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A CONSPECTUS ON DIFFERENT TYPES OF SPECTROPHOTOMETRIC AND CHROMATOGRAPHIC APPROACH FOR NOVEL HYPNOTIC DRUG-TASIMELTEON

KARTHIK RAJA R*, KAVITHA J* AND K MANIKANDAN

Department of Pharmaceutical Analysis, SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur, Chengalpattu district – 603 203, Tamil Nadu, India

***Corresponding Author: Dr. J.Kavitha: E Mail: kavitha0208@gmail.com**

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ABSTRACT

Objective: The ultimate aim of this current study is to review on different Spectrophotometric and chromatographic approaches for evaluating a novel hypnotic drug- Tasimelteon. To review the different analytical techniques conducted to determine the Tasimelteon. The available Spectrophotometric method of Tasimelteon stated in this article has accurate and precise results. High performance liquid chromatographic method mentioned in the article was robust enough to give out accurate and precise reports within a short run time. Liquid chromatographic/ mass spectrophotometric methods performed on human plasma shows precise results with specific limits. Reversed phase-high performance liquid chromatographic methods reported are accurate and precise for Tasimelteon. This article encapsulates a few developed and validated analytical methods available for the determination of Tasimelteon.

Keywords: Tasimelteon, Ramelteon, Spectrophotometric, Chromatographic

INTRODUCTION

Tasimelteon is a novel chemical entity globally approved for the sleep-wake disorder (Non-24hrs) **[1]**. The United States Food & Drug Administration licensed the use

of this medication in 2014; it is marketed under the trade name Hetlioz. Adults with irregular sleep-wake cycles (non-24-hour cycles) get a sleep-wake rhythm disorder **[2]**. In the propionamide subclass of 1-benzofurans, Tasimelteon, the amide hydrogen is substituted by [(1R,2R) group-2-(2,3-dihydro-1-benzofuran-4-yl] cyclopropyl] ($C_{15}H_{19}NO_2$) **[3][4]**. It has a biological role like an agonistic effect on melatonin receptor **[5]**. Tasimelteon is selective binds with MT1 and MT2 receptors and activates the MT production which leads to improvement in the sleep cycle **[6]**. Reported techniques are grouping depending on the bulk and formulated market products and combination with other drugs. UV-spectrophotometric method and chromatographic techniques. Chemical structures of Tasimelteon are shown in **Figure 1 [7]**. The other related drug to Tasimelteon is Ramelteon **[8]**. Solubility profile of Tasimelteon is very soluble in methanol, 95% ethanol, ACN, Isopropanol, PEG-300 **[9]**.

Elemental analysis, IR and UV spectroscopy, H1, C13 and COSY NMR spectroscopy, heteronuclear various quantum cohesion and heteronuclear various bond connection, and spectrometry (MS, such as Mass spectrometric) have all successfully shown the chemical composition of Tasimelteon. Tasimelteon chemical composition, solid phase shape, and absolute and relative stereo configuration all were established in addition using single-crystal X-ray diffraction research.

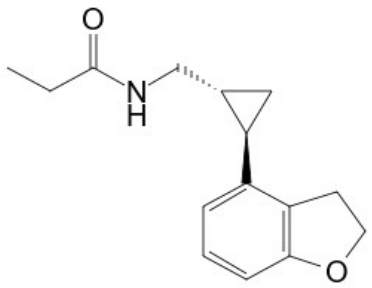

Figure 1: Chemical structure of Tasimelteon

ANALYTICAL TECHNIQUES

Spectrophotometry

A Spectrophotometer is an instrument that measures the amount of light that an analyte (the component under investigation) absorbs at a specific wavelength in order to calculate its concentration. Light from the ultraviolet and visible portions of the electromagnetic spectrum is used in Ultraviolet/ visible (UV/ Vis) spectrophotometry. This wavelength can enhance the energy levels of the ground state electrons in molecules or atoms, which results in absorption at wavelengths unique to each molecule.

Chromatography

High-performance liquid chromatography (HPLC), which is a well-known technology for separating analytes. HPLC is a

compelling innovation for investigating a wide scope of tests. The dissemination of (test) between a versatile stage and a fixed stage is the reason for HPLC division. The particles are eased back while going through the fixed stage, contingent upon the compound design of the analyte. The time an example spends on a segment is controlled by the particular intermolecular collaborations between its atoms and the pressing material. Subsequently, different parts of an example elute on various occasions. Subsequently, the example fixings can be isolated.

Reverse phase (RP) – HPLC includes the division of atoms dependent on their hydrophobicity. Sections that are utilized comprise of an alkylsilica-based, non-polar sorbent connected with carbon-18 (C_{18}) that permits division dependent on the hydrophobic restricting of the solute atom from the portable stage to the immobilized hydrophobic ligands connected to the sorbent. Different sections might be utilized, for example, carbon-8 or cyano, the two of which have a more prompt extremity.

Liquid chromatography coupled with Tandem Mass Spectrophotometer (LC-MS/MS) is a fantastic analytical technique that combines the isolating power of fluid chromatography with the sensitive and specific mass examination capability of triple quadrupole mass spectrometry. A portable stage traveling through at high strain extracts analytes of interest through a stationary stage. Different movement rates are influenced by the substance connection between the parts of the example, the fixed stage and the portable stage, through the LC section, affecting a division. The diverse spectrum of permanent stage and portable stage mixes considers reworking a partition to accommodate a variety of complex layouts. Following elution from the LC section, the mass spectrometer is synchronized. The LC section profluent is nebulized, desolvated, and ionized in the mass spectrometer for an LC-MS/MS framework, resulting in charged particles. These charged particles are then forced to flow through a vacuum tube.

