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New Method for Spectrophotometric Determination of Furosemide in Pure Form and in Pharmaceutical Formulations

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Abstract— *An accurate, simple, fast and cheap spectrophotometric method has been developed for the determination of Furosemide (FUR) in pharmaceutical pure and dosage forms. The method is based on the reaction of 2,4- Di hydroxyl Benz aldehyde (DHBA) with Furosemide in the presence of Ethyl alcohol. This reaction produces a complex yellow colored product which absorbs maximally at 430 nm. Beer's law was obeyed in the range of 3.3 – 82.69 µg/mL with molar absorptivity of 1.749×10^3 L $mole^{-1}$ cm^{-1} Sandell's sensitivity 0.11 µg.cm^{-2}. The effects of variables such as temperature, concentration of color producing reagent, and stability of color were investigated to optimize the procedure. The results are validated statistically. The proposed method was applied to commercially available tablets, and the results were Pharmaceutical formulations.*

Keywords— ***Furosemide; 2,4 Di hydroxyl Benz aldehyde; Spectrophotometry; Beer's law; complex.***

I. INTRODUCTION

Furosemide or Frusemide (4-chloro-N-furfuyl -5-sulfamayl- anthranilic acid is formally a sulfonamide, an antibacterial agent(Fig.1) .However the intense and fast dieresis produced by this drug, has extended its application as a powerful acidic diuretic for diverse treatment in human and veterinary medicine. Furosemide is often classified as a loop diuretic due to its predominate action in the nephron [1].

Fur acts inhibiting of sodium on Henle, s 100g and inhibiting the co-transportation of sodium, potassium and chloride, and causes excretion of calcium, magnesium and bicarbonate ion. Intense and fast dieresis may also mask the ingestion of other doping agents by reducing their concentration in urine [2].

Fur have a large number of analytical technique to determinate it in pharmaceutical and biological samples a number of spectrophotometric method have also been reported for furosemide [3-8].

Also electrochemical detection and capillary electrophoresis have been used to quantify fur [9-11].

HPLC is generally the method of choice for diuretics quantitation, due to the required

time and cost of the analysis [12-13].

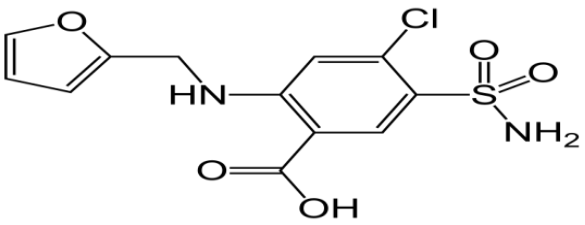

Fig 1: Chemical Structure of Furosemide

Although there are several highly sophisticated instrumental methods were reported but are suffered by time of analysis, cost per analysis, sophistication and most importantly the skilled analyst to handle the instruments. The present method offers a simple, sensitive, cost effective method for the determination of FUR in any common QC laboratory.

II. EXPERIMENTAL

Reagents and apparatus

- Furosemide (99.9%) pure reference substance, produced by Lupin, India)
- Stock solution (1 mg/mL): 100 mg FUR was dissolved in ethyl alcohol in a 100 mL volumetric flask.
- Stock solution (1 mg/mL): 100 mg DHBA was dissolved in ethyl alcohol in a 100 mL volumetric flask.
- Analytical balance
- UV-Vis Spectrophotometer Model SP3000 OpTMA from Korea olumetric flask.

Principle of the method

We studied the best volume and concentration of the FUR, DHBA, universal con.H_2SO_4 on the formation yellow complex.

FUR-DHBA method

To different aliquots of DHBA solution corresponding to 0.5 - 2.0 ml were transferred into a series of 10ml volumetric flasks. 0.5 - 2.0 ml of FUR solution and Universal con.H_2SO_4 were added to each flask diluted to volume with C_2H_5OH respectively and the temperature was allowed to rise to 25C°. each flasks and were kept aside for 10 min for the reaction to complete. The absorbance of bottle Yellow colored complex was measured at 430 nm against the reagent blank.

Analysis of pharmaceutical formulations

20 tablets were accurately weighted finely powdered and dissolved into sufficient volume of solvent. The mixture was stirred well and filtered through Whatman filter paper No. 42 and the filtrate was diluted with solvent added universal con.H_2SO_4 in 10 ml volumetric flask. The temperature was allowed to rise to (25±2)C° and absorbance was measured after 10 min of mixing against blank at λ_{max} = 430nm.

III. RESULTS AND DISCUSSION

Preliminary investigations have been shown that FUR react with DHBA in con.H_2SO_4 to give Yellow colored complex which absorbs at λ_{max}=430 nm as shown in (Fig 2).

