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A Review on Residual Solvent Determination In Esomeprazole Using Gas Chromatography

Rahul P. Varade [1], Hrushikesh C. Suryawanshi [2], Swpnil B Hiray[3], Yogesh V. Patil[4]

Matoshri College of Pharmacy

ABSTRACT :

Residual solvents are unwanted chemicals (solvents) employed or during the process of production of a excipients, drug or pharmaceutical formulation and cannot be totally eliminated by realistic means in the end product. They may be toxic in nature. Hence, determination of residual solvents becomes an essential aid to the quality control of pharmaceuticals. In this review on determination of residual solvent in esomeprazole. Its molecular formula is (C17H19N3O3S) The drug's side effects are dizziness, confusion, rapid or irregular heartbeat, muscle jerking movements, jittery sensation, watery or bloody diarrhea.

Keywords: Esomeprazole, Gas chromatography, Residual solvents, Head Space, Pharmaceutical formulation, Pharmaceutical analysis

Introduction

Pharmaceutical analysis is a critical branch of analytical chemistry that ensures the safety, efficacy, and quality of drug substances and drug products. It involves the application of various techniques for the identification, quantification, and characterization of active pharmaceutical ingredients (APIs), excipients, impurities, and degradation products. With the increasing complexity of modern medicines, stringent regulatory requirements demand robust and reliable analytical methods to monitor drug quality at every stage of development, production, and storage[1].

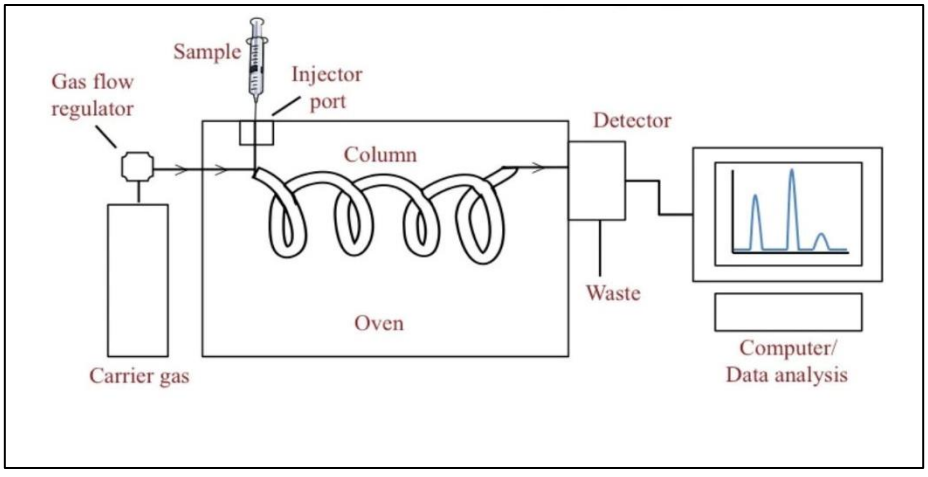
Gas Chromatography

Gas chromatography is a phrase to describe the collection of analytical separation methods utilized for the analysis of volatile materials in the gas state. In gas chromatography, the sample constituents are dissolved within a solvent and vaporized for the purpose of separating the analytes by partitioning the sample between two phases a stationary phase and a mobile phase. The mobile phase is an inert chemically gas used to transport the analyte molecules through the hot column. Gas chromatography is one of the only chromatography techniques that doesn't use the mobile phase to interact with the analyte. The stationary phase is either a solid adsorbent, which is referred to as gas-solid chromatography (GSC), or a liquid on an inert support, which is referred to as gas-liquid chromatography (GLC)[2,3,4].

Principles:

The separation principle in GC is "partition." The component to be separated mixture is vaporized and blended with mobile gaseous phase. The more soluble component in stationary phase moves slower and is eluted later. The less soluble component in stationary phase moves quicker and eluted first. No two components share same partition coefficient conditions. Therefore the components are resolved based on partition coefficient. Partition coefficient is the ratio between solubility of a substance divided between two immiscible liquids at constant temperature[5].

Figure No. 1: Instrumentation of Gas Chromatography



Instrumentation:

Carrier Gas

The carrier gas functions as the mobile phase. It is supplied through a pressure regulator, pressure gauge, molecular sieve filter, and flow controller to ensure a stable and clean flow into the column.

An ideal carrier gas must:

- Be chemically inert
- Be easily available and cost-effective
- Offer high purity to prevent contamination
- Ensure consistent and accurate results
- Be suitable for the selected detector[6,7].

Commonly used gases include helium, nitrogen, hydrogen, and carbon dioxide. Helium is considered optimal due to its inertness and high efficiency, though nitrogen is more economical. Hydrogen has good thermal conductivity but poses flammability risks.

Sample Injection System

The injection port is located at the head of the column and is maintained at a temperature 20–50 °C above the boiling point of the analyte to ensure vaporization.

Injection modes

- Split injection

Divides the sample, sending only a fraction into the column while venting the remainder. Useful for concentrated samples but less sensitive.

