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Research article

Hydrotropic solubilization: a green review on - analytical approach for hydrotropic solubilization technique via spectrophotometric estimation of API

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ABSTRACT

The pharmaceutical industry is increasingly focused on developing environmentally sustainable analytical methods that minimise the use of hazardous chemicals while maintaining analytical reliability. Poor aqueous solubility of many active pharmaceutical ingredients (APIs), including Esomeprazole and Levosulpiride, presents significant challenges during analytical method development. Conventional analytical methods frequently require toxic organic solvents such as methanol and acetonitrile, leading to environmental and occupational concerns. Hydrotropic solubilization has emerged as an effective and eco-friendly alternative for enhancing the aqueous solubility of poorly water-soluble drugs. This review discusses the concept, mechanism, classification, and applications of hydrotropic agents in pharmaceutical analysis. Special emphasis is placed on the analytical challenges associated with Esomeprazole and Levosulpiride and the potential application of hydrotropic solubilization for their spectrophotometric estimation. The review highlights recent developments in green analytical chemistry and demonstrates how hydrotropic techniques contribute to sustainable pharmaceutical quality control practices.

Keywords: Hydrotropy, Green analytical chemistry, Esomeprazole, Levosulpiride, UV spectrophotometry, Sodium benzoate, Pharmaceutical analysis.

INTRODUCTION

Analytical chemistry plays a critical role in pharmaceutical development, quality assurance, and regulatory compliance. Reliable analytical methods are essential to ensure the safety, efficacy, and quality of pharmaceutical products. Traditionally, chromatographic techniques such as HPLC and LC-MS have been widely employed due to their high sensitivity and selectivity. However, these techniques require expensive instrumentation and large quantities of hazardous organic solvents [1, 2].

The growing concern regarding environmental sustainability has led to the emergence of Green Analytical Chemistry (GAC), which focuses on minimising hazardous chemicals, reducing waste generation, and improving analyst safety. Among various green analytical approaches, hydrotropic solubilization has gained significant attention as an effective technique for improving the solubility of poorly water-soluble drugs without using organic solvents [3, 4].

Green analytical chemistry

Green Analytical Chemistry is based on the principles of reducing environmental impact while maintaining analytical performance. The major objectives include:

Reduction of toxic solvents.

Minimization of waste generation.

Energy-efficient analytical procedures.

Safer working environments.

Sustainable laboratory practices.

Hydrotropic solubilization satisfies several principles of green analytical chemistry by replacing organic solvents with environmentally friendly aqueous systems [5, 6].

Concept of hydrotropy

Hydrotropy is defined as the enhancement of aqueous solubility of poorly soluble compounds by the addition of high concentrations of hydrotropic agents.

The phenomenon was first described by Carl Neuberg in 1916. Hydrotropic agents improve drug solubility through weak intermolecular interactions such as:

Hydrogen bonding

π–π interactions

Dipole–dipole interactions

Molecular aggregation

Unlike surfactants, hydrotropes do not form micelles and therefore provide a simple and efficient solubilization mechanism [7, 8].

Classification of hydrotropic agents

Anionic hydrotropes

Sodium Benzoate

Sodium Salicylate

Sodium Cumene Sulfonate

Sodium Xylene Sulfonate

Non-Ionic hydrotropes

Urea

Nicotinamide

Caffeine

Mixed hydrotropic systems

Combination of two or more hydrotropic agents to achieve synergistic solubilization effects.

Mechanism of Hydrotropic Solubilization

Several theories have been proposed:

Self-Association Theory

Hydrotropic molecules aggregate and create hydrophobic microenvironments that accommodate poorly soluble drugs [9].

Complex formation theory

Weak complexes are formed between hydrotropic molecules and drug molecules through non-covalent interactions [10].

Structure modification theory

Hydrotropes alter the hydrogen-bonded network of water, enhancing drug solubility.

Esomeprazole: Pharmaceutical and Analytical Perspective

Esomeprazole is a proton pump inhibitor widely used for treating:

Gastroesophageal reflux disease (GERD)

Peptic ulcer disease

Helicobacter pylori infections

Zollinger–Ellison syndrome [11].

Analytical challenges

Poor aqueous solubility

Acid instability

Dependence on organic solvents for analysis

These limitations make Esomeprazole a suitable candidate for hydrotropic solubilization-based analytical methods.

Levosulpiride: Pharmaceutical and Analytical Perspective

Levosulpiride is a selective dopamine D2 receptor antagonist and prokinetic agent [12].

Therapeutic uses

Functional dyspepsia

Gastroesophageal reflux disease

Delayed gastric emptying

Gastrointestinal motility disorders [13].

Analytical challenges

Practically insoluble in water

Significant spectral overlap with Esomeprazole

Requirement of organic solvents for conventional analysis

Hydrotropic techniques can effectively address these challenges.

Analytical Methods Reported for Esomeprazole and Levosulpiride [14].

UV spectrophotometric methods

Simultaneous equation methods

Derivative spectrophotometry

Absorbance ratio methods [15].

Chromatographic methods

RP-HPLC

HPLC-UV

LC-MS/MS

Although these methods provide accurate results, they often require hazardous solvents and costly instrumentation.

Applications of Hydrotropy in Pharmaceutical Analysis

Hydrotropic solubilization has been successfully applied to:

Ibuprofen

Diclofenac Sodium

Ciprofloxacin

Amoxicillin

Aceclofenac

Esomeprazole

Various BCS Class II and IV drugs [16].

Benefits include

Elimination of toxic solvents

Reduced analytical cost

Improved safety

Simplified sample preparation

Environmental sustainability [17].

Advantages of hydrotropic spectrophotometric methods

Eco-friendly

Economical

Rapid analysis

Simple operation

Reduced solvent toxicity

Improved analyst safety

Suitable for routine quality control [18].

Future perspectives

Hydrotropic solubilization has significant potential for future pharmaceutical analysis. Continued research is expected to:

Develop novel hydrotropic agents.

Improve mixed hydrotropic systems.

Enhance sustainability metrics.

Expand applications to complex pharmaceutical formulations.

significant improvement in the EDSS to 1. [19].

CONCLUSION

Hydrotropic solubilization represents a promising green analytical approach for the analysis of poorly water-soluble drugs. The technique effectively enhances aqueous solubility while eliminating the need for hazardous organic solvents. For drugs such

as Esomeprazole and Levosulpiride, hydrotropic spectrophotometric methods provide a simple, economical, and environmentally sustainable alternative to conventional analytical techniques. Adoption of hydrotropic methods can contribute significantly to greener pharmaceutical quality control and support global sustainability initiatives.

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