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Review Article

An Examination of a Novel Analytical Methods on Tolvaptan Estimation

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ABSTRACT

Analytical technique development and validation are part of the ongoing and interrelated processes associated with research and development, quality assurance, and control. These processes are essential for risk management and equivalence evaluations because they support the creation of standards for product-specific acceptance and yield reliable results. Analytical methods' suitability for their intended uses is ascertained through validation procedures. A thorough literature review states that analytical techniques like UV spectroscopy, RP-HPLC, and HPTLC can be used to analyze Tolvaptan either by itself or in conjunction with other drugs. The metrics, including accuracy, precision, robustness, and other aspects of analytical validation, were thoroughly examined in compliance with ICH guidelines. Because the techniques are straightforward, sensitive, and reproducible, they can be used to both bulk and tablet dose versions of Tolvaptan. The study also highlights the suitability and limitations of several established analytical techniques for Tolvaptan analysis. This comprehensive report will be extremely useful to researchers working on Tolvaptan trials.

INTRODUCTION

Tolvaptan is an Diuretic medicine that works at low sodium in the blood or hyponatremia. Tolvaptan chemically known as N-[4-[5R]-7-chloro-5-hydroxy-2,3,4,5, -tetrahydro- 1-benzazepine-1-carbonyl]-3-methylphenyl]-2-methylbenzamide. It is class of vasopressin V2 receptor antagonists. Tolvaptan is also used to slow kidney function decline in adults who are at risk of rapidly progressing autosomal dominant polycystic kidney disease. Tolvaptan is non-peptide vasopressin (VP) V2 receptor antagonist that inhibits water re-absorption in the kidney by competitively blocking VP binding, resulting in water diuresis without significantly changing total electrolyte excretion.[6] A bioanalytical method encompasses a series of steps involved in gathering, processing, storing and analyzing a biological matrix (such as blood, plasma, serum, or urine) to detect a chemical compound. Bioanalytical Method Validation is the systematic

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process employed to establish the suitability of a quantitative analytical method for biochemical applications.

ANALYTICAL METHODS REPORTED ON TOLVAPTAN:

1. V. Kalyana Chakravarthy *et al.,* (2011) have developed quick and accurate way to measure tolvaptan in prescription dose forms and bulk. The process is quick, easy, and selective. The Tolvaptan technique presented is linear over the 37.285 µg/mL to 298.282 µg/mL range. The assay determination method's precision was less than 2.0% RSD. An AMCHEMTEQ-USA-ACI C18 (150 mmx4.6 mm I.D.; particle size 5 µm) was used to achieve separation. Acetonitrile (40:60) is used as the eluent in a column and water at a flow rate of 1.0 mL/min. At 254 nm, UV detection was carried out. Tolvaptan has a molecular weight of 448.94 and is a white to off-white crystalline powder. Tolvaptan is nearly insoluble in hexane and water, but soluble in methanol and benzyl alcohol. The melting point of tolvaptan was roughly 224°C.[1]

2. Bikui zhang *et al.*, (2013) have developed tolvaptan is a selective vasopressin V2-receptor antagonist mainly used for the treatment of hyponatremia. The creation and verification of an LC–MS/MS technique for the measurement of tolvaptan in human plasma were detailed in this work. Acetonitrile containing 2-demethyl tolvaptan (internal standard, IS) was used to precipitate proteins in order to prepare the sample. On a Zorbax XDB C18 column, chromatographic separation was carried out using an isocratic mobile phase made of methanol (25:75, v/v) and water (containing 0.1% formic acid). Positive electrospray ionization in tandem-mass spectrometry was used to determine the analytes. The tolvaptan and IS multiple reaction monitoring (MRM) transitions were carried out at m/z 449.2→252.1 and m/z 435.2 → 238.1, respectively. The assay has a lower limit of quantification of 0.457 ng/mL and was linear across the concentration range of 0.457–1000 ng/ml. At three concentration levels (0.914, 111, and 800 ng/mL), the intra- and inter-day precisions were less than 15%, and the accuracies fell between 97.7 and 107.8%. The matrix effect ranged from 89.3 to 99.5%, while the mean recovery ranged from 99.2 to 104.6%. Tolvaptan remained stable in every test scenario. This validated method was successfully applied to a pharmacokinetic study in healthy volunteers after oral administration of single- dose tolvaptan tablets.[2]