- Splitless injection

Delivers the entire sample into the column. Best suited for trace analysis of dilute samples.

- On-column injection

Introduces the liquid sample directly into the column without vaporization in the injector, minimizing thermal degradation.

- Automatic injection systems

Improve reproducibility and allow unattended operation for multiple samples[8,9].

Columns

Columns serve as the separation unit and may be:

- Packed columns: Contain inert solid supports coated with stationary liquid phase. Dimensions: 1.5–10 m in length, 2–4 mm internal diameter.
- Capillary columns: Narrow tubes (0.1–0.5 mm ID) with lengths up to 100 m. Two types exist:
- Wall-coated (WCOT): Stationary phase coated directly on the inner wall.
- Support-coated (SCOT/PLOT): A support material is applied to the inner wall to hold the stationary phase[10,11].

Column Conditioning

Columns must be equilibrated before analysis by continuously passing hot carrier gas through them for several hours (up to 24 h). A well-conditioned column ensures baseline stability.

Temperature Control

The column oven regulates temperature during separation. Low boiling compounds elute at lower temperatures. High boiling compounds require higher temperatures and often a programmed heating cycle to improve peak shape and resolution. [12].

Detectors

The solute particles which are eluted and the carrier gas leave the column and proceed to the detector. The detector generates electrical signals proportional to the concentration of the solute component. The signals are amplified and registered as peaks at intervals in the chromatograph.

Thermal conductivity detector:

TCD relies on the fact that heat lost from a filament is a function of the thermal conductivity of the stream of surrounding gas and its own specific heat. If carrier gas only flows, heat loss to metal block remains constant, filament T also remains constant. When analyte species move over the filament usually thermal conductivity varies, hence resistance varies which is detected by Wheatstone bridge setup. The difference in control and sample filament temperature is detected and a signal is obtained[13].

Electron capture detector:

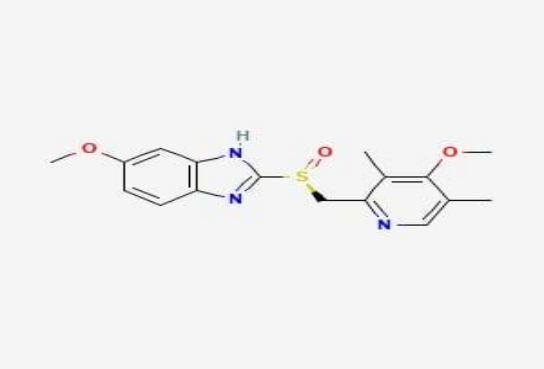
Molecules of compounds, that have electron affinity, vary in their electron absorbing ability. The same is used in this detector to identify the compounds [14].

Residual solvents:

Residual solvents in pharmaceuticals are explained as organic volatile chemicals used or can be generated during the process of manufacture of drug substances or excipients, or during preparation process of drug products. The residual solvents don't appear to have been completely eliminated by realistic manufacturing methods. Proper selection of the solvent for synthesizing a drug substance or an excipient would be helpful in increasing the yield, or defining the properties such as crystal form, purity, and solubility. Thus, the solvent may in general at times be a necessary ingredient in the process of synthesis.. Hence, determination of residual solvents becomes a challenging analytical problem in pharmaceutical analysis and control. Unknown residual

solvents are usually found during normal quality control analyses. A mistake may result while current official methods are employed in their analysis. Therefore, it is necessary to design a rapid, sensitive methodology that identifies, and quantitates all residual solvents present in pharmaceuticals[15].

DRUD PROFILE:

Name of drug	Esomeprazole
Structure	
Drug categories	Protan Pump Inhibitors
Molecular formula	$C_{17}H_{19}N_3O_3S$
Molecular weight	345.4 g/mol
Melting point	155°C
Appearance	White crystalline powder
Mechanism of action	Esomeprazole is a proton pump inhibitor (PPI) that binds to and irreversibly inhibits the H+/K+ ATPase enzyme in the stomach's gastric parietal cells. This prevents the proton pump from secreting hydrochloric acid into the stomach, which reduces gastric acidity.
Absorption	Rapidly absorbed from the gastrointestinal tract after oral administration

Side effect	headache nausea diarrhea gas constipation dry mouth

Literature Review:

SR. No	Drug	Method	Column	Mobile Phase	Detector	Ref.
1	Esomeprazole	GC-FID	DB-624(30m×0.32mm,1.8 µm)	Helium	FID	16
2	Esomeprazole	GC-HS	DB-WAX (30M×0.25mm0.25 µm)	Nitrogen	FID	17
3	Esomeprazole	GC-FID	DB-1 (30M×0.25mm0.25 µm)	Helium	FID	18
4	Esomeprazole	GC-HS	DB-624(30M×0.53mm,3.0 µm)	Helium	FID	19
5	Esomeprazole	GC-MS	DB-FFAP(30M×0.25mm,0.25 µm)	Helium	MS	20
6	Esomeprazole	GC-FID	ZB-WAX(60m× 0.32mm,1.8 µm)	Nitrogen	FID	21

Conclusion :

The measurement of residual solvents in Esomeprazole by Gas Chromatography (GC) is an important step in the verification of the safety, efficacy, and regulatory compliance of the active pharmaceutical ingredient (API). Literature shows that headspace GC, with its low sample preparation, high sensitivity, and capacity to analyze volatile analytes, is the analytical method of choice for the detection of Class 1, 2, and 3 solvents according to ICH Q3C guidelines. Choice of right stationary phase, optimised oven temperature programme, and appropriate detector (typically flame ionization detector) improves accuracy and reproducibility.

