretic methods

- Capillary Electrophoresis (CE)
- Slab Electrophoresis
- Gel Electrophoresis
- Paper Electrophoresis
- Immuno-electrophoresis
- Zone Electrophoresis
- Iso-electric focusing.

Esomeprazole is proton pump inhibitor (PPI) and potent inhibitor of gastric acidity which are widely used in the therapy of gastroesophageal reflux and peptic ulcer disease. Esomeprazole therapy is associated with a low rate of pransist and asymptomatic serum aminotransferase elevations and rate causes of clinically apparent liver injury. Esomeprazole is the S – isomer

of omeprazole, with gastric proton pump inhibitor activity. In the acidic compartment of parietal cell, esomeprazole is protonated and converted in to the active achivalsulfenamide; the active sulfenamide forms one or more covalent disulfenamide bonds with the proton pump hydrogen – potassium adenosetriphosphatase (H^+/K^+ATPase), thereby inhibiting its activity and the parietal cell secretion of H^+ into the gastric lumen, the final step in gastric acid production. H^+/K^+ATPase is an integral membrane protein of the gastric parietal cell.

Esomeprazole is a 5 – Methoxy -2-{[(4 – methoxy – 3,5 – dimethyl pyridine -2-yl)methyl]sulfinyl} -1H benzimidazole that has S configuration at the sulphur atom. An inhibitor of gastric acid secretion, it is used (generally as its sodium or megnisium salt ex: esomeprazole megnisium or esomeprazole sodium) for the treatment of gastro – oesophageal reflux disease, and Zollinger – Ellison syndrome. The esomeprazole molecular formula is $C_{17}H_{19}N_3O_3S$ and its molecular weight is 345.4g. The melting point of Esomeprazole is 155^oC. It was very slightly soluble in water. General method reported that are used in the analysis of esomeprazole analysis are HPLC, HPTLC, UPLC, TLC, UV Spectroscopy, Infra-red Spectroscopy, NMR Spectroscopy, LC-MS, which are summarized.



Structure of esomeprazole

Analytical determination

1. High Performance Liquid Chromatography (HPLC)

HPLC is the advanced analytical technique in the pharmaceutical analysis, which is predominantly used in pharmaceutical industries[7-8] for the large variety of samples. It is the method of choice for determining the purity of new drug candidates, monitoring changes or scale-ups of synthetic procedures, evaluating new formulations, and scrutinizing quality control of final drug products.

S. no.	Stationery phase	Mobile phase	Flow Rate and Method of detection	Results	References
1	BDS HypersilC_{18} column, 250mm X 4.6mm, 5µm particle size.	Methanol and 50 mM phosphate buffer 35:65(v/v)	1.0ml/min At 213nm	R_t-8.33min Accuracy-99.90% LOD-15 ng/mL LOQ-25 ng/mL	Farah Kahn et al.[13]
2	Xterra RP18 column, 150mm X 4.6mm, 5µ particle size.	0.005 mole of sodium perchlorate, 5mL N-butyl amine in milli-Q grade water a pH of 8.7 which is mixed with Acetonitrile and Methanol.	1.5 mL/min, UV at 305nm.	R_t-6 min Accuracy-100.2% Linearity-0.9999	PalavaiSripal Reddy et al.[14]
3	SUPELCO C_{18} – DB column, 250mm X 4.6mm, 5µm particle size.	0.01M phosphate buffer pH7.5: ACN: methanol 40:50:10 v/v, addition of 0.1% triethyl amine	0.8 ml/min, UV at 303nm.	R_t-4.6 min, Linearity-0.9999 LOD-0.016µg/ml LOQ-0.048µg/ml	ChandrakantSojitra et al.[15]
4	C_{18}	Methanol and Acetonitrile 40:60	1ml/min, UV at 260nm.	R_t-3.425min, Linearity-0.9999 LOD-0.0386µg/ml LOQ-0.0216µg/ml	HarithaGali et al.[16]
5	SUPELCO 516 C_{18} DB column, 250mm X 4.6mm, 5µ particle size	Phosphate buffer (20mM pH-7.4 adjusted with sodium hydroxide): Acetonitrile: methanol20:20:60 (%v/v).	1ml/min UV at 275nm	R_t-3.09 min, Linearity-0.9993 LOD-0.0733µg/ml LOQ-0.2227µg/ml	DarshanGohil et al.[17]