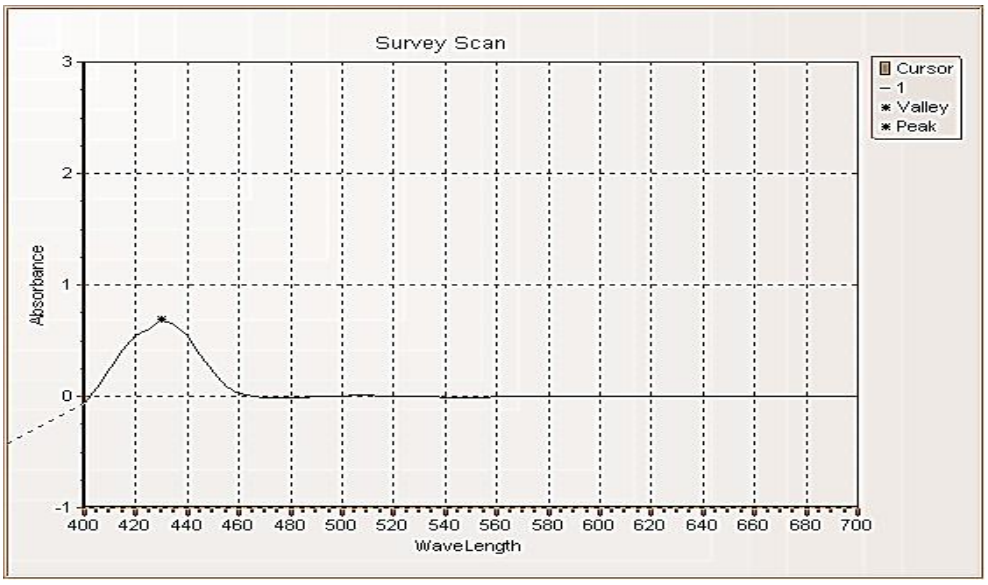

Fig.2: Absorption spectrum of FUR-DHBA formation

The optimum reaction conditions for quantitative determination of the ion pair complexes were established via number of preliminary experiments. Several parameters such as amount of con.H_2SO_4 added, reagent concentration, temperature, sequence of addition and color stability.

Effect of time on the stability of the color (FUR-DHBA) complex:

Developed color was stable up to 24 hours which was considered sufficient time for an analyst to carry out analysis (Figure 3)

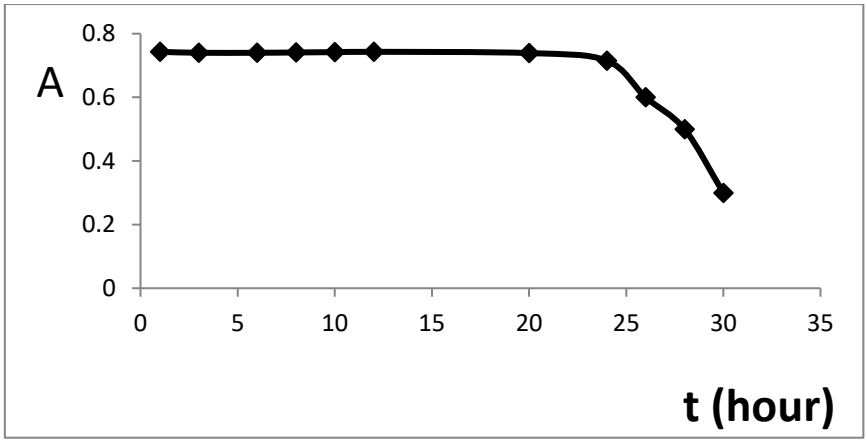

Fig.3:Effect of time on the color development

Effect of amount of con.H_2SO_4 :

The optimum of amount of con.H_2SO_4 for the assay of drugs was studied.

0.7ml of con.H_2SO_4 sufficient for complete color development for (FUR-DHBA) complex as shown in (Figure 4).

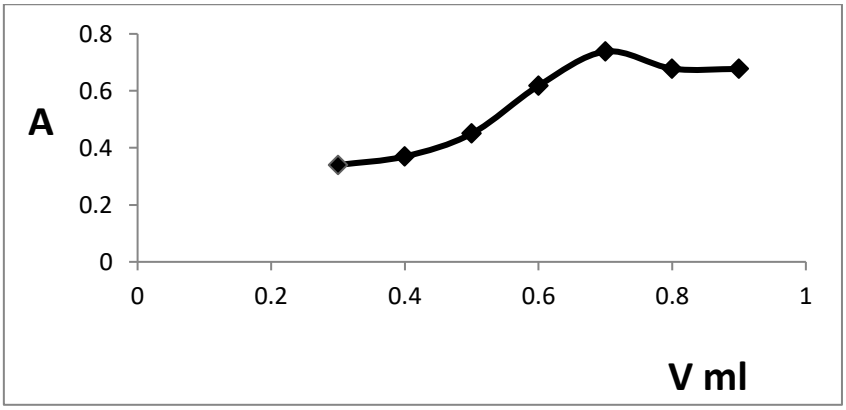

Fig.4: Effect of amount of con.H_2SO_4.

