



ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF ESOMEPRAZOLE IN DRUG AND DOSAGE FORM: A REVIEW

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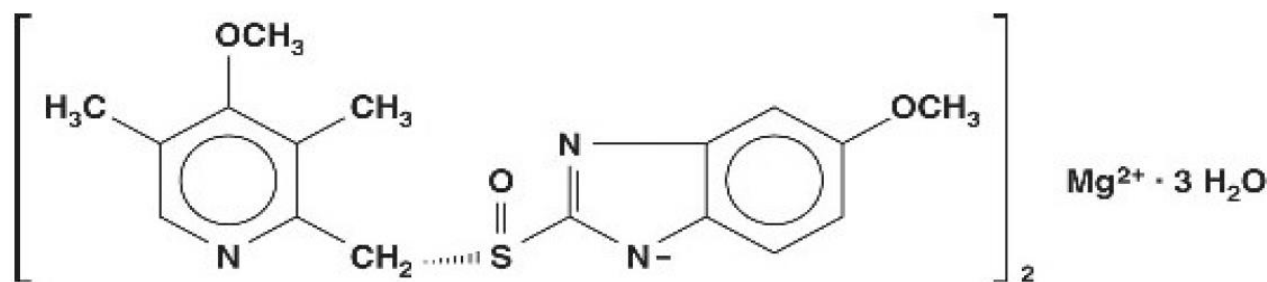
Abstract: Esomeprazole magnesium trihydrate (ESO), bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1-H-benzimidazole-1-yl)magnesium trihydrate ^{Figure 1}, A compound called esomeprazole magnesium trihydrate prevents the secretion of stomach acid. When treating conditions related to gastric oesophageal reflux, ESO is an affordable option. The first single optical isomer proton pump inhibitor, omeprazole, has an S-isomer called ESO. It has a good pharmacokinetic profile compared to omeprazole and generally offers better acid control than contemporary racemic proton pump inhibitors. Esomeprazole and omeprazole show significant similarities with respect to of pharmacokinetics, mechanism of action, and clinical efficacy. In the US, omeprazole is prescribed to treat peptic ulcer disease, gastroesophageal reflux disease, and the prevention of stress ulcers¹. Gastroesophageal reflux disease (GERD), but is especially suitable for people with GERD who have recurring, chronic symptoms that can be disruptive and last a long time². Literature survey reveals esomeprazole magnesium trihydrate that is determined by RP-HPLC, LC-MS/MS, UPLC, UVHPLC, UPLC—MS/MS and UV Spectrophotometry

Keywords: Esomeprazole, HPLC, LC-MS/MS, UPLC, UVHPLC, UPLC—MS/MS, UV

INTRODUCTION

Method development and validation are an iterative process. The influence of operating parameters on the performance of the method can be assessed at the validation stage which was not done during development/optimization stage of the method. The most significant point raised for validation is that the validity of a method can be demonstrated only through laboratory studies. Guidelines from the United States Pharmacopoeia (USP), International Conference on harmonization (ICH), Food and Drug Administration (FDA) etc., provide guidelines for performing such validations in pharmaceuticals. Results from method validation is used to judge the quality, reliability and consistency of analytical results³. Esomeprazole magnesium trihydrate is the first proton pump inhibitor designed as a single optical isomer for treating acid-

related disorders. It offers better pharmacokinetics and acid suppression than omeprazole. The medicine treats gastroesophageal reflux illness, erosive reflux esophagitis, and peptic ulcers.



A variety of methods have been used to estimate and validate ESO both alone and in combination⁴. The most frequent separation technique in HPLC is reversed-phase chromatography. The reversed-phase method's versatility and ability to handle compounds with varying polarities and molecular masses contribute to its popularity. Reversed phase chromatography has analytical and preparative uses for biological separation and purification. Reversed phase chromatography is highly effective at separating hydrophobic molecules like proteins, peptides, and nucleic acids. This review discusses the significance of RP-HPLC in analytical method development, including methodologies and essential chromatographic parameters that must be tuned for efficiency. In high-performance liquid chromatography, a compound with lower affinity for the stationary phase travels faster and covers a longer distance, while a compound with higher affinity moves slower and covers a shorter distance. This differential migration facilitates effective separation and analysis of sample components. High-performance liquid chromatography (HPLC) proves invaluable in pharmaceutical analysis, efficiently isolating and quantifying major medications, reaction impurities, synthesis intermediates, and degradants. As a preeminent analytical tool, HPLC excels in identifying, measuring, and separating diverse sample components soluble in liquid. Its precision is paramount for both quantitative and qualitative drug product analysis, playing a pivotal role in determining drug product stability. By offering a meticulous approach to characterizing pharmaceutical samples, HPLC stands as an indispensable technique in ensuring the quality and safety of medicinal formulations in the field of analytical chemistry⁵. Liquid chromatography—tandem mass spectrometry (LC—MS/MS) is becoming a popular technology for analyzing prescription medicines. LC-MS/MS is the only practical measuring approach for substances without natural chromophores or fluorophores, providing enhanced specificity and sensitivity compared to immunoassay. LC-MS/MS is considered a superior technology to immunoassay because to its higher specificity and sensitivity; however, the main disadvantages of LC-MS/MS are the high instrument costs, increased technical complexity, and analytical speed and turnaround⁶. Ultra-high performance liquid chromatography (UPLC) has revolutionized analytical separation procedures, allowing for faster findings without losing quality. UPLC, a derivation of HPLC, works on the idea that decreasing column packing particle size leads to increased efficiency and resolution⁷.