6	C_{18} analytical column, 250mm X 4.6mm, 5µm particle size.	Acetonitrile and Phosphate buffer (pH-7.4±0.05 adjusted with 5% potassium hydroxide) 50:50 (v/v).	1.0 mL/min UV at 302nm.	R_t-6.5 min, Accuracy-100.56% Linearity-0.9991 LOD-0.0015µg/mL LOQ-0.04µg/mL	Muhammad Tariq Khalil et al.[18]
7	Thermo RP8 Column, 4.6 x 150mm, 3.5 µm particle size	Acetonitrile and Phosphate buffer 35:65 (v/v).	1.0 ml/min At 283nm.	R_t-4.288min, Linearity-0.999 LOD-0.12µg/ml LOQ-0.08µg/ml	T. Santhosh Kumar et al.[19]
8	C_8 column, 250mm X 4.6mm, 5 µm particle size.	Acetonitrile and Phosphate buffer (pH-7.6) 35:65 (v/v).	1.0 ml/min UV at 280nm.	R_t-7.4min, Accuracy-99.15%	Sharifa Sultana et al.[20]
9	Phenomenex ODS 2 C_{18} column, 150 X 4.6 mm, 5µm particle size.	Methanol and 0.1% Ortho phosphoric acid 40:60 %v/v.	0.8 mL/min UV at 285nm.	R_t-7.20 min, Linearity-0.9966 LOD-50.57 ng/mL.	Satyadev TNVSS et al.[21]
10	PhenomenexC_{18}column, 250 X 4.6 mm, 5 µm particle size, with gard column (4 X 3mm I.D., Phenomenex)	Acetonitrile and phosphate 60:40 v/v (pH-7).	1.0 mL/min UV at 205nm.	R_t-3.4 min, Linearity-0.9992	ArmaganOnal et al.[22]
11	HypersilC_{18}, 250 X 4.6 mm,	Methanol: acetonitrile 90:10 v/v	1.0 ml/min UV at 240nm.	R_t-3.40±0.05 min Linearity-0.9985 LOD-0.315539µg/ml LOQ-0.956178µg/ml	Jinesh A Doshi et al.[23]
12	C_{18}Phenomenex column, ODS Column 250mm X 4.6mm, 5µ	Acetate buffer : acetonitrile: methanol 55:35:10 (v/v)	1.0mL/min UV at 290nm	R_t-6.76min Linearity - 0.999 Accuracy-	Dilip G Maheshwari et al.[24]

	particle size.			99.81 LOD-0.3µg/mL LOQ-1.5µg/mL	
13	Kromasil 100 C_{18}column 250 X 4.6mm, 5µ particle size.	Acetonitrile and Phosphate buffer 55:45 (v/v).	1.0 mL/min UV at 301nm.	R_t-4.09 min Accuracy-99.86% Linearty-0.999 LOD-0.25µg/mL LOQ-0.781µg/mL	Girish G Rathi et al.[25]
14	Hypersil C_{18} column 250 X 4.6 mm, 5µm particle size.	Methanol: Acetonitrile: 0.05 M phosphate buffer (pH 7 adjusted with potassium hydroxide) 45:10:45 (v/v/v).	1.0 mL/min UV at 302nm.	R_t-5.92 min Linearty-0.9998 LOD-0.0102µg/mL LOQ-0.0309µg/mL.	Nazar Muhammad Ranjha et al.[26]
15	C_{18} column 150cm X 4.6mm, 3.5µm particle size.	Acetonitrile: buffer (0.3% formic acid) in 25:75 and 30:70 (v/v).	1.1ml/min UV at 302nm.	R_t-3.25min, Linearty-0.999, LOD-1.02mg/L LOQ-5.18mg/L.	K. S. Kumar et al.[27]

*UV – Ultra-Violet, R_t – Retention time, LOD – Limit of Detection, LOQ – Limit of Quantitation.

2. Ultra-Violet spectroscopy

S. NO.	Detection wavelength	Solvent	Linearity range	LOD	References
1	303 nm	Methanol	5-35µg/ml	0.3µg/ml	PatilShamkat S et al.[28]
2	301 nm	Methanol + Distilled water	5-20µg/ml	-	S. Lakshmana Prabu et al.[29]
3	305 nm	Sodium hydroxide	5-25µg/ml	0.734µg/mL	Gowtham Reddy Cheruku et al.[30]
4	299 nm	Methanol	1-6µg/ml	0.116µg/ml	Sunil Singh et al.[31]
5	291.5 nm	Methanol	5-25µg/ml	0.78µg/ml	Brijen Vaghela et al.[32]

6	301 nm	Methanol	5-30µg/ml	-	Suvarna A. Barse et al.[33]
7	296 nm	Methanol	1-40µg/ml	3.3σ/S	Rajan V. Rele et al.[34]
8	291 nm	Methanol	5-30µg/ml	0.16µg/ml	Bhavna A Patel et al.[35]

*LOD – Limit of detection.

