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CHEMICAL-TOXICOLOGICAL ANALYSIS OF PREGABALIN (LYRICA) IN BIOLOGICAL FLUIDS USING A GAS CHROMATOGRAPH (CRYSTALLUX-4000M)

Khusanov Azamat Sotivoldievich

Abstract: This article presents a detailed methodological approach to the chemical-toxicological analysis of pregabalin (commercially known as Lyrica) in biological fluids using the gas chromatographic system CrystalLux-4000M. Due to pregabalin's increasing misuse and inclusion in the list of psychotropic substances in many countries, the need for precise, sensitive, and reliable analytical methods is more pressing than ever. The article describes the procedures for sample preparation, extraction techniques, chromatographic conditions, and identification parameters for pregabalin in fluids such as blood plasma and urine. It also highlights the analytical advantages of the CrystalLux-4000M, particularly its thermal stability, high resolution, and applicability in forensic and clinical toxicology.
Keywords: Pregabalin, Lyrica, gas chromatography, CrystalLux-4000M, biological fluids, toxicological analysis, forensic chemistry.

INTRODUCTION

In recent years, pregabalin (commercially known as Lyrica) has become increasingly prevalent not only as a pharmaceutical for the treatment of neuropathic pain and epilepsy but also as a substance of abuse. Its central nervous system effects—ranging from sedation to euphoria—have contributed to its misuse, particularly among individuals with a history of opioid or benzodiazepine dependence. In light of this, pregabalin has been placed under legal control in numerous jurisdictions.

Toxicological laboratories face growing challenges in accurately detecting pregabalin, especially in forensic cases involving intoxication or drug-facilitated crimes. Gas chromatography (GC), particularly when used with high-performance instruments such as the CrystalLux-4000M, offers a viable solution for detecting pregabalin at trace levels in biological matrices. This article focuses on the methodological framework for GC-based analysis of pregabalin, emphasizing the sensitivity, specificity, and forensic reliability of this approach [1].

MATERIALS AND METHODS

Pregabalin is a gamma-aminobutyric acid (GABA) analog with the chemical formula C8H17NO2. It is structurally similar to gabapentin but exhibits a higher binding affinity to the α2δ subunit of voltage-gated calcium channels. Unlike many classic psychotropics, pregabalin is not significantly metabolized in the liver, and approximately 90% of the administered dose is excreted unchanged in urine. This pharmacokinetic profile simplifies its detection in biological fluids but also necessitates a highly sensitive analytical method due to its rapid clearance.

Traditional immunoassays often fail to detect pregabalin due to lack of cross-reactivity, making instrumental analysis essential. Gas chromatography, while less commonly used for non-volatile compounds, can be applied effectively with proper derivatization techniques.

RESULTS AND DISCUSSION

Biological samples, most commonly blood plasma and urine, are collected using standard clinical protocols. Due to pregabalin's high water solubility and protein binding of less than 10%, plasma filtration and urine centrifugation are adequate initial steps [2].

Extraction typically follows a liquid-liquid extraction (LLE) or solid-phase extraction (SPE) method, where pH is adjusted to optimize partitioning of pregabalin into the organic phase.

Derivatization is achieved using BSTFA (N,O-Bis(trimethylsilyl)trifluoroacetamide), converting pregabalin into its more volatile trimethylsilyl (TMS) derivative, thereby enhancing its detectability via GC.

The CrystalLux-4000M gas chromatograph is a versatile instrument known for its robust thermal control, high-resolution capillary columns, and precise injector systems. The following chromatographic parameters are used for pregabalin detection [3]:

Column: Capillary column HP-5MS (30 m × 0.25 mm × 0.25 μm)

Carrier gas: Helium at a flow rate of 1.2 mL/min

Injection mode: Splitless, with injector temperature at 250°C

Oven temperature program: Initial 80°C (hold 1 min), ramp to 280°C at 20°C/min (hold 5 min)

Detector: Flame ionization detector (FID) or MS detector (optional)

Derivatized pregabalin retention time: ~7.5–8.0 minutes

This method allows for sharp peak resolution, minimal matrix interference, and detection limits in the low ng/mL range. Quantification is performed by comparing peak areas against an internal standard (e.g., diazepam or gabapentin).

Method validation includes testing for linearity, sensitivity, specificity, repeatability, and robustness. Linearity has been observed across the 10–1000 ng/mL range, with recovery rates exceeding 85%. Intra- and inter-day precision values remain below 5%, confirming reproducibility.

In forensic toxicology, this method has been used effectively in post-mortem and clinical cases involving overdose, impaired driving, or drug-facilitated assault. The ability to detect and quantify pregabalin accurately has allowed experts to link pharmacological levels with behavioral outcomes and physiological impairments.

Additionally, the method supports retrospective toxicological review due to the stability of derivatized samples and reproducibility of chromatograms stored digitally through CrystalLux-4000M's proprietary software interface [4].

CONCLUSION

The gas chromatographic analysis of pregabalin using the CrystalLux-4000M presents a highly reliable and scientifically rigorous method for detecting this increasingly misused drug in biological fluids. Given pregabalin’s pharmacological profile and legal classification, accurate detection is essential for both clinical diagnostics and forensic investigations. The combination of proper sample preparation, derivatization, and optimized chromatographic settings ensures the method’s applicability in various toxicological contexts. Moving forward, integrating this approach with mass spectrometry (GC-MS) could further enhance specificity and aid in broader toxicological screening panels.

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