Effect of reagent concentration

The effect of (DHBA) concentration on the color development was investigated (1.0) mL of (DHBA) reagent produced maximum color intensity (Figure 5).

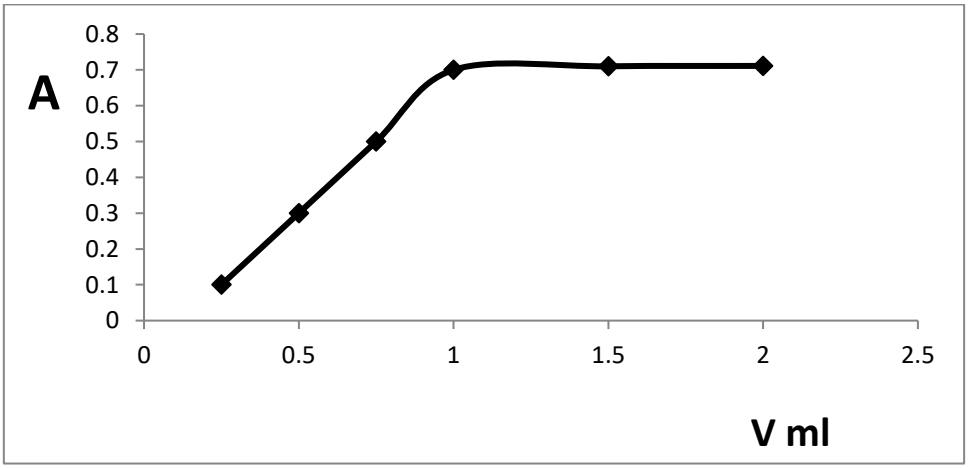

Fig.5: Effect of (DHBA) concentration on the absorbance of (FUR-DHBA) complex.

Molar Ratio Determination of (FUR-DHBA) complex

The molar ratio was determined using the molar ratio method [14] and continuous variation methods[15] .the ratio were found to be 1:1 for FUR:DHBA(Figures 6 and 7)

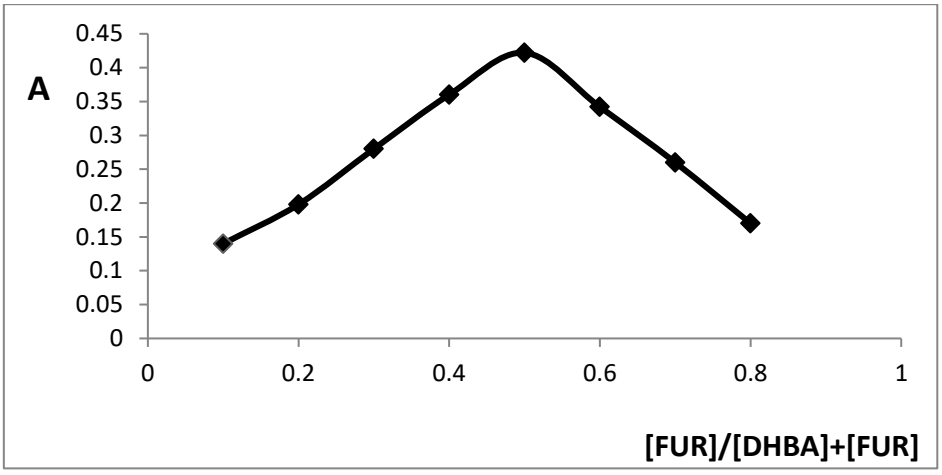

Fig.6: Continuous variation plot for (FUR-DHBA) complex.

