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Novel Uv Spectrophotometer Methods For Quantitative Estimation Of Carvedilol (CDL) and Ivabradine (IVD) Using Mixed Hydrotropy Solubilization

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1. INTRODUCTION

Carvedilol (CDL) and Ivabradine (IVD) are widely used in the treatment of cardiovascular diseases, particularly in managing heart failure, hypertension, and angina. Carvedilol is a non-selective beta-blocker and alpha1-adrenergic blocker, which works by reducing the heart rate, lowering blood pressure, and improving the heart's ability to pump blood. It is commonly prescribed for conditions such as heart failure, post-myocardial infarction, and hypertension. On the other hand, Ivabradine, a selective inhibitor of the If current in the sinoatrial node, primarily reduces the heart rate without affecting myocardial contractility, making it an essential medication for managing chronic heart failure and angina pectoris. Both drugs often act synergistically in cardiovascular treatments, and their combination can significantly improve patient outcomes in terms of both survival and quality of life (Gonzalez et al., 2013; Crea et al., 2012).

Simultaneous estimation of carvedilol and ivabradine in pharmaceutical dosage forms presents a significant analytical challenge. Both drugs have distinct chemical properties, with carvedilol being highly lipophilic and Ivabradine being more hydrophilic, which leads to differences in their solubility and absorption spectra. These differences make it difficult to develop a single, efficient method for their simultaneous quantification. Furthermore, traditional estimation techniques, such as UV-spectrophotometry, often struggle with resolving the overlapping absorbance peaks of these two drugs in mixed formulations. To overcome this issue, researchers have increasingly turned to mixed hydrotropic solubilizing agents, which are capable of enhancing the solubility of both poorly soluble and hydrophilic drugs.

Hydrotropic solubilization involves the use of hydrotropic agents, which are typically organic salts capable of increasing the solubility of certain drugs by forming hydrotropic complexes. The combination of two or more hydrotropic agents (i.e., mixed hydrotropes) can lead to synergistic effects, improving the solubility of drugs that are otherwise difficult to dissolve in water. These mixed hydrotropes allow the dissolution of both carvedilol and ivabradine without the need for organic solvents, making the process more eco-friendly and cost-effective. Additionally, hydrotropic solubilization avoids the use of toxic solvents, which is a significant advantage over traditional methods (Patel et al., 2011).

In recent years, the simultaneous estimation of carvedilol and ivabradine using mixed hydrotropic agents has gained attention due to its simplicity, efficiency, and environmental sustainability. This technique has been employed successfully in UV-spectrophotometric methods, where mixed hydrotropes enhance the solubility of both drugs, allowing their effective quantification in complex formulations. The use of hydrotropic solubilization enables the accurate estimation of both drugs, despite their differences in solubility, and offers a valuable tool for routine analysis in pharmaceutical quality control. By combining hydrotropic solubilization with the precision of UV-spectrophotometry, this method promises to streamline the analysis of fixed-dose combinations of carvedilol and ivabradine, ensuring their consistent quality and efficacy in clinical settings (Rani et al., 2016).

The simultaneous estimation of carvedilol and ivabradine using mixed hydrotropic solubilizing agents represents an advanced and promising approach to overcoming the challenges associated with drug analysis in combined dosage forms.

This method offers a sustainable, efficient, and accurate solution for the quality control of cardiovascular drugs and enhances the therapeutic monitoring of patients undergoing treatment with these medications.

2. MATERIAL AND METHODS

CDL and IVD standard were obtained from Pharmaceutical Company. Methanol, acetonitrile were procured from Rankem, RFCL Limited, New Delhi, India. Ammonium acetate AR, sodium citrate and sodium benzoate AR grade, etc were procured from Central Drug House (P) Limited, New Delhi, India. The 0.45- mm pump nylon filter was obtained from Advanced Micro devices (Ambala Cantt, India). Reverse osmosis water was used throughout the study. Other chemicals used were of analytical or HPLC grade. Glyxambi Tab (10mg/5mg) was purchased from local market.