3. Infra-red Spectroscopy

S. no.	Wavenumber	Group	Reference
1	3417 cm^{-1} 2949 cm^{-1} 1612-1507 cm^{-1} 3321-3350 cm^{-1} 1611-1422 cm^{-1} 1032-1015 cm^{-1} 2913 cm^{-1} 1584 cm^{-1} 1472 cm^{-1} 1373 cm^{-1}	C=N N-H C=C O-H $COO^{—}$ C-O C-H C-N CH_2 CH_3	Milica Pantic et al.[36]
2	1347 cm^{-1} 1416 cm^{-1} 1727-1686 cm^{-1} 1227 cm^{-1}	OH CH C=O CO	A K. Vynckier et al.[37]

4. Nuclear magnetic resonance spectroscopy

S. no.	Wavenumber	Group	Reference
1	890 cm^{-1} 950 cm^{-1} 1100 cm^{-1} 1260 cm^{-1} 1300 cm^{-1} 1380 cm^{-1} 1500 cm^{-1} 1632 cm^{-1}	Ether group present aromatic ring C-C Ether groups Thiocarboxyl group Chain vibration of two Aromatic rings Symmetric bending of Methyl group Asymmetric bending of Methyl group Stretching of the Aromatic rings	Gaetano F. Bellia at al.[38]

5. Thin-Layer Chromatography (TLC)

S. NO.	Derivatization Agent	Stationery phase Mobile phase Detection method	Retention factor (R_f) LOD	Reference
1	Iodine	Silica gel G, Dichloromethane - methanol - 2.67Mammonia (5:0.3:2 v/v/v) UV-visible spectrophotometer	0.77 0.35µg/ml	Nafisur Rahman et al.[39]

2	Camag TLC scanner	silica gel F254 (10 cm × 10 cm) plates, ethyl acetate: methanol: benzene: acetonitrile (5: 4: 8:3, v/v/v/v), A Camag TLC scanner in reflectance-absorbance mode from 250-350 nm	0.93 1.73 ng/spot	Pakinaz Y. Khashaba et al.[40]

*LOD – Limit of Detection**.**

6. High Performance Thin-Layer Chromatography (HPTLC)

S. no.	Derivatization Agent	Stationery phase Mobile phase Detection method	Retention factor (R_f) LOD	Reference
1	CAMAG TLC scanner III	Aluminium plates with silica gel 60 F_{254} (20 cm X 10 cm), Ethyl acetate: methanol: ammonia (9:1:0.5, v/v/v), CAMAG TLC scanner III at 216nm.	0.64±0.02 3.3 σ/S	Pravin D. Pawar et al.[41]
2	CAMAG TLC scanner III	Silicagel precoated aluminium plate 60 GF_{254} plates (20x10 cm with 250µm thickness), Acetonitrile: Chloroform: Ammonia (12:7. 5:0. 5) (v/v/v), CAMAG TLC scanner III at 222nm.	0.48 85. 07 ng/spot	P. Asha et al.[42]
3	CAMAG TLC scanner III	aluminium backed silica gel 60 F_{254} TLC plates (10cm x 10cm), ethyl acetate: ammonia, 8: 0.8 (v/v), CAMAG TLC scanner III at 301nm.	0.6 0.37 ng	S.A. Gosavi et al.[43]

*LOD – Limit of Detection**.**

7. Liquid Chromatography-Mass Spectroscopy (LC-MS)

S. NO.	Internal Standard	Sample preparation, Stationary phase, Mobile phase.	Flow rate, Detection (m/z), LOQ	Reference
1	Ezmos	Used Methanol as solvent, Develosil phenyl phase-	0.9 mL/min, MRM,	Suresh Reddy

		UG-5 (150 X 4.6 cm, 3µm) column, 1% Ammonia solution buffer and acetonitrile.	2.303 ppm.	Yelampalli et al.[44]

*LOQ – Limit of Quantitation, MRM – Multiple Ion Monitoring, Ezmos – Esomeprazole.