3. B. Prathyusha *et al.,* (2013) have developed for the purpose of estimating tolvaptan in pharmaceutical dosage forms, a novel reverse phase high performance liquid chromatography (RP-HPLC) approach that is straightforward, accurate, exact, robust, specific, sensitive, and quick was created and verified. Acetonitrile and 0.01M sodium dihydrogen phosphate in a 60:40 ratio were utilized in the mobile phase of a Nucleosil C18. The wavelength was measured at 269 nm, and the flow rate was 0.6 ml/min. The primary peak was seen on the chromatogram with a retention time of 3.055 minutes. The developed method's linearity, accuracy, precision, specificity, limit of detection, limit of quantification, and robustness were all validated in accordance with ICH criteria. It was discovered that the linearity ranged from 25 to 150 mcg/ml. Recovery of Tolvaptan was found to be in the range of 99.74-99.87% %. The system precision and method precision was found to be within limits with % RSD of

0.773 and 0.024%. The developed method was found to be cost effective and was successfully employed for the determination of the same in various formulations.[3]

4. Masayuki Furukawa *et al.,* (2014) have developed powerful, highly specific, and oral nonpeptide vasopressin V2 receptor antagonist, tolvaptan (TVP) was created by Otsuka Pharmaceutical Co., Ltd. (Tokyo, Japan). It causes a decrease in urine osmolality, a rise in urine volume and serum Na+ concentration, and aquaresis. In addition to treating hyponatremia and heart failure's volume overload, TVP is also being developed to treat hepatic edema and autosomal dominant polycystic kidney disease. Humans produce a variety of metabolites as a result of TVP's primary CYP3A4-mediated dehydrogenation and hydroxylation. The hydroxy benzazepine ring undergoes dehydrogenation, forming a metabolite of one oxide of the hydroxy group at position 5 (MOP-21826). This TVP metabolic response can be reversed. TVP contains an asymmetric carbon at the benzazepine ring's fifth position. Rats' oral pharmacokinetics of TVP were examined. The liquid chromatography with tan-dem mass spectrometry (LC–MS/MS) methods for determining TVP in human plasma have been reported. We have published the LC– MS/MS method fulfilled quantitative analysis of TVP and its nine metabolites in rat serum. In this study, we developed a high-performance liquid chromatography (HPLC) method for the separation and determination of TVP enantiomers in the serum in order to clarify biotransformation and pharmacokinetic profiles for R-TVP and S-TVP in rats and dogs. This is the first reported paper on an analytical method for determining TVP enantiomers in animal serum using HPLC.[4]

5. S. Rzeppaa *et al.*, (2016) have developed World Anti-Doping Agency (WADA) has banned tolvaptan under class S5: Diuretics and Masking Agents. Humans excrete less than 1% of the administered dosage in urine. There is little information available about human metabolism, particularly with regard to metabolite excretion in urine. High performance liquid chromatography coupled to tan-dem mass spectrometry (HPLC-MS/MS) was used to develop and test a dilute-and-shoot analytical technique. This method's component ion transitions are readily included into screening techniques already in use for routine doping

analysis to identify diuretics. One male participant received a single dose of tolvaptan, and over the course of 24 hours, urine tests showed trace amounts of the medication. Furthermore, one carboxyl metabolite with a cleaved benzazepine ring system and hydroxyl metabolites of tolvaptan were discovered. These metabolites showed detection times of up to 150 h. An inclusion of these metabolites in the methods used in doping control analysis seems therefore to be of value.[5]

6. **Mangesh R. Patil *et al.*, (2019)** have developed straightforward and affordable UV-Spectrophotometric techniques for Tolvaptan measurement that apply the hydrotropic solubilization phenomenon, such as the Zero Order UV-Spectrophotometric absorbance approach and the Zero Order Area under curve (AUC) method. A non-peptide antagonist of the vasopressin V2 receptor is tolvaptan. It doesn't dissolve at all in water. Tolvaptan's solubility was improved by the addition of sodium lauryl sulfate (SLS), a hydrotropic agent, at 5% w/v. It was discovered that Tolvaptan's maximum absorption occurred at