ANALYTICAL METHODOLOGIES

Vivek Jain reported validation of RP-HPLC method for the estimation of esomeprazole in bulk and pharmaceutical dosage form. The separation was achieved on Thermo C18 analytical column (250 mm × 4.6 mm i.d., 5.0 μm) using acetonitrile and methanol in the ratio 50:50 v/v as mobile phase and at a flow rate of 1.0 ml/min. Detection was carried out using a UV detector at 300nm. The method was validated for accuracy, precision, specificity, linearity and sensitivity. The standard curve was linear over the concentration range of 5-25 μg/ml with r² close to one (0.999). The limit of detection (LOD) and limit of quantitation (LOQ) obtained were 0.100 μg/ml and 0.314 μg/ml respectively. The mean percentage recoveries obtained for ESO was 99.78% and RSD was <1. The proposed method was highly

reproducible, reliable, rapid, robust and specific. The suggested HPLC approach was discovered to be suitable for routine quantitative HPLC analysis of ESO in pharmaceutical dosage form, and it was validated in accordance with the International Conference on Harmonization (ICH) Q2B Guidelines. It was demonstrated that the results of linearity, precision, accuracy, and specificity were within the bounds. ESO can be selectively quantified with this method without interference from other formulation excipients. The suggested approach was very robust, fast, accurate, repeatable, and specific. Therefore, its application for the routine measurement of ESO in the pharmaceutical dose form is made possible by a high percentage of recovery and a run time of less than seven minutes⁸.

T. Santhosh Kumar developed and validated for the determination of Esomeprazole (Eso), and Domperidone (Dom) in capsule formulation. The method uses a Waters HPLC system with a Thermo RP8 column (4.6 x 150 mm and 3.5 μ m), a flow rate of 1 ml/min, and a load of 20 μ l. The mobile phase was composed of acetonitrile and phosphate buffer at a ratio of 35:65. The detection was carried out at 289 nm. The study was conducted to provide a sensitive, precise, and accurate RP-HPLC method for analyzing Esomeprazole and Domperidone in pharmaceutical dosage forms. The retention times for Esomeprazole and Domperidone were determined to be 4.288 and 2.946, respectively. After injecting each sample five times, the drug solution's peak area was consistent and had a low coefficient of variation. A good linear association ($r = 0.999$) was found between the concentrations and their corresponding peak regions. The proposed HPLC method was found to be highly exact, as indicated by a %RSD of less than 1.00. The approach was resilient, as evidenced by little fluctuation in analysis results with changes in flow rate, mobile phase composition, and temperature. The proposed RP-HPLC method for estimating Esomeprazole and Domperidone in capsule dosage proved accurate, precise, linear, robust, easy, and cost-effective⁹.

Shanmugam Gopinath A sensitive and high-throughput LC-MS/MS technique has been developed and validated to detect esomeprazole and naproxen in human plasma, using ibuprofen as an internal reference. Solid-phase extraction was utilized to extract analytes and internal standards from human plasma. The XBridge C18 column separated in 4.0 min using a mobile phase of acetonitrile-25mM ammonium formate (70:30, v/v). ESI/MS/MS in negative ion mode detected esomeprazole, naproxen, and isoproterenol at m/z 344.19-194.12, 229.12-169.05, and 205.13-161.07. The calibration curves for esomeprazole and naproxen were linear, ranging from 3.00 to 700.02 ng/mL and 0.50 to 150.08 ng/mL respectively. The intra- and inter-batch precision and accuracy across four quality control levels satisfied the requirements of US FDA guidelines. The SPE-LC-MS/MS technique successfully detects esomeprazole and naproxen in human plasma. The method's quick analytical time allows for high throughput. Using the Oasis HLB SPE cartridge, the SPE method yielded quantifiable and reproducible results for both analytes. Endogenous plasma components did not cause interference in plasma samples. Validation data shows that the developed method is highly precise and accurate. The validation characteristics indicate that the approach is suitable for bioequivalence research, providing the requisite sensitivity, precision, and accuracy.¹⁰