ANALYTICAL METHODS FOR TASIMELTON AND RAMELTEON

Analytical methods for estimating Tasimelteon in bulk that is simple, accurate, precise, and quick. The maximum Tasimelteon concentration was reported to be 225.0 nm in acetonitrile and double distilled water (50:50). The amplitude and Area under the curve of the spectrum have been taken into account in all five methods of UV-Spectrophotometry based on Zero Order, First Order, and Second Order derivatives.

Tasimelteon obeyed linearity in the concentration range of 4-20 µg/mL in all five methods, with a correlation coefficient of 0.999. According to the International Conference on Harmonization (ICH) requirements, all of the procedures were validated. All of the offered approaches were found to be linear, accurate, precise, and robust, as well as sensitive enough.

A unique degradation product was found using the LC-MS-IT-TOF system in addition to the previously mentioned ones. The development and validation of a highly sensitive liquid chromatography connected with spectrometry (LC-MS/MS) method for the simultaneous detection of Ramelteon as well as its biologically active form M-II in human plasma using this method, a clinical pharmacokinetic body of research shows Chinese volunteers produced encouraging outcomes.

RP-HPLC was used to develop a new method for estimating Tasimelteon. The average retention duration was discovered to be 2.482 minutes. The analytical method was verified using ICH guidelines (ICH, Q2 (R1)), with a LOQ value of 9.92.

Table 1: Analytical methods for the estimation of Tasimelteon

S. No	Agent/Drug	Mode/technique	Report
1.	Tasimelteon [9]	UV-visible spectrophotometric	➢ Wavelength: 225nm ➢ Solvent: ACN:Double distilled water (50:50) ➢ Linearity range: 4 to 20µg/ml ➢ Correlation coefficient : 0.999
2.	Tasimelteon [10]	RP-HPLC	➢ Wavelength: 265nm ➢ Stationary phase: Thermosil (5µm), 184.5×150mm ➢ Mobile phase:- methanol : water (65:35%v/v) ➢ Flow rate: 0.8ml/min ➢ Injection volume: 20µl ➢ Linearity range: 30 - 150 µg/ml ➢ Correlation coefficient: 0.997% ➢ LOD: 2.97µg/ml ➢ LOQ: 9.92µg/ml
3.	Ramelteon [11]	UV-visible spectrophotometric	➢ Wavelength: 287nm ➢ Solvent: methanol ➢ Linearity range: 10-50µg/ml
4.	Tasimelteon [12]	LC-MS/MS (liquid -liquid extraction)	✓ Stationary phase: Agilent zorbax,eclipse, C18(4.6×50mm,5µm) ➢ Mobile phase:- ACN: 0.02% formic acid buffer (85:15%v/v/v) ➢ Flow rate: 0.5 ml/min ➢ Linearity range: 0.30 to 299ng/ml ✓ 20mg TASIMELTEONcapsule- • Cmax:- 314±147ng/ml • Tmax:- 0.54±0.22 hrs
5.	Tasimelteon [13]	LC-DAD METHOD	➢ Wavelength: 281nm

			➢ **Mobile phase: ACN: Acetate buffer (0.025M PH 4.5): H_2O (40:10:50%v/v/v).** ➢ **Stationary phase: Ascentis express pentaflurophenyl propyl (F5) -bonded fused-core particle column (100×4.6mm, 2.7µm).** ➢ **Flow rate: 0.8ml/min**
6.	**Tasimelteon [13]**	**UPLC (ruggedness assessment)**	✓ **Mobile phase: 0.1%(v/v) formic acid in water: 0.1%(v/v) formic acid in ACN (60:40%v/v)** ✓ **Stationary phase:monolithic silica (chromolith® high-resoultion RP-18e, 100×4.6mm)**
7.	**Tasimelteon [13]**	**LC/MS-IT-TOF**	**To elucidate the degradation products.**
8.	**Ramelteon [14]**	**HPLC**	➢ **Wavelength: 285nm** ➢ **Stationary phase: OSD column** ➢ **Mobile phase: ACN:0.45M phosphate buffer [Ph-6.8] (40:60%v/v)** ➢ **Flow rate: 1.2ml/min** ➢ **Linearity range: 500-1500 µg/ml** ➢ **RT: 7min**

Several medications and pharmaceutical formulations have lately been released in the pharma business all around the world. For the most part, researchers have recorded the development of analytical methods as well as integrity indication parameters. Tasimelteon active pharmaceutical ingredient and dosage formulations have not been assessed for the research indicated above.

CONCLUSION

This article encapsulates different analytical methods available for the assessment of Tasimelteon and its related drug Ramelteon. Review of reported spectroscopic and chromatographic approaches for identifying novel hypnotic drugs that have been developed and validated. Only a few methods like UV-Vis, RP-HPLC, and LC-MS are available for Tasimelteon estimation. The mobile phase containing ACN, and formic acid were commonly used in most of the chromatographic techniques to provide high resolution in the report. Development of greener methods for the estimation of Tasimelteon is recommended.

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CONFLICT OF INTEREST

The authors declare that NO conflict of interest among us.

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