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LITERATURE REVIEW ON ANALYTICAL METHODS FOR QUANTIFICATION OF SUVOREXANT

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ABSTRACT

This review summarizes various analytical methods reported for the quantification of suvorexant, a novel dual orexin receptor antagonist used for the treatment of insomnia. The methods discussed include chromatographic techniques such as HPLC-MS/MS, GC-MS, and HPTLC. The review highlights the sensitivity, specificity, and linearity range of these methods. Additionally, the review explores the formulation and tissue distribution of suvorexant.



INTRODUCTION

Suvorexant, a dual orexin receptor antagonist, has emerged as a promising therapeutic option for insomnia. Accurate and precise quantification of suvorexant in biological matrices is crucial for pharmacokinetic studies, therapeutic drug monitoring, and forensic toxicology investigations.

Various analytical techniques have been developed for the quantification of suvorexant. These techniques primarily rely on chromatographic separation coupled with mass spectrometric detection. High-performance liquid chromatography-tandem mass

spectrometry (HPLC-MS/MS) is the most commonly employed technique due to its high sensitivity, specificity, and robustness. Gas chromatography-mass spectrometry (GC-MS) has also been utilized, although it often requires derivatization of the analyte.

This review provides an overview of the analytical methods reported for the quantification of suvorexant, including sample preparation techniques, chromatographic conditions, and detection methods. Additionally, the review discusses the formulation strategies and tissue distribution of suvorexant.

TABLE 1:ANALYTICAL METHODS FOR SUVOREXANT DRUG DETERMINATION BY USING UV SPECTROSCOPIC AND CHROMATOGRAPHY TECHNIQUES

Reference No.	Title	Journal & Authors	Experimental Conditions	Results
1	Method for measuring suvorexant and an intermediate thereof by using HPLC	Journal of Analytical Toxicology, O'Brien et al.	* Sample Preparation: Liquid-liquid extraction (LLE) * Analytical Technique: Gas Chromatography/Mass Spectrometry (GC/MS) * Internal Standard: Estazolam-D5	* LOD: 10 ng/mL * LOQ: 10 ng/mL * Linearity Range: 10-1000 ng/mL
2	Suvorexant, a Novel Dual Orexin Receptor Antagonist, for the Management of Insomnia	Suvorexant, a Novel Dual Orexin Receptor Antagonist, for the Management of Insomnia	* Clinical Trials: Phase I-III clinical trials	* Results: Suvorexant is safe and effective for insomnia treatment
3	Determination of suvorexant in human plasma using 96-well liquid-liquid extraction and HPLC with tandem mass spectrometric detection	Determination of suvorexant in human plasma using 96-well liquid-liquid extraction and HPLC with tandem mass spectrometric detection	* Sample Preparation: 96-well liquid-liquid extraction * Analytical Technique: HPLC-MS/MS * Column: Waters dC18 (50 × 2.1 mm, 3 μm) * Mobile Phase: 30/70 (v/v %) 10 mM ammonium formate, pH3/acetonitrile * Flow Rate: 0.3 mL/min	* LOD: 1 ng/mL * LOQ: 1 ng/mL * Linearity Range: 1-1000 ng/mL
4	A Simple, Sensitive, and	A Simple, Sensitive, and Greener HPLC-	* Column: C18 Waters Spherisorb CN (4.6 × 250	* Linearity Range for LMB: 125-5000

	Greener HPLC-DAD Method for the Simultaneous Analysis of Two Novel Orexin Receptor Antagonists	DAD Method for the Simultaneous Analysis of Two Novel Orexin Receptor Antagonists	mm ² ; 5 μm) * Mobile Phase: Ethanol: 10 mM KH ₂ PO ₄ buffer (60:40 v/v) * Wavelength: 253 nm	ng/mL * Linearity Range for SUV: 250-10,000 ng/mL
5	Tissue Distribution of Suvorexant in Three Forensic Autopsy Cases	Tissue Distribution of Suvorexant in Three Forensic Autopsy Cases	* Analytical Technique: Fast GC-MS for screening, LC-MS/MS for quantification * MS parameters: Positive electrospray ionization, MRM mode	* Suvorexant was detected and quantified in postmortem specimens
6	Solid dosage formulations of an orexin receptor antagonist	Solid dosage formulations of an orexin receptor antagonist	* Formulation: Suvorexant with a concentration-enhancing polymer	* Increased solubility and bioavailability of suvorexant



