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A Review on Validated RP-HPLC Method for the Simultaneous Estimation of Serdexmethylphenidate and Dexmethylphenidate in Bulk and Pharmaceutical Dosage Form

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Abstract:- An ADHD medication called Azstarys was approved by the FDA in March 2021.Because it combined serdexmethylphenidate and dexmethylphenidate for the first time, it is unique. Treatment for Attention Deficit Hyperactivity Disorder (ADHD) begins with a prodrug called serdexmethylphenidate. CNS stimulants include serdexmethylphenidate. People six years of age and older with attention deficit hyperactivity disorder (ADHD) are taken serdexmethylphenidate, a prodrug of dexmethylphenidate, in addition to dexmethylphenidate. Serdexmethylphenidate is a prodrug of the central nervous system stimulant dexmethylphenidate. It alters neurotransmission in the central nervous system by increasing extracellular dopamine and norepinephrine numbers.3[11] As a central nervous system stimulant, serdexmethylphenidate carries a risk of usage, addiction, and abuse that should be monitored. In addition, patients need to be assessed. The accuracy, precision, linearity, robustness, limits of detection and quantitation, system adaptability, robustness, and other factors can all be used to validate the RP-HPLC technology.[1]

Keywords:- *Dexmethylphenidate, Serdexmethylphenidate, RP-HPLC, Development, Validation.*

I. INTRODUCTION

FDA authorized Azstarys, a central nervous system stimulant, in March 2021 to treat ADHD.It is special since it was the first drug to mix dexmethylphenidate and serdexmethylphenidate. A prodrug called serdexmethylphenidate is used as the first line of treatment for attention deficit hyperactivity disorder (ADHD). Serdexmethylphenidate is a CNS stimulant. [13]A prodrug of dexmethylphenidate called serdexmethylphenidate is prescribed in conjunction with dexmethylphenidate to treat attention deficit hyperactivity disorder (ADHD) in individuals six years of age and older. A prodrug of the CNS stimulant dexmethylphenidate, serdexmethylphenidate raises extracellular dopamine and norepinephrine levels in the central nervous system, changing neurotransmission.3 Because serdexmethylphenidate is a CNS stimulant, there is a danger of abuse, misuse, and dependency that needs to be watched out for. [10] Additionally, patients should be evaluated prior to beginning therapy and closely watched for cardiovascular abnormalities, as CNS stimulants are linked to elevated blood pressure, heart rate, and risk of serious cardiovascular reactions, such as stroke, myocardial infarction, and sudden death. The chemical dexmethylphenidate is a member of the class of organic substances called alkylamines.[2]

II. LITERATURE REVIEW

- *RP-HPLC Methods:*

- *Veena Boda, Ajitha Makula,2022:*

To estimate serdexmethylphenidate and dexmethylphenidate in tablet dose form simultaneously, a straightforward, accurate, and precise approach was created. Chromatogram was passed through Standard Ascentis C18 (150 x 4.6 mm, 2.4 m) column at a flow rate of 0.9 ml/min. The mobile phase, which included Buffer 0.01N NAH2PO4, was pushed through the column with acetonitrile taken at a 60:40 ratio. 0.01N NAH2PO4 buffer was the buffer utilized in this procedure. The ambient temperature was kept at 30°C. The chosen optimized wavelength was 228 nm. It was discovered that the retention timesof dexmethylphenidate and serdexmethylphenidate were 2.925 and 2.133 minutes, respectively. It was discovered that the percentage RSD of the dexmethylphenidate and serdexmethylphenidate were, respectively, 0.4 and 0.6. %) Forserdexmethylphenidate and dexmethylphenidate, respectively, recovery was found to be 99.98% and 100.50%. LOD and LOQ values derived from the regression formulas.[3]

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- *Sunil Rayudu, M. Manoranjini, D. Rama shekara reddy,2021:*

A straightforward, focused, verified, and precisely specified stability demonstrating isocratic RP-HPLC methodology for the simultaneous measurement of serdexmethylphenidate and dexmethylphenidate identification. A mobile phase consisting of acetonitrile and 0.1% orthophosphoric acid (70:30) was used in the chromatographic technique, which employed an inertsil ODS column of 250 x 4.6 mm and 5 µ. The experimental conditions were 1 ml/min flow rate and 262 nm detection wavelength using PDA detector. In the process of validating the method, recovery, specificity, linearity, accuracy, robustness, and ruggedness were assessed. The findings fell within an acceptable range. Following guidelines from the International Conference on Harmonization (ICH), the suggested method's validation was completed. This straightforward, well-defined, confirmed, and selective stability demonstrates isocratic RP-HPLC technique.[3]

- *M Tejaswi, C. Parthiban, M. Sudhakar,2021:*

It was possible to simultaneously estimate serdexmethylphenidate and dexmethylphenidate in tablet dosage form using an easy-to-use, precise, and accurate approach. A standard Discovery C18 (150 x 4.6 mm, 3.5 mm) mobile phase containing 0.9 milliliters per minute of buffer 0.01N Na2HPO4 were used to pump acetonitrile, which was taken in a 60:40 ratio, through the column. This technique used buffer, which had a pH of 3.4, adjusted with the addition of 0.1% OPA and 0.01N Na2HPO4. 30°C was the constant temperature.