Shravan Kumar Malisetty The simultaneous detection of aspirin and esomeprazole magnesium in pharmaceutical formulations has been accomplished through the development and validation of a stability-indicating ultra-performance liquid chromatography (UPLC) method. The column utilized was an Agilent Zorbax XDB (50 4.6 mm i.d., 1.8 mm particle size). In a straightforward gradient elution, the mobile phase was a combination of 0.2% orthophosphoric acid, methanol, and acetonitrile. At 210 nm, ultraviolet (UV) detection was carried out. The two medications were eluted at retention times of 2.4 and 2.8 minutes for aspirin and esomeprazole, respectively. The total run time was 6 minutes. Aspirin's linearity was found to be between 32 and 98 mg/ml, while esomeprazole magnesium's was found to be between 4 and 12 mg/ml. Aspirin and esomeprazole magnesium were reported to have percentage recoveries of 99.1e100.5 and 99.2e100.1, respectively. Even in real samples, the technique was able to distinguish clearly between the medication and degradation products. A liquid chromatographic approach has been devised to quantify both AS and ES in mixed dose forms using specific stability indicators. The validated method accurately detects and quantifies AS and ES with specificity, precision, robustness, and linearity.¹¹

Gowtham Reddy Cheruku For the medication esomeprazole in bulk and pharmaceutical dosage form, an exact and simple technique was created. The solvent that was employed was NaOH. It was discovered that the maximum wavelength (λ_{\max}) of esomeprazole was 305 nm. The validation was carried out in accordance with the Limit of Detection (LOD), Limit of Quantification (LOQ), accuracy, linearity, and precision requirements provided by the ICH of Technical Requirements for Pharmaceuticals for Human Use (ICH). The recovery rate (%) for esomeprazole was 100.20%. For esomeprazole, linearity was noted between 5 and 25 $\mu\text{g}/\text{mL}$, respectively. For esomeprazole, the regression coefficient (r^2) is 0.9963, and the regression equation is $y=0.0407x-0.0122$. Precision within and between days was examined, and results for the relative standard deviation were less than 2. The LOD and LOQ values were obtained using the regression equation. For esomeprazole, the LOD value was determined to be 0.734 $\mu\text{g}/\text{mL}$ and the LOQ value to be 2.224 $\mu\text{g}/\text{mL}$. Both the method's validity and the comparatively dependable results it produces support this validity. It can be used to estimate esomeprazole in both the academic and private sectors.¹²

Raja Haranadha Babu Chunduri For the purpose of simultaneously quantifying esomeprazole, rabeprazole, and levosulpiride in human plasma, a high throughput ultra-pressure liquid chromatography—mass spectrometry (UPLC—MS/MS) method with good sensitivity and selectivity has been developed and validated. Lansoprazole is used as the internal standard (IS). Using methyl tert-butyl ether: ethyl acetate (80:20, v/v), which affords a high recovery, the analytes and IS were extracted from 50 mL of human plasma using a liquid-liquid extraction process. On a Hypersil gold C18 column, chromatographic separation of analytes and IS was accomplished using a gradient mobile phase comprising of 2mM ammonium formate/acetonitrile. To elute all the analytes and IS in the allotted runtime of one minute, the flow rate was adjusted to 0.5 mL/min. Target compound detection was carried out using positive electrospray ionization (ESI) in multiple reaction monitoring (MRM) mode on a triple quadrupole mass spectrometer. The developed technique exhibits good precision and accuracy over the concentration ranges of 0.1—2000 ng/mL for each analyte, according to method validation results. A series of stability assays, including bench top, auto sampler, dry extract, long-term storage stability, and freeze-thaw cycles, were used to determine the stability of the compounds. The broad range of linearity, high recovery, quick extraction, and short run time of this approach are all major benefits. Additionally, this technique offers exceptional sensitivity, with each analytes LLOQ as low as 0.1 ng/mL. Ultimately, the method's high sample throughput capabilities stems from its easy sample preparation and fast chromatographic duration. We may infer that the current method is helpful for pharmacokinetic/bioequivalence investigations with the appropriate precision and accuracy based on the outcomes of all the validation parameters.¹³

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