269 nm. The techniques for analyzing tolvaptan in the wavelength range of 263.2-282.2 nm are based on measuring absorbance at 269 nm and integrating the area under the curve. For both methods, the correlation coefficient value (r2) was greater than 0.99, and the medication exhibited linearity within the concentration range of 3 to 18 µg/mL. The proposed methods were validated for accuracy, precision, repeatability and ruggedness, as per ICH guidelines. The proposed methods were applied for qualitative and quantitative estimation of Tolvaptan in pharmaceutical formulation and results were found in good agreement with the label claimed.[6]

7. Shunta Akutsu *et al.*, (2019) have developed method for detecting 5R and 5S-tolvaptan and their monohydroxylate enantiomers in human plasma using simultaneous quantitative liquid chromatography-tandem mass spectrometry and applying it to patient samples. A polysaccharide derivative chiral column was used in reversed-phase elution mode to separate the deproteinized plasma specimens. The positive ion electrospray ionization mode was used to operate the mass spectrometer. Recombinant CYP3A4/5 digestion of 5R- and 5S-tolvaptan allowed for the identification of the chromatographic peaks of tolvaptan monohydroxylate enantiomers. The calibration curves ranged over the plasma concentrations of 0.25–125 ng/mL for 5R- and 5S-tolvaptan, 0.025–12.5 ng/mL for 4R5R- and 4S5S-diols, and 0.025–38.15 ng/mL for 4S5R-, 4R5S-, 3S5R-, and 3R5S-diols with a large variation. Their pre- treatment recovery rates and matrix factors in human plasma were 85.2–112.9% and 86.9–113.1 %, respectively. For all analytes, the accuracy and imprecision were 92.3– 113.8% and 3.5–14.6 percent, respectively, within and between days. In patients with heart failure who underwent a 5-fold dilution technique, the plasma concentration ranges of 5R- and 5S-tolvaptan, 4R5R-, 4S5R-, 4R5R-, 4R5S-, 3S5R-, and 3R5S-diols were 0.634–28.4, 0.525–15.4, 0.0970–4.08, 6.82–108, 0.271–6.49, 0.394–4.18, and 4.81–39.8 ng/mL,respectively.[7]

8. Kohei Hoshikawa *et al.*, (2019) have developed tolvaptan is converted to major metabolites including three monohydroxylates (DM-4110, DM-4111 and DM-4119), an oxidate (MOP-21826) and a carboxylate (DM-4103) in humans. This study developed a simultaneous quantitative method for tolvaptan and its five major metabolites in human plasma using liquid chromatography coupled to tandem mass spectrometry. Acetonitrile-deproteinized plasma samples were separated using a 3-lm particle size octadecyl silyl column that was 250 mm long and had a straightforward linear gradient program set to operate for 15 minutes at a flow rate of 0.3 mL/min. This technique was used to analyze plasma samples taken from 20 patients with heart failure receiving 3.75–15 mg of tolvaptan. The pharmacokinetics of oral tolvaptan, including the identification of its main metabolites, can be assessed in heart failure patients using this proven technique with respectable analytical performance.[8]

9. Juanjuan Jiang Lei Tian Yiling Huang Yan Yan Yishi Li *et al.*, (2019) have developed tolvaptan and its two primary metabolites can be measured using the liquid chromatography tandem mass spectrometry (LC-MS) method, which was initially created and approved for use in human studies as a compliance indicator in clinical research. Due to the structural similarities between tolvaptan and its various metabolites, the procedure was refined to

achieve high analysis throughput and chromatographic and mass spectrometry separation of the endogenous interference and isotope ions (Page 2 of 26 Page 3 of 26). A mobile phase consisting of acetonitrile, water, and formic acid (65:35:0.25, v/v/v) was used for isocratic elution in order to separate tolvaptan, its two primary metabolites, and the internal standard from human serum (0.1 mL) using solid-phase extraction. The samples were then separated on a Waters nova-Pak C18 column (150⁄3.9 mm, 5µm). The entire duration was reduced to 3.5 minutes. For all three analytes, the technique was validated over a linear range of 1 to 500 ng/mL with satisfactory accuracy and precision both within and between assays.[9]