Solubility

Solubility of CDL and IVD was determined at 25±1°C. Accurately weighed 10mg CDL and IVD was added in different 10 ml volumetric flask containing different solvent and placed at mechanical shaker for 8 hrs. After 8 hrs filter both solution were filtered through whatman filter paper No. 41. The filtrates were diluted suitably and analyzed visually (Kim et al., 2010).

Determination of Solubility Enhancement by UV VIS. Spectroscopy

Solubility studies were performed in distilled water 2M Sodium acetate, 8M Urea, 2M Sodium Citrate, 2M Sodium Benzoate, 2M Ammonium Acetate, 2M Sod. Citrate, 2M Sodium acetate: 2M Sodium Benzoate, 2M Urea: 2M Sodium acetate, 2M Sodium citrate: 8M Urea, 2M Sodium citrate: 8M Urea, 2M Ammonium Acetate: 2M Sod. Citrate at room temperature (25 ± 2^0 C). An excess amount of drug was added to 100ml of solvent in screw-capped glass vials; these were mechanically shaken for 48 hours at 25°C until equilibrium was achieved. Aliquots were withdrawn, filtered through a membrane filter (0.45µ) and spectrophotometrically analyzed for solubility (Madan et al., 2015).

Linearity range and calibration graph

Preparation of Standard Stock Solution (Stock-A)

Standard stock solutions were prepared by dissolving separately 100 mg of each drug in 80`mL mixed hydrotropic solution containing 2M Ammonium Acetate: 2M Sod. Citrate (1:1) and the flask was sonicated for about 10 min to solubilize the drug and the volume was made up to 100ml with mixed hydrotropic agent to get a concentration of 1000 µg/ml (Stock-A) for both drugs (Niraimathi et al., 2015).

Preparation of Sub Stock Solution (Stock-B)

Aliquots of 2.5 ml withdrawn with help of pipette from standard stock solution A of CDL and IVD and transferred into 25 ml volumetric flask separately and diluted up to 25 ml with RO Water that gave concentration of 100µg/ml (Stock-B).

Preparation of Working Standard Solution

Aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml and 1.0ml withdrawn with help of pipette from standard stock solution (Stock-B) separately in 10 ml volumetric flask and volume was made up to 10 ml with RO Water. This gave the solutions of 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml and 10µg/ml respectively for CDL.

1.0 ml, 2.0 ml, 3.0 ml, 4.0 ml and 5.0 ml from sub stock solution (Stock-B) were taken separately in 10 ml volumetric flask and volume was made up to 10 ml with RO Water. This gave the solutions of 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml and 25µg/ml respectively for IVD.

Selection of wavelength for linearity

Solutions of 2µg/ml of CDL and 20µg/ml IVD were prepared separately. Both the solutions were scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance of CDL and IVD was observed at 216.0 nm and 232.0 nm, respectively. CDL and IVD showed linearity in the concentration range of 2-10 µg/ml and 10-50µg/ml at their respective maxima. Calibration curve was plotted, absorbance versus concentration (Savale; 2017).

