

Development of New Spectrophotometric methods for the determination of Indapamide in Bulk and Pharmaceutical formulations

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Abstract: Three simple, precise and accurate UV methods have been developed for the estimation of Indapamide in bulk and pharmaceutical formulation. Indapamide on condensation with p-dimethylamino cinnamaldehyde (PDAC) and p-dimethylamino benzaldehyde (PDAB) in the acidic medium produces bottle-green and blue colored complex, which showed absorption maxima at 682.0nm and 602.0nm in Method A, B and Method C applied Area Under Curve (AUC) for the analysis of Indapamide in the wavelength range of 238-248nm. Drug followed the linearity range of 6-16µg/ml, 50-250µg/ml and 1-18µg/ml for Method A, B and C respectively. Results of analysis were statistically validated with recovery studies and were found to be satisfactory.

Keywords: Indapamide, UV spectroscopy, PDACA, PDAB, Area Under Curve.

Introduction

Indapamide is an orally administered diuretic and antihypertensive drug.^[1] Its diuretic and natriuretic effects are mainly due to the presence of o-chlorobenzenesulfonamide, a molecule present in various diuretics. However, a varied side chain gives the drug characteristic properties. Indapamide represents an indolinyl ring which uniquely exhibits free-radical scavenging activity as well as a direct vasodilator action. It is an antihypertensive agent administered to individuals with mild to moderate hypertension.^[2] Indapamide is chemically 3-(aminosulfonyl)-4-chloro-N-(2,3-dihydro-2-methyl-1H-indol-1-yl)benzamide^[3] and the structural formula is shown in Figure 1. It is an official drug in United states pharmacopoeia 2005^[4] and British Pharmacopoeia 1995.^[5] Literature survey reveals

that, only few spectrophotometric^[6-10] and bio-analytical methods by LC-MS and HPLC were found using human plasma^[11], blood^[12] and biological fluids^[13] for the quantitative estimation of Indapamide in bulk and pharmaceutical formulations have been developed. Hence an attempt has been made to develop new UV methods for its estimation in bulk and pharmaceutical formulation with good accuracy, simplicity and precision.

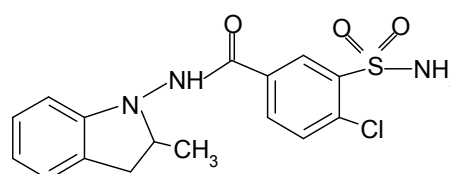


Figure 1: Chemical Structure of Indapamide

Experimental

Materials and method

Pure sample of Indapamide was obtained from Supra chemicals, Navi Mumbai, India as gift sample. A Shimadzu UV-1700 UV/VIS Spectrophotometer was used with 1cm match quartz cell. Tablets of 2.5mg were procured from local pharmacy.

Preparation of Standard solution

The pure drug of about 100mg was weighed accurately and dissolved in 100ml of methanol to give the standard stock solution of 1000 μ g/ml (Stock A). Aliquots of standard stock solution were pipetted out and suitably diluted with methanol to get a final concentration of the standard solution.

Estimation of Indapamide with PDAC and PDAB^[14]

Two sets each of five flasks containing appropriate dilutions of Indapamide from the stock 'A' to obtain a concentration range of 6-16 μ g/ml and 50-250 μ g/ml were prepared. To each flask which was immersed in ice bath, 0.5 ml of Con.H₂SO₄ was added and the temperature was allowed to rise to 20⁰ C followed by addition of 0.5 ml of PDAC reagent in the first set of each flasks and 2.0 ml of PDAB in the second set of

each flasks and were kept aside for 5 min for the reaction to complete. The volume was made up to 10 ml with distilled water. The absorbances of bottle green and blue colored complex were measured at 682.0nm and 602.0nm against the reagent blank (Figure 2, 4) and the calibration curves were plotted (Figure 3, 5).

Area Under Curve Method (AUC)

The AUC method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 238.0nm and 248.0nm (Figure 6). Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. The wavelength range is selected on the basis of repeated observation so as to get the linearity between area under curve and concentration. Suitable dilutions of Stock A of the drug were prepared and scanned in the spectrum mode in the wavelength range 400-200nm and the calibration curve was plotted (Figure 7).