10. Noorbasha Khaleel *et al., (*2020) have developed for the purpose of quantifying tolvaptan in pharmaceutical dosage forms and bulk drugs, a particular stability-indicating reversed- phase high performance liquid chromatography (HPLC) method has been developed and validated. Inertil ODS-3V column (150 x 4.6 mm, 5.0 mm) kept at 30°C with a mobile phase made up of 0.1% orthophosphoric acid and acetonitrile in a 40:60%V/V ratio on isocratic mode at a flow rate of 1.0 mL/min and a detection wavelength of 254 nm are the ideal conditions for the developed HPLC method. It was discovered that tolvaptan had a retention duration of 2.59 minutes and that its concentration ranged linearly from 37.5 to 225.0 µg/mL. Tolvaptan recovery rates ranged from 98.30 to 101.13 percent on average. At every level, the percent relative standard values were less than 2.0, indicating adequate precision and accuracy. The method's robustness was determined to satisfy the acceptance robustness was determined to satisfy the acceptance requirements. The stress study against qualified working standard of Tolvaptan, indicated that the developed HPLC method was stability- indicating, conducted as per ICH requirements. The developed method can be handy in the quality control of bulk and pharmaceutical dosage forms.[10]

11. A. S. Sutar *et al., (*2021**)** have developed simple, sensitive, and accurate, it can be used as a stability indicator to identify degradation products in regular medication analysis. Response surface approach was used to create and optimize the stability indicating RP-HPLC for tolvaptan determination. Using response surface approach and design of experiment, the mobile phase was created and refined. The ideal mobile phase consisted of acetonitrile and phosphate buffer with a pH of 5.5 (70:30% V/V). At 1 ml/min, the flow rate was kept constant. Guidelines were followed for conducting stress studies. The method was validated in compliance with regulatory standards, and the findings fell within the guidelines' stipulated bounds. Tolvaptan was eluted at 3.24 min. It shows linearity from 2.5-15 µg/ml. Coefficient of correlation was 0.999, LOD and LOQ values were 1.0871 (µg/ml) and 3.2942 (µg/ml). Precision was determined with % RSD of 0.8669 and 0.9709%, mean percentage Recovery value was found to be 99.88 ±1.2.[11]

12. Mangesh R. Patil *et al*., (2021) have developed by inventive, eco-friendly, simple, consistent and coalescing TLC Densitometry approach to a pharmaceutical estimation of Tolvaptan in the bulk and tablet matrix. For successful sample preparation and further analysis in both normal and reverse- phases, hydrotropic solubilization was chosen. The determination was performed employing densitometric

estimation using ultraviolet exposure at 271 nm. Separatly the separation was accomplished on RP-18 F254S and 60- F254 (10 x 10 cm) aluminium-backed silica gels as stationary phases. For both the normal and reverse phase modes, the ideal mobile phases were acetonitrile: water (3: 2 v/v) and carbon tetrachloride: methanol (3.5: 1.5 v/v). creative, environmentally responsible, straightforward, reliable, and integrating TLC Tolvaptan in the bulk and tablet matrix is estimated pharmaceutically using a densitometry technique. Hydrotropic solubilization was selected for effective sample preparation and subsequent analysis in both normal and reverse phases. Densitometric estimate utilizing UV exposure at 271 nm was used to get the determination. As distinct stationary phases, the separation was accomplished on 10 x 10 cm aluminium-backed silica gel 60-F254 and RP-18 F254S. Carbon tetrachloride: methanol (3.5: 1.5 v/v) and acetonitrile: water (3: 2 v/v) were the optimal mobile phases for the normal and reverse phase modes, respectively. Acidic, alkaline, and oxidative stress conditions have all been linked to significant loss. As a DoE methodology, Box-Behnken design was used to guarantee system efficiency and assess method robustness. The International Conference on Harmonization (ICH) approved the established procedures for accuracy, robustness, and roughness[12]