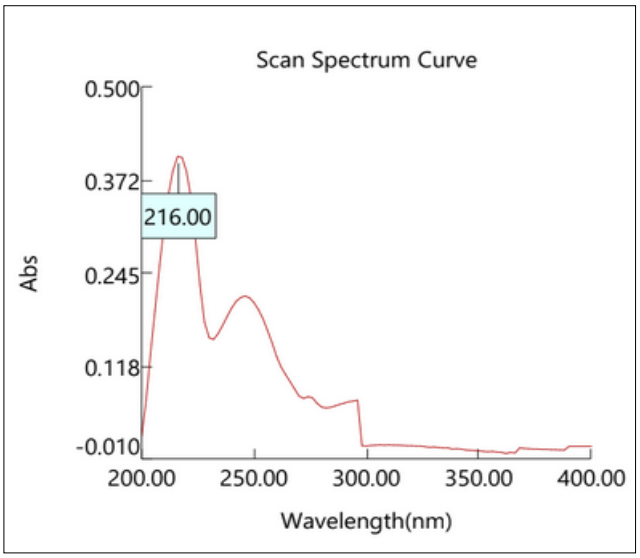

Figure 1: Determination of λ_{max} of CDL

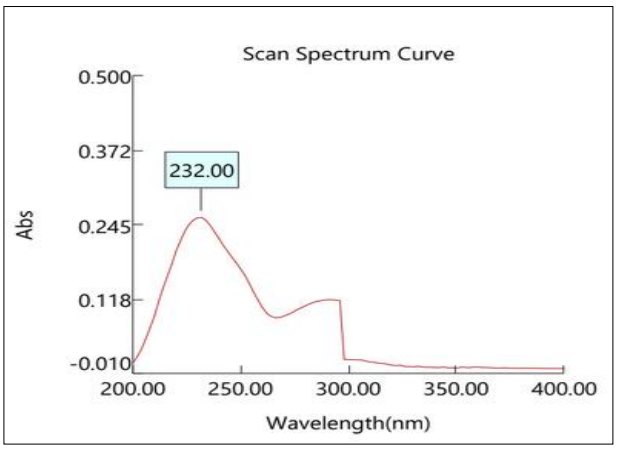

Figure 2: Linearity of IVD

Simultaneous equation method

Study of overlay spectra

Working standard solution from the standard stock solution prepared in concentration 2µg/ml of CDL and 20µg/ml of IVD were scanned in the spectrum mode over the range of 200-400 nm against RO Water as blank and the overlain spectra of the two were recorded.CDL showed an absorbance peak at 216.0 nm, whereas IVD at 232.0 nm. The overlain spectra also showed isoabsorptive points at 222.0 nm. Due to difference in absorbance maxima and having no interference with each other so both drug can be simultaneously estimated by simultaneous equation method (Gummadi et al., 2012).

Where, A_1 and A_2 are absorbances of mixture at 216.0 nm and 232.0 nm respectively, ax_1 and ax_2 are absorptivities of CDL at λ_1 (216.0 i.e. λ_{max} of CDL) and λ_2 (232.0 i.e. λ_{max} of IVD) respectively and ay_1 and ay_2 are absorptivities of IVD at λ_1 and λ_2 respectively. C_{IVD} and C_{CDL} are concentrations of CDL and IVD respectively. Figure 3 represent the overlain spectra of both the drugs in 2:30 ratio and the criteria for obtaining maximum precision [i.e. absorbance ratio $(A_2/A_1)/ax_2/ax_1$ and ay_2/ay_1] by this method were calculated and found to be outside the range of 0.1-2.0 which is satisfied for both the CDL and IVD

$$C\ CDL = \frac{A1ay2 - A2ay2}{ax1ay2 - ax2ay1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eq.(1)$$

$$C\ IVD = \frac{A1ax2 - A2ax2}{ax1ay2 - ax2ay1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eq.(2)$$