8. Ultra Performance Liquid Chromatography (UPLC)

S. no.	Sample	Description	Detection	Reference
1	Bulk substance and tablet dosage form	Column: HypersilGoldC18 column (50 mm X 3.0 mm, 1.9 µm particle size), Mobile phase:methyltert-butylether :ethylacetate(80:20,v/v), Flow rate – 0.5mL/min, LLOQ-0.100ng/ml	MRM, ESI.	Raja Haranadha Babu Chunduri et al.[45]
2	Bulk substance and tablet dosage form	Column: UPLC BEH C18 column (2.1 × 50 mm, 1.7 µm particle size), Mobile phase: acetonitrile and 0.1% formic acid and 5 µM ammonium Formate, Flow rate: 0.40ml/min.	MRM.	Hsin Tian et al.[46]
3	Aspirin and Esomeprazole magnesium in combined tablet	Column: Agilent Zorbax XDB column (50 × 4.6 mm i.d., 1.8 µm particle size), Mobile phase: 0.2% orthophosphoric acid, methanol, and acetonitrile, Simple gradient elution, Retention time – 2.4 min, Linearity – 32 – 98 µg/ml.	UV at 210nm.	Shravan Kumar Malisetty et al.[47]

*LLOQ – Lower Limit of Quantitation, MRM – Multiple Ion Monitoring, ESI – Electrospray ionization, UV – Ultra – Violet.

9. Gas Chromatography-Mass Spectrometry (GC-MS)

S. No.	Stationery phase,	Linearity range, Retention time	LOD, LOQ	Reference
1.	Column- DB-5 capillary column (30m X 0.32mm i.d. X 1.0 µm film).	Linearity- 0.9998 Peak- 50mg/mL, Flow rate- 1.46 mL/min Injective range- 0.5-2 µL.	LOD-3ppm LOQ-10ppm Scanned range- 265 (m/z), Validation- SIM SCAN mode- TIC	Nandhuri V.V. S. S. Raman et al.[48]

2.	Column- DB-5 capillary column (30m X 0.53mm i.d. X 5.0 µm film).	Linearity- 0.9989 Flow rate-3.0 mL/min	LOD-1.5ppm LOQ-5ppm Validation-SIM,SIR	M. Yogeshwarreddy et al.[49]

*LOD – Limits of Detection, LOQ – Limit of Quantification, SIM – Selected Ion Monitoring, SIR – Selected Ion-Recording, TLC – Total Ion Chromatogram.

DISCUSSION AND REPORT

In this review article we have investigated the analytical techniques used in the determination of different pharmaceutical dosage forms Also we discussed about the drug profile of the drug Esomeprazole and its analytical methods of determination in different pharmaceutical dosage forms. The main objective of this review is to compile the recent literatures on of esomeprazole on its analytical methods of determination in different pharmaceutical dosage forms.

From the various surveys about the drug esomeprazole on its analytical methods of determination in different pharmaceutical dosage forms.We have concluded that the analytical development plays a vital role in the development of various pharmaceutical dosage forms. Esomeprazole the drug used as proton pump inhibitor in the treatment of ulcer patients as an antiulcer agent and is available in limited pharmaceutical dosage forms (i.e. tablets).

As the formulation of esomeprazole in different formulation is still under development, the analytical determination of esomeprazole and its metabolites has taken a keen interest of various scientist and researchers to develop a simple and efficient analytical method for the determination of esomeprazole in pharmaceutical dosage forms. According to our information collected from different articles we came to a conclusion that the chromatographic techniques (HPLC/LC-MS – Both Normal Phase and Reverse Phase) has produced efficient results in the determination of esomeprazole. The HPLC/LC-MS is the most preferably used methods in the determination of Esomeprazole as well.

The HPLC/LC-MS method and UV spectroscopy method were developed and validated for the analysis of Esomeprazole in pharmaceutical preparations were found to be reliable, simple, fast, true and precise. Statistically compared, the HPLC/LC-MS method is more precise and accurate than the UV method. Because both recommended methods are specific,

simple, fast, precise and accurate, they can be successfully applied for routine quality control analysis in pharmaceutical dosage forms of Esomeprazole.

The Infra-Red spectroscopy and Nuclear Magnetic Resonance spectroscopy gives details about the bonding between the atoms and its wavenumbers are also discussed. The scientists and research scholars had done efficient work on the Esomeprazole.

CONCLUSION

The present review discussed about different analytical approach employed for the assessment of Esomeprazole. Profuse examination have been accomplished including HPLC, TLC, HPTLC, UPLC, UV/Vis-Spectroscopy, Infra-Red spectroscopy, NMR spectroscopy, LC-MS for evaluation of Esomeprazole in bulk and in its combination with other drugs for pharmaceutical formulations and also biological fluids.

Liquid chromatography with UV detection has been found to be most studied for estimation of Esomeprazole in bulk as well as pharmaceutical dosage forms, while hyphenated LC-MS methods reported for determination of Esomeprazole and its metabolite in plasma and other biological fluids. Few chromatography approaches like stability indicating HPLC, HPTLC, UPLC, and TLC are also reported. Few simple UV spectrophotometric methods may be used for routine analysis of Esomeprazole alone and in combination with other drugs. These compiled data may of use or research for further studies in analysis of Esomeprazole.

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