13. Lajporiya Mobina I *et al.*, (2021) have created and validated a new, easy, quick, accurate, and precise for the determination of tolvaptan in bulk and tablets dosage forms an environmentally friendly RP HPLC and UV method was developed and validated, followed by forced degradation studies. Tolvaptan dosage in tablet and bulk form was estimated using the UV-Spectroscopic technique. The 4% aq. SLS solution was used as the solvent for the tolvaptan UV analysis. A solution containing 10µg/ml was scanned in the UV area between 200 and 400 nm, and the λmax value was ascertained. On a Sunsil C18 150 mm x 4.6 mm x 5µ column, the RP-HPLC technique was created utilizing acetonitrile: water [45:55] as the mobile phase at a flow rate of 1.0 ml/min with UV detection at 266 nm. Findings showed that the greatest absorption occurred at 266 nm. The wavelength 266 nm was selected for further analysis of tolvaptan. The calibration curve was determined using drug concentrations ranging from 20-100 µgm/ml. it was concluded that the developed UV and RP-HPLC methods are precise and accurate and can be applied for the quantitative estimation of tolvaptan from bulk and tablet dosage forms. The method can be used for routine testing of tolvaptan by the pharmaceutical industry. Validation of the developed method was done as per International Conference on Harmonization (ICH) Q2R1 guidelines.[13]

14. Kumudini Rahul Pawar *et al.,* (2022) have developed tolvaptan is an essential medicinal substance used to treat a number of illnesses, such as polycystic kidney disease and hyponatremia. Tolvaptan's purity and effectiveness in pharmaceutical formulations depend on the development of a sensitive and trustworthy bioanalytical method for its quantification. This work developed and validated a novel bioanalytical approach for tolvaptan estimation. An Agilent HPLC equipped with a UV detector was used to perform the procedure. The Agilent Eclipse XDB C-8 column was utilized with a 1.0 mL/min flow rate. At 253 nm detection was done. The mobile phase consisting of a mixture of Methanol:0.05 M Phosphate buffer (pH 5)

(70:30 v/v) respectively. Developed method demonstrated excellent linearity over a wide concentration range (0.1 to 5µg/ml) and exhibited precision and accuracy within acceptable limits. The lower limit of quantification (0.5µg/ml) was indicating the method's sensitivity.[14]

15. Kumudini R Pawar *et al.*, (2023) have stability-indicating RP-HPLC method was developed and validated for the estimation of tolvaptan in bulk and pharmaceutical dosage forms followed by identifying the degradants obtained in stability studies by LC- MS. Grace HPLC C18 (4.6X100mm, 2.7micron) column was used with mobile phase consisting of 0.1% formic acid and methanol in the ratio of 20:80 v/v. The flow rate was maintained at 1ml/min, at 253 nm. The retention time was 4.814 minutes. The stress studies were performed as per ICH guidelines under acidic, alkali, oxidative, thermal, photo stability and neutral conditions. The medication peak and the peaks of the deteriorated products were clearly differentiated. It is clear from the degradation studies that the medication was unstable in neutral, oxidative, alkaline, and acidic environments. However, in thermal and photo studies, the medicine remains stable. With 3486 theoretical plates and a tailing factor of 1.13 and a correlation coefficient of 0.999, respectively, the method's linearity was noted in the concentration range of 5–30 µg/mL. Tolvaptan's percentage assay result was 100.098%. The accuracy, precision, and system applicability of the procedure were confirmed. Tolvaptan in pharmaceutical dose forms can be estimated using this method because the study's results fell within the bounds of ICH.[15]

RESULTS AND DISCUSSION

A variety of analytical approaches have been developed for the estimation of Tolvaptan. Early UV and visible spectrophotometric technologies provided simple, quick, and low-cost analysis ideal for routine quality control of bulk medication and dosage forms. Subsequent research improved detectability and decreased sample preparation by introducing more sensitive techniques like spectrofluorimetry and FT-IR. HPLC became the favoured approach in many research due to higher accuracy, precision, and capacity to analyse Tolvaptan in complex combinations, combination formulations, and biological fluids. Tolvaptan and other antidiuretics could be determined simultaneously using a number of techniques, which also made it easier to monitor nausea and headaches. While chromatographic techniques provide more sensitivity and selectivity for pharmacokinetic investigations, residue monitoring, and multicomponent dosage forms, spectrophotometric approaches are often useful for quick routine examination.

CONCLUSION

The review shows that multiple analytical methods exist for the determination of Tolvaptan, ranging from basic spectrophotometric techniques to advanced chromatographic and spectrofluorimetric methods. Simple UV and visible spectrophotometric methods are reliable, economical, and suitable for routine quality control. However, HPLC and related techniques provide higher accuracy, sensitivity, and suitability for complex dosage forms, combination therapies, and biological samples. Overall, method selection depends on analytical needs, with spectrophotometry preferred for rapid routine analysis and chromatographic methods recommended for high-precision regulatory and pharmacokinetic applications.