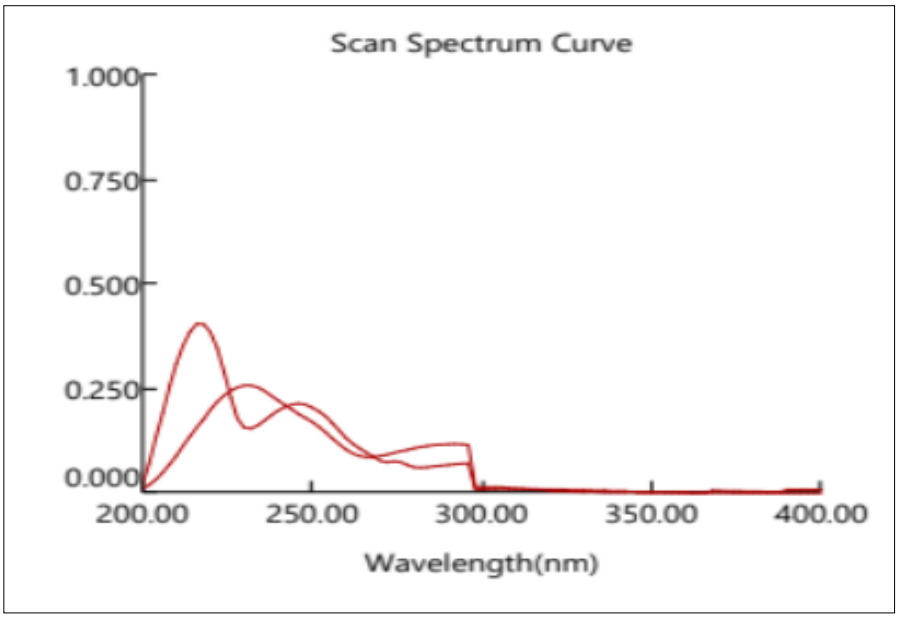

Figure 3: Overlay Spectra of CDL and IVD

Validation of simultaneous equation method (ICH; 2005)

Linearity

Linearity of both drugs was established by response ratios of drugs. Response ratio of drug calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio.

Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of CDL and IVD to preanalysed tablet solutions. The resulting solutions were then re-analysed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels.

Precision

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to Day and analyst to analyst) and reproducibility. Repeatability was performed by analyzing same concentration of drugs for five times. Day to Day was performed by analyzing 5 different concentration of the drug for three days in a week.

Analysis of tablet sample

Twenty marketed tablets (Ivabrad C) of CDL and IVD were weighed and ground to a fine powder; amount equal to 2mg of CDL was taken in 10 ml volumetric flask. The IVD present in this amount of tablet powder was 30mg. Then 8 ml of 2M Ammonium Acetate: 2M Sod. Citrate (1:1) solution was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was made up to the mark with hydrotropic solution. After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with RO Water to get the final concentrations of both drugs in the working range. The absorbances of final dilutions were observed at selected wavelengths and the concentrations were obtained from simultaneous equation method. The procedure was repeated for five times.

Table 1: Result of Linearity of Carvedilol (CDL) and Ivabradine (IVD)

	Method	
Parameter	**CDL**	**IVD**
Working λ	216.0 nm	232.0 nm
Beer's law limit (µg/ml)	2-10	10-50
Correlation Coefficient (r^2)*	0.999	0.999

Slope (m)*	0.099	0.022
Intercept (c)*	-0.003	-0.005

*value of five replicate

Table 2: Results of Recovery Studies

Recovery Level %	**% Recovery (Mean±SD)***	
	CDL	**IVD**
80	98.97±0.459	98.78±0.714
100	97.02±1.835	99.17±0.334
120	99.18±0.580	99.09±0.343

*Average of three determination

Table 3: Results of Precision

Parameter		**(Mean±SD)***	
		CDL	**IVD**
Precision*	Repeatability	96.81±0.110	98.20±0.120
	Day-to-Day	97.81±0.062	99.59±0.015
	Analyst-to-Analyst	99.23±0.151	99.06±0.041
	Reproducibility	97.64±0.080	99.50±0.144

*Average of five determination

Table 4: Analysis of Tablet Formulation of CDL and IVD

Drug	**Label claim (mg)**	**Amount found (mg)**	**Label claim (%)**	**S.D.**	**% RSD**
CDL	2	1.97	98.5	0.152	0.225
IVD	30	29.58	98.6	0.223	0.263

3. RESULTS AND DISCUSSION

In this study, the simultaneous estimation of Carvedilol (CDL) and Ivabradine (IVD) using UV-Vis spectroscopy with mixed hydrotropic solubilizing agents was successfully performed. The method was validated for linearity, recovery, precision, and tablet formulation analysis, which are crucial for ensuring the accuracy and reliability of the results. The linearity results, as shown in Table 1, confirm the effectiveness of the proposed method for both Carvedilol and Ivabradine. The correlation coefficient (r^2) for both drugs was very close to 1, indicating a strong linear relationship between concentration and absorbance within the specified range (2–10 µg/ml for CDL and 10–50 µg/ml for IVD). The slopes of 0.099 for Carvedilol and 0.022 for Ivabradine further demonstrate that the method is sensitive to changes in concentration, with Carvedilol showing a greater sensitivity than Ivabradine. The recovery data (Table 2) indicated that the method provides accurate results across a wide range of concentrations (80%, 100%, and 120%). The percentage recovery for Carvedilol and Ivabradine ranged from 97.02% to 99.18% and 98.78% to 99.09%, respectively, which are within the acceptable limits of 98%–102%.