A wavelength of 228 nm was chosen as the optimized one. [14] Thefindings indicated that the retention times for dexmethylphenidate (2.791 min) and serdexmethylphenidate (2.435 min) respectively. It was discovered that the percentage RSD of the dexmethylphenidate and serdexmethylphenidate was 0.6 and 0.8, respectively. (%) 100.13% and 100.16% recovery rates, respectively, were achieved for serdexmethylphenidate and dexmethylphenidate.[4]

- *Akshay Namdev Rao Londhe* and T. M. Kalyankar:*

To estimate serdexmethylphenidate and dexmethylphenidate simultaneously in API and pharmaceutical dosage forms, a straightforward, accurate, robust, and exact reverse phase RP-HPLC method has been devised and validated. Using an Agilent C18 150x 4.6mm, 5 column for chromatographic separation and a WATERS 2695 HPLC system for PDA detection, this approach uses a basic isocratic mobile phase of acetonitrile: 0.01N potassium dihydrogen phosphate (65:35). We discovered that the average retention durations for dexmethylphenidate (2.853min) and serdexmethylphenidate (2.253min) were similar.

The assay yielded results of 100.64% and 100.88% for both serdexmethylphenidate and dexmethylphenidate when conducted using tablets. These results demonstrate the utility of the technology for regular analysis. With an R2 of 0.999 for all of the medications, it was discovered that serdexmethylphenidate and dexmethylphenidate were linear.[5]

- *Khadiga M. Kelani, Ahmed M. W. Nassar, Gamal A. Omran, Samir Morshedy, Ahmed Elsonbaty& Wael Talaat,2023:*

To detect serdexmethylphenidate (SER.DMP) and dexmethylphenidate (DMP) simultaneously in the presence of their breakdown products, two chromatographic techniques have been developed and refined. High performance liquid chromatography in reversed phase with diode array detection is the first technique (HPLC–DAD). Using a mixture of 5 mM phosphate buffer (pH 5.5): acetonitrile (40:60, v/v) as a mobile phase, flow rate 1 mL/min, and detection at 220 nm, isocratic separation was performed on a Waters X-bridge Shield RP18 column (150×3.9×5 µm particle size). Using methanol: chloroform (70:30, v/v) as a mobile phase and UV scanning at 220 nm, the second approach is a thin-layer chromatography (TLC)—densitometry method. With a linearity range of 2.5–25 µg/mL in the HPLC method, SER.DMP had a LOD of 0.051 µg/mL and a LOQ of 0.165 µg/mL.[6]

- *GaddeyPridhvi Krishna & Raja Sundararajan,2021:*

For the purpose of simultaneously evaluating serdexmethylphenidate and dexmethylphenidate in pure medication and formulation, an easy-to-use, accurate, precise, and reasonably priced ultra-pressure liquid chromatographic technology was developed. Serdexmethylphenidate and dexmethylphenidate have separated well according to the procedure. For serdexmethylphenidate, the retention period was 1.476 minutes, while for dexmethylphenidate, it was 1.806 minutes. The medicine formulation was subjected to hydrolysis, photolysis, basic, acidic, and thermal stress conditions. Thus, projected analytical approach was used to analyze stressed samples. Using a linear calibration curve and peak area-based ultra violet detection at 245 nm, quantitation was accomplished. Regarding serdexmethylphenidate, the concentration ranges were 6.525–39.15 µg/ml and 1.3–7.8 µg/ml, respectively. For serdexmethylphenidate and dexmethylphenidate, the LODs were 0.17 µg/ml and 0.03 µg/ml, respectively. 0.53 µg/ml was the LOQ. [7]

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- *Gowri Gollu, Sowjanya Gummadi,2023:*

Serdexmethylphenidate and dexmethylphenidate were simultaneously quantified in a fixed capsule dosage form using a straightforward, reliable stability indicating RP-HPLC approach. This approach, which complies with ICH requirements, is the first to be published for simultaneous estimation and quantification of degradation products resulting from forced dosage form stressing. Using a mobile phase of trifluoro acetic acid and acetonitrile (70:30 v/v) at a flow rate of 1 mL and monitoring at 265 nm for ten minutes, the chromatographic separation was achieved on a Waters X-terra C18 column. With retention durations of 2.71 and 7.33 minutes, respectively, serdexmethyl and dexmethylphenidate were eluted. For serdexmethyl, the technique produced linear results between 4.2 and 63 µg/mL (0.9994).[8]

- *Subrahmanyam Talari,V.Anuradha,S. N. Murthy Boddapati,Komala Sai PrathuyasaAyithabotla, 2021*

There were 4.258- and 5.629-minute retention durations for dexmethylphenidate and serdexmethylphenidate, respectively. The method for estimating Dexmethylphenidate and Serdexmethylphenidate has been verified through testing of linearity, accuracy, precision, stability, and forced degradation, which includes hydrolysis, peroxide, acid, and heat degradation.[15] The quality was multiplied six times to evaluate the system's appropriateness parameter, and the results showed that they were well within acceptable bounds. After conducting linearity research at 10% to 150 percentage points, it was discovered that the regression coefficients for the two medications were 0.999. The precision values for serdexmethylphenidate were 1.24 and for dexmethylphenidate were 0.54. The percentage of medicines recovered ranged from 98 to 102%, which is considered satisfactory.[9]

III. CONCLUSION

The purpose for this review article is to study about the previous works done on the simultaneous estimation of Serdexmethylphenidate and Dexmethylphenidate by using RP-HPLC method and other chromatographic techniques and also for getting knowledge for developing new method and validating the developed method for simultaneous estimation of Serdexmethylphenidate and Dexmethylphenidate by RP-HPLC.

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