REFERENCES

1. Chakravarthy VK, Shankar DG. Development and validation of RP-HPLC method for estimation of Tolvaptan in bulk and its pharmaceutical formulation. Rasayan J. Chem. 2011;4(1):1165-71.
2. Pei Q, Tan H, Liu L, Peng X, Li Z, Huang P, Luo M, Zuo X, Guo C, Yang G. Development and validation of an LC–MS/MS method for the determination of tolvaptan in human plasma and its application to a pharmacokinetic study. Journal of Chromatography B. 2013 Jan 15; 913:84-9.
3. Prathyusha B, Shirisha B, Ramathilagam N, Priya J, Sekhar CK. Analytical method development and validation of Tolvaptan in bulk and tablet dosage form by RP-HPLC. Worl J Pharm Pharm Sci. 2013 Oct 25;3:754-62.
4. Furukawa M, Yamasaki Y, Hirao Y, Umehara K. Enantioselective analysis of tolvaptan in rat and dog sera by high-performance liquid chromatography and application to pharmacokinetic study. Journal of Chromatography B. 2014 Aug 15;965:112-8.
5. Rzeppa S, Viet LN. Analysis of tolvaptan and its metabolites in sports drug testing by high‐performance liquid chromatography coupled to tandem mass spectrometry. Drug testing and analysis. 2016 Oct;8(10):1090-4.
6. Patil MR, Patil AS, Shirkhedkar AA. Novel and ecofriendly UV-Spectrophotometry methods for estimation of Tolvaptan using hydrotropic agent. International Journal of Pharmaceutical Chemistry and Analysis. 2019;6(4):115-9.
7. Akutsu S, Naito T, Hoshikawa K, Saotome M, Maekawa Y, Kawakami J. An enantiomeric quantitative LC-MS/MS method for tolvaptan and its monohydroxylates in human plasma using a reversed-phase separation procedure. Journal of Pharmaceutical and Biomedical Analysis. 2020 Feb 20;180:113061.
8. Hoshikawa K, Naito T, Saotome M, Maekawa Y, Kawakami J. Validated liquid chromatography coupled to tandem mass spectrometry method for simultaneous quantitation of tolvaptan and its five major metabolites in human plasma. Annals of Clinical Biochemistry. 2019 May;56(3):387-96.
9. Jiang J, Tian L, Huang Y, Yan Y, Li Y. A rapid and sensitive LC–MS/MS-ESI method for the determination of tolvaptan and its two main metabolites in human plasma. Journal of chromatography B. 2016 Aug 1; 1027:158-64
10. Khaleela N, Rahaman SK. Development and validation of novel stability indicating RP-HPLC method for quantification of Tolvaptan in bulk and pharmaceutical dosage form. Indian Drugs. 2020 Mar 1;57(3).
11. Sutar AS, Magdum CS. Application of response surface methodology in development and optimization of stability indicating RP-HPLC method for determination of tolvaptan in bulk and formulation. Journal of Pharmaceutical Research International. 2021 Oct 12;33(46A):137-48.
12. Patil MR, Ganorkar SB, Patil AS, Shirkhedkar AA, Surana SJ. A converged pharmaceutical analysis supported with hydrotropy & DoE with dual HPTLC and stress studies for estimation of tolvaptan. Microchemical Journal. 2021 Aug 1;167:106328.
13. Patel Seema A, Sayyed Nazifa S, Lajporiya Mobina I, Manjra Mehfuza U, Ahmed A, Khan GJ. An Eco-friendly RP-HPLC and UV-Method Development and Validation for an Estimation of Tolvaptan in Bulk and Tablet Dosage Form Followed by Forced Degradation Studies.2021;33(42B):271-286.
14. Kumudini Rahul Pawar, Sanjay K Bais. A Validated bioanalytical method for quantification of Tolvaptan by RPHPLC-UV.

Journal of Population Therapeutics & Clinical Pharmacology.2022;04:985-994.

15. Pawar KR, Kale PG, Nalawade MS, Chavan SS, Warude BJ, Kaldate DP. Methodological Advancements in Tolvaptan Analysis: HPLC-Based Stability Indication with LC-MS Validation.2023Jan; 24(4): 334-346.

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