The low standard deviations (SD) reflect the precision and consistency of the method, confirming its suitability for routine analysis.

The precision data, shown in Table 3, demonstrates the reliability of the method. The repeatability, day-to-day, analyst-to-analyst, and reproducibility studies all yielded small variations, as evidenced by the low standard deviations and % RSD. The precision results for Carvedilol and Ivabradine fall within acceptable limits, further validating the robustness and consistency of the method across different conditions and operators. Table 4 presents the analysis of tablet formulations for Carvedilol and Ivabradine. The amount found for both drugs was very close to the labeled claim (98.5% for Carvedilol and 98.6% for Ivabradine), indicating that the drug content in the tablets is in line with the manufacturer's specifications. The low % RSD values (0.225 for Carvedilol and 0.263 for Ivabradine) further confirm the method's reliability and precision in determining the active pharmaceutical ingredients in the formulations.

4. CONCLUSION

The developed method for the simultaneous estimation of Carvedilol and Ivabradine using mixed hydrotropic solubilizing agents is both accurate and precise, as demonstrated by the results of linearity, recovery, precision, and tablet formulation analysis. The method is suitable for routine analysis in quality control laboratories, ensuring the correct dosage of both drugs in pharmaceutical formulations. Further, the findings emphasize the reliability of this approach for assessing the content of both drugs in combination dosage forms.

REFERENCES

[1] Crea, F. et al. (2012) Ivabradine for the treatment of chronic heart failure. *Journal of the American College of Cardiology*, 59, 1136–1144.

[2] Gonzalez, J.A. et al. (2013) Carvedilol in the management of heart failure. *Journal of Clinical Hypertension*, 15, 508–515.

[3] Kim JY, Kim, J.Y., Papp, M., Park, K., Pinal, R. (2010) Hydrotropic solubilization of poorly water-soluble drugs. *Journal of Pharmaceutical Sciences*, 99, 3953–3965. DOI: 10.1002/jps.22241, PubMed: 20607808.

[4] Patel, K.R. et al. (2011) Hydrotropic solubilization: A green approach for solubilization of poorly soluble drugs. *Asian Journal of Pharmaceutical and Clinical Research*, 4, 5–8.

[5] Madan JR, Pawar, K.T., Dua, K.T. (2015) Solubility enhancement studies on lurasidone hydrochloride using mixed hydrotropy. *International Journal of Pharmaceutical Investigation*, 5, 114–120. DOI: 10.4103/2230-973X.153390, PubMed: 25838997.

[6] Rani, R. et al. (2016) Simultaneous estimation of carvedilol and ivabradine by UV spectrophotometric method in pharmaceutical dosage forms. *Journal of Pharmaceutical Analysis*, 6, 273–278.

[7] Niraimathi V, Suresh, A.J. & Alageswaran, A. (2015) UV spectrophotometric determination of fenofibric acid by using hydrotropy. *International Journal of Pharmaceutical Sciences and Research*, 6, 451–458.

[8] Savale SA (2017) Simultaneous determination of curcumin and gefitinib in pure form by using UV spectrophotometric method. *Hygeia*, 9, 1–8.

[9] Gummadi S, Thota, D., Varri, S.V., Vaddi, P., Rao, V.L. (2012) Development and validation of UV spectroscopic methods for simultaneous estimation of ciprofloxacin and tinidazole in tablet formulation. *International Current Pharmaceutical Journal*, 1, 317–321.

[10] ICH Guidelines: Validation of Analytical Procedures (2005) Text and methodology, Q2.