As the results obtained were satisfactory, the methods were applied for the pharmaceutical formulations.

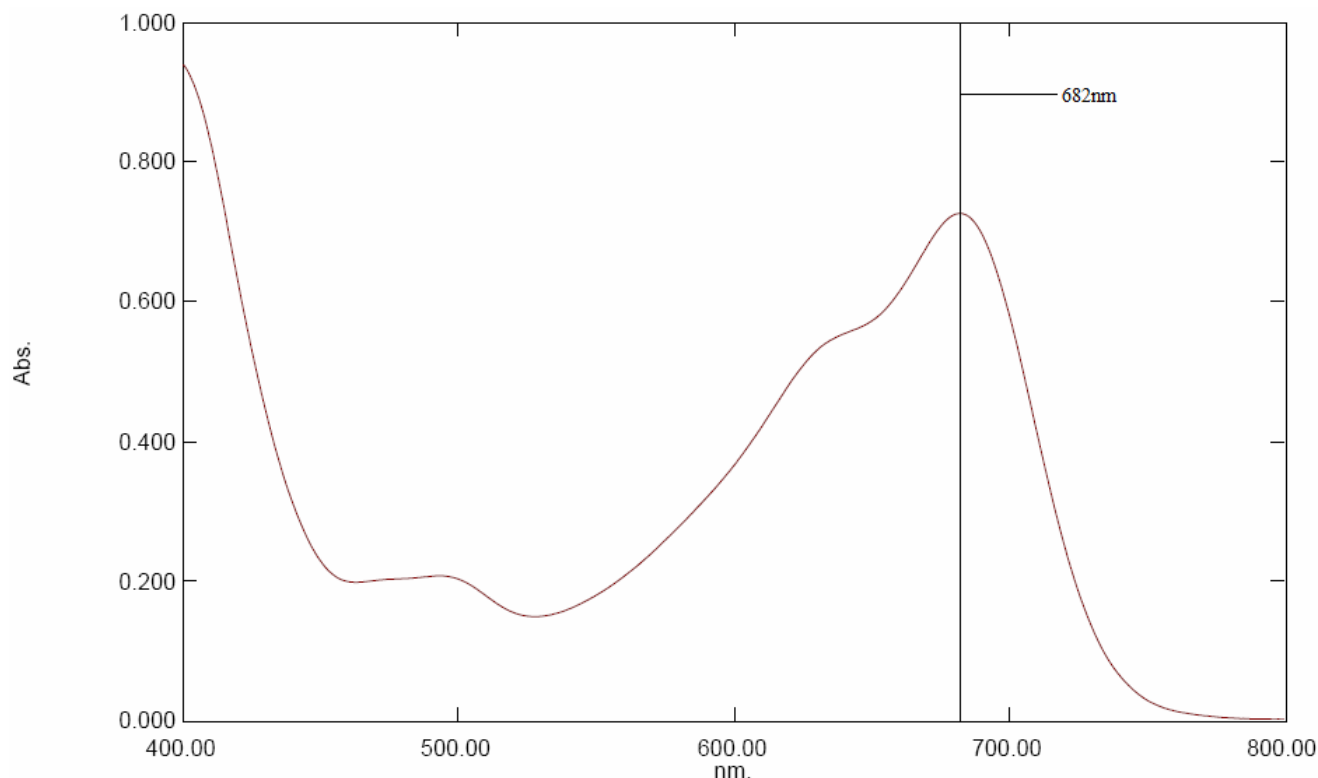


Figure 2: Spectra for Indapamide at 682.0 nm with PDAC

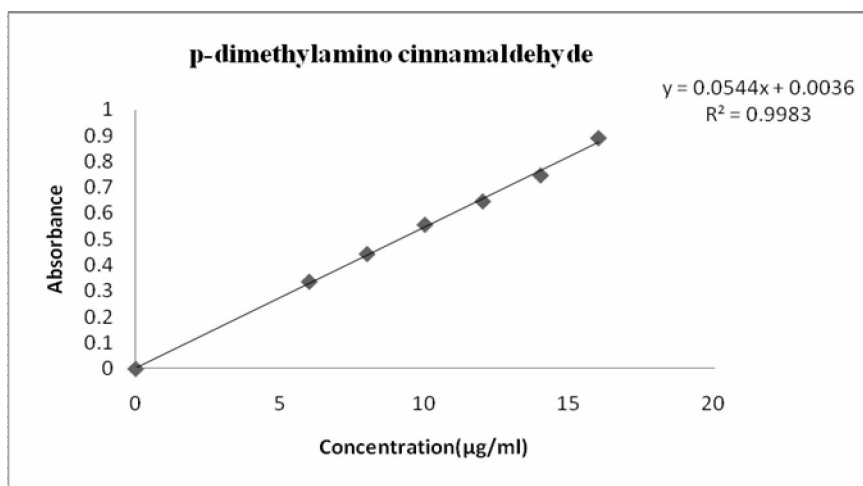


Figure 3: Calibration curve for Indapamide at 682.0 nm with PDAC

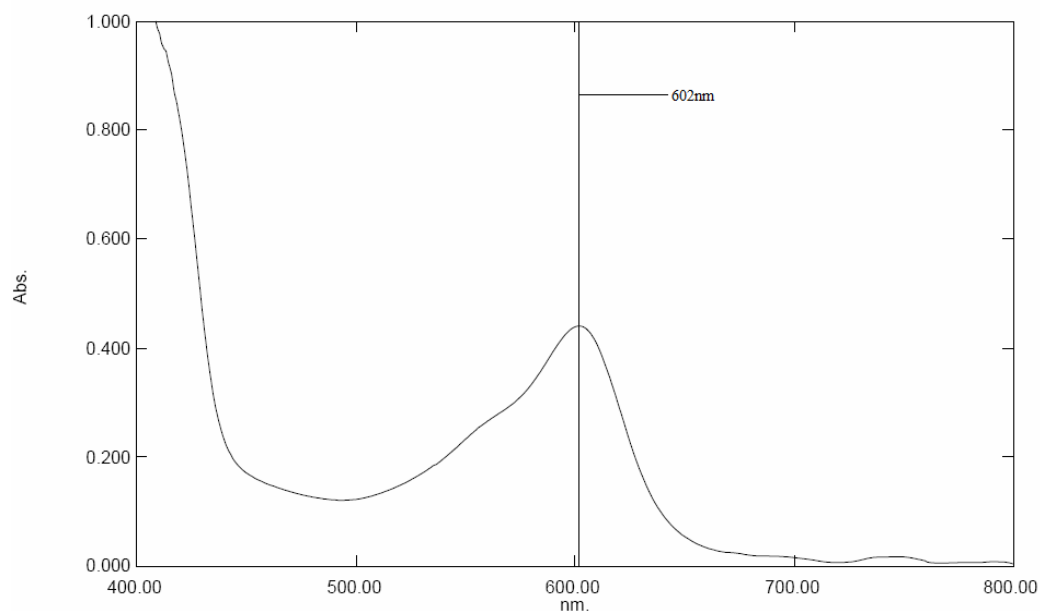


Figure 4: Spectra for Indapamide at 602.0 nm with PDAB

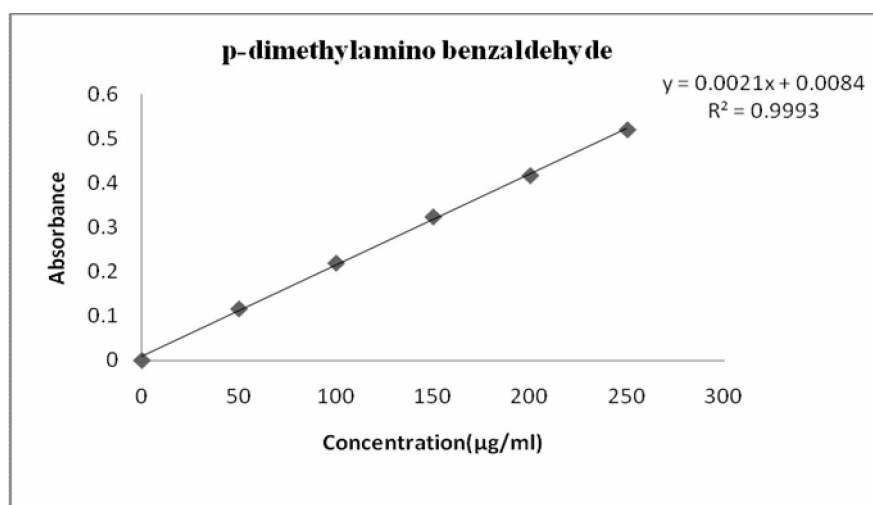


Figure 5: Calibration curve for Indapamide at 602.0 nm with PDAB

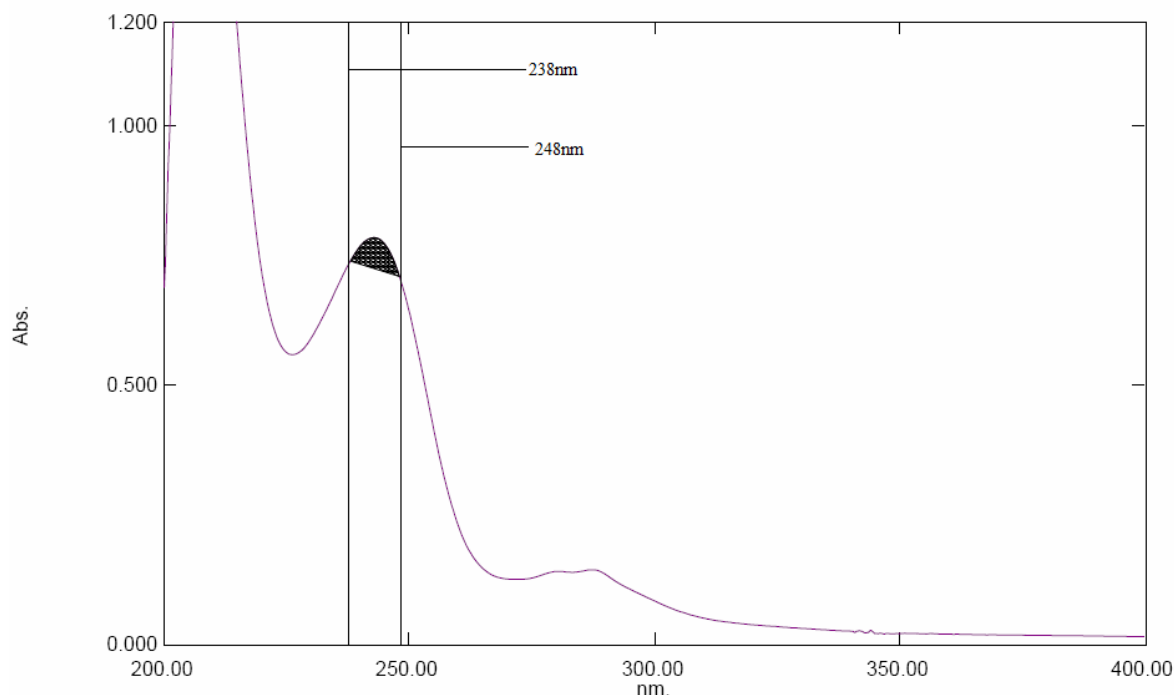


Figure 6: Spectra for Indapamide at 238-248nm in methanol by AUC

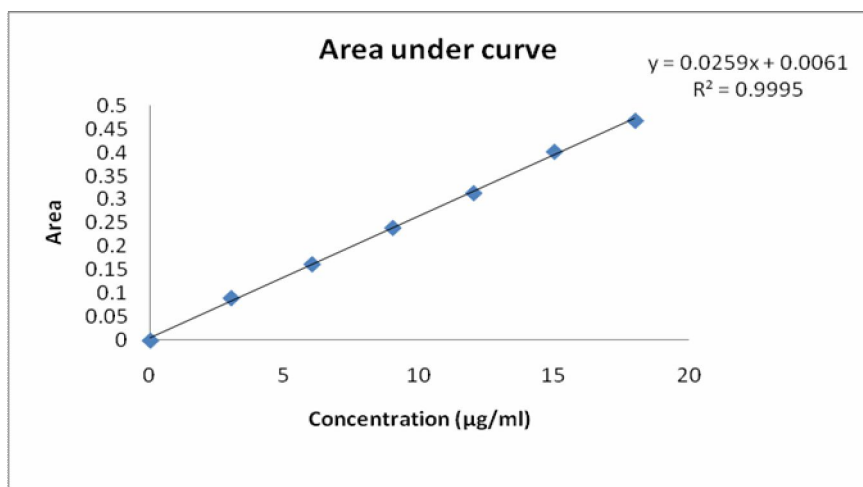


Figure 7: Calibration curve for Indapamide at 238-248nm in methanol by AUC

Preparation and analysis of the Tablet formulation

For the estimation of Indapamide in tablet formulation by three methods, 20 tablets were weighed and triturated to fine powder. Tablet powder equivalent to 25mg of Indapamide was weighed, dissolved and further diluted with sufficient quantity