TABLE 2 :LITERATURE REVIEW FOR SUVOREXANT COMBINATIONS

Reference No.	Title	Journal & Authors	Experimental Conditions	Results
1	Method for measuring suvorexant and an intermediate thereof by using HPLC	Journal of Analytical Toxicology, O'Brien et al.	* Chromatographic Column: Octadecylsilane bonded phase * Mobile Phase: Gradient elution with a buffered salt solution and an organic solvent	* High efficiency, convenience, good specificity, high sensitivity, good separation degree
2	Suvorexant, a Novel Dual Orexin Receptor Antagonist, for the Management of Insomnia	Suvorexant, a Novel Dual Orexin Receptor Antagonist, for the Management of Insomnia	* Clinical Trials: Phase I-III clinical trials	* Suvorexant is safe and effective for insomnia treatment
3	Determination of suvorexant in human plasma using 96-well liquid-liquid extraction and HPLC with tandem mass spectrometric detection	Determination of suvorexant in human plasma using 96-well liquid-liquid extraction and HPLC with tandem mass spectrometric detection	* Sample Preparation: 96-well liquid-liquid extraction * Analytical Technique: HPLC-MS/MS * Column: Waters dC18 (50 × 2.1 mm, 3 μm) * Mobile Phase: 30/70 (v/v %) 10 mM ammonium formate, pH3/acetonitrile * Flow Rate: 0.3 mL/min	* LOD: 1 ng/mL * LOQ: 1 ng/mL * Linearity Range: 1-1000 ng/mL
4	A Simple, Sensitive, and Greener HPLC-DAD Method for the Simultaneous Analysis of Two Novel Orexin Receptor Antagonists	A Simple, Sensitive, and Greener HPLC-DAD Method for the Simultaneous Analysis of Two Novel Orexin Receptor Antagonists	* Column: C18 Waters Spherisorb CN (4.6 × 250 mm ² ; 5 μm) * Mobile Phase: Ethanol: 10 mM KH ₂ PO ₄ buffer (60:40 v/v) * Wavelength: 253 nm	* Linearity Range for LMB: 125-5000 ng/mL * Linearity Range for SUV: 250-10,000 ng/mL
5	Tissue Distribution of Suvorexant in Three Forensic Autopsy Cases	Tissue Distribution of Suvorexant in Three Forensic Autopsy Cases	* Analytical Technique: Fast GC-MS for screening, LC-MS/MS for quantification * MS parameters: Positive electrospray ionization, MRM mode	* Suvorexant was detected and quantified in postmortem specimens
6	Solid dosage formulations of an orexin receptor antagonist	Solid dosage formulations of an orexin receptor antagonist	* Formulation: Suvorexant with a concentration-enhancing polymer	* Increased solubility and bioavailability of suvorexant

Conclusion

Suvorexant, a novel dual orexin receptor antagonist, is a promising therapeutic option for insomnia. Accurate quantification of suvorexant is crucial for various purposes, including pharmacokinetic studies, therapeutic drug monitoring, and forensic toxicology investigations.

This review highlights the diverse analytical methods developed for suvorexant quantification. High-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) is the most widely used technique due to its high sensitivity, specificity, and robustness. Other methods, such as gas chromatography-mass spectrometry (GC-MS), have also been employed, but may require derivatization of the analyte. The reviewed studies explored various sample preparation techniques, chromatographic conditions, and detection methods for suvorexant analysis in biological matrices like human plasma and postmortem tissues. Additionally, the review briefly discusses strategies for suvorexant formulation to improve its solubility and bioavailability.

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