REFERENCES:

1. Shirey R. Unknown residual solvents identification in drug products by headspace- Gas chromatography-mass spectrometry, J. High Resol chromatogr 1995: 18: 495-9.
2. Kolb, B: Ettre, L. S. Static Headspace-Gas Chromatography: Theory and Practice: Wiley-VCH: New York, 1997; pp 3-4.
3. Premnath, S.M. & Zubair, M. (2024, January 11) Chromatography. Statpearls- NCBL Bookshelf.
4. Grote C, Pawliszyn. Unknown residual solvents identification in drug products by Headspace solid phase microextraction gas chromatography. J Anal Chem 1997. 69. 587-98.
5. Page B, lacroix G. Unknown residual solvents identification in drug products by headspace solid phase microextraction gas chromatography-mass spectrometry. J Chrmatogr. 1993. 648:199-211.
6. Masoom Raza Siddiqui, Rajkumar Singh, Anuj Bhatnagar, Jetendra kumar, Manu Chaudhary, Determination of residual solvents in docetaxel by headspace gas chromatography, Arabian Journal of Chemistry, 10, 2017, 2479-2484.
7. Gas chromatography: principles, characteristics and process creative protemics blog. (2020 January 10)
8. Jyothsna Modugula and Podili venkata seshagiri, Analytical Method Development and validation of residual solvents in methocarbamol by gas chromatography (gc/fid) with head space, world journal of pharmacy and pharmaceutical sciences, 8, 2019, 1268-1284.
9. Clecio S. Ramos, Development and validation of a headspace gas chromatographic method for determination of residual solvents in five drug substances, International Journal of Pharmaceutical Science Invention, 2, 2013, 36-41.
10. Nanduri V. V. S. S. Raman ,Kura Ratnakar Reddy, Adapa V. S. S. Prasad ,Karipeddi Ramakrishna. Development and Validation of a GC–MS Method for the Determination of Methyland Ethyl Camphorsulfonatesin Esomeprazole Magnesium.
11. Hymer CB,(2003) Residual solvent testing: A review of gas chromatographic and alternative techniques. Pharm Res; 23:337-44.
12. Raghani, A. R. High speed gas chromatographic analysis of solvents in pharmaceutical using solid phase microextraction.J. Pharm. Biomed. Anal. 2002, 29. 507.
13. Rocheleau, M.J., Titley, M. Bolduc, Measuring residual solvents in pharmaceutical samples using fast gas chromatography techniques. J. J.Chromatogr. B. 2004, 805, 77.

14. Feng XZ, Han Gc, Qin J;Yin SM, Chen Z, Determination of Residual Solvents in Linezolid by Static Headspace GC, Journal of chromatographic science, 54, 2016, 487-491.

15. Klick, S., Skold, A. Validation of generic analytical procedure for determination of Residual solvents in drug substances. J. Pharma. Biomed. Anal. 2004.36, 401.

16. Joshi, O., Gide, P. Analytical Method Development to Determine Residual Solvents in Esomeprazole by Gas Chromatography (GC/FID) with Headspace. IJPPR Human Journals, 2017; Vol. 10 (1):12–17.

17. Pandey, S., Pandey, P., Kumar, R., Singh, N.P. Residual Solvents Determination by Head-Space Gas Chromatography with Flame Ionization Detector in Omeprazole API. Brazilian Journal of Pharmaceutical Sciences, vol. 47, no. 2, Apr./June 2011.

18. Mishra, G., Saxena, V.S., Jawla, S., Srivastava, V.K. Method Development and Validation for the Determination of Residual Solvents in Omeprazole API by Using Headspace Gas Chromatography. Asian Journal of Pharmaceutical and Clinical Research, 2014; 7(1):54–56.

19. Battu, P.R., Reddy, M.S. Residual Solvents Determination by HS-GC with Flame Ionization Detector in Omeprazole Pharmaceutical Formulations. International Journal of PharmTech Research, 2009.

20. ICH. Q3C(R8) Impurities: Guideline for Residual Solvents. International Council for Harmonisation; Step 4 (2021).

21. Cheng C, et al. A generic static headspace GC method for ICH Q3C Class 2 & 3 residual solvents in drug substances. J Pharm Biomed Anal. 2010.

22. Pankaj verma, N.V. satheesh Madhav, Vinay k Gupta: A Review article on Pharmaceutical Validation and Process Control ;vol 1 : 2012