of methanol. It was sonicated for 20 min and then filtered through Whatmann filter paper no. 41 to get the stock solution of 1000µg/ml. Various dilutions of the tablet solution were prepared and analyzed for six times and the

concentration was calculated by using the calibration curve for three methods (Table 2).

Validation of the methods^[15]

All the methods were validated according to ICH guidelines by carrying out analysis of six replicate samples of tablet. Recovery studies were carried out at three different levels i.e. 80%, 100% and 120% by adding the pure drug to previously analyzed tablet powder sample. From the amount of drug found, percentage recovery was calculated (Table 1).

Table 1: Optical characteristics and other parameters

Parameters	Method A	Method B	Method C
$\lambda_{\max}$ / wavelength range	682.0	602.0	238.0-248.0
Linearity range ($\mu\text{g/ml}$)	6-16	50-250	1-18
Molar absorptivity (litre, mole ⁻¹ cm ⁻¹)	2.03×10^4	7.88×10^2	1.5×10^4
Sandell's sensitivity ($\mu\text{g/cm}^2$ -0.001absorption units)	1.79×10^{-5}	4.6×10^{-4}	3.73×10^{-5}
Coefficient of Correlation	0.9983	0.9993	0.9995
Slope* (m)	0.0544	0.0021	0.0259
Intercept* (c)	0.0036	0.0084	0.0061
Accuracy (%RSD)			
80%	0.7246	0.5119	0.7803
100%	0.7683	0.6947	1.0004
120%	0.7602	0.5123	0.7297
Precision (%RSD)			
Intra-day	0.7268	0.7990	0.9116
Inter-day	0.7833	1.0946	0.9764
LOD	0.113	3.170	0.50
LOQ	0.342	9.610	1.50

*y = mx + c; when x is the concentration in mg/ml and y is absorbance unit.

Table 2: Results of Indapamide formulation

METHOD	Brand Name	Label claimed (mg)	Amount found (mg)	%Recovery $\pm$ SD**
A	Lorvas	2.5	2.493	99.71 $\pm$ 0.8199
B		2.5	2.485	99.41 $\pm$ 0.8333
C		2.5	2.482	99.27 $\pm$ 1.1148

**Average of six determinations

Results and Discussion

All the three methods A, B and C for the estimation of Indapamide in tablet formulation were found to be accurate and reproducible. Linearity was found in the concentration range of 6-16 $\mu\text{g/ml}$, 50-250 $\mu\text{g/ml}$ and 1-18 $\mu\text{g/ml}$ with correlation coefficient 0.9983, 0.9993 and 0.9995 for the methods A, B and C respectively. The optical characteristics such as linearity range, molar absorptivity, sandell's sensitivity, percentage relative standard deviation of recovery studies and precision in each method were calculated and the results were reported in Table 1. Also the regression characteristics like slope (m), intercept (c) and correlation coefficient (r) were calculated and are presented in Table 1. The accuracy of the methods was assessed by recovery studies at three different levels i.e. 80%, 100% and 120%. The values of standard

deviation were satisfactory and the recovery studies were close to 100%. The %RSD value was less than 2, an indicative of the accuracy of the methods.

Conclusion

Thus, it can be concluded that the methods developed in the present investigation were simple, sensitive, accurate, rapid and precise. Hence, the above said methods can be successfully applied for the estimation of Indapamide in pharmaceutical formulation.

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