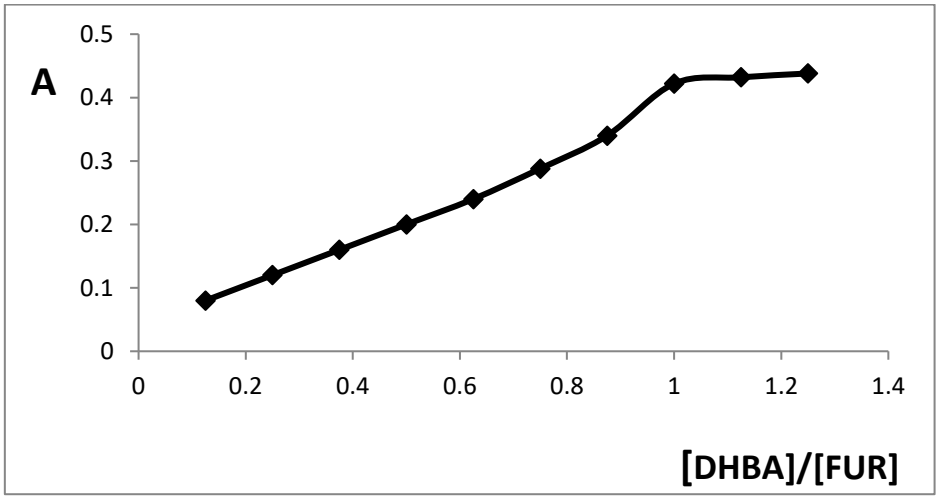

Fig.7: Molar ratio plot for (FUR-DHBA) complex.

Linearity and sensitivity

A liner relation was obtained between absorbance and concentration of FUR in the range of 3.3 – 82.69 µg/ml (Fig 8). The graphs show negligible intercept and they are described by the regression equation Y= m x + C (where Y the absorbance of 1 cm layer ,m is the slope ,C is the intercept and x is the concentration of the measured solution in µg/ml)obtained by the least-square method[16].The high molar absorptivity of the resulting colored complex indicate the good sensitivity of the method. The Beer's law limits , Sandell's sensitivity, molar absorptivity ,linear regression equation ,correlation coefficient and detection limit[17] determined for the method are given in Table 1.

Beer's law was obeyed in the range More than 99% recover of FUR was obtained in the presence of possible excipients and ingredient in FUR formulations (Tables 1 and 2).

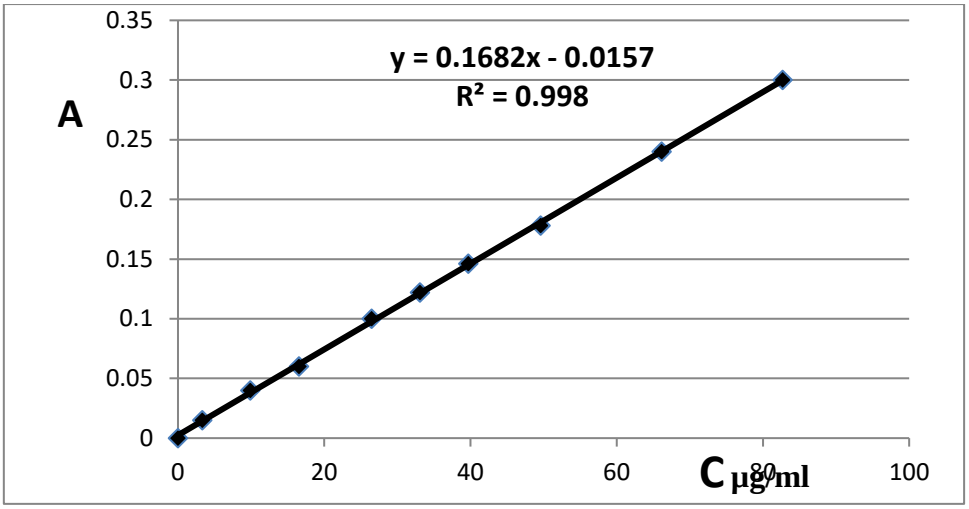

Fig.8: Calibration range for Furosemide

Table 1: Optical characteristics and statistical data for the regression equation of the proposed method.

Parameter	Value
λ_{max}	430 nm
Beer's law limit (µg/mL)	3.3 – 82.69
Molar absorptivity (L mole^{-1} cm^{-1})	1.749×10^{3}
Sandell's sensitivity (µg/mL per 0.001 A)	0.11
Regress ion equation (Y*)	
Slope (m)	0.1682
Intercept (c)	0.0157
Correlation coefficient	0.998
Relative standard deviation**	1.74
Limit of Detection (µg/mL)***	2.69
Limit of quantitation (µg/ml)	8.96

*Y= m x + C; Where x is the concentration of analyte (µg/mL) and Y is absorbance unit; **: Calculated from six determinations; ***: Calculated as per ICH guidelines

Accuracy and precision

The results obtained are summarized in Table 2.The low values of relative standard deviation (RSD) indicate good precision and reproducibility of the method. The average precent recoveries obtained were 99.03-100.33% indicating good accuracy of the methods[18,19].

Table 2: Study of precision and accuracy of the proposed method.

FUR Taken (µg/ml)	FUR Found (µg/ml)	Stander deviation SD	Relative Stander deviation R.S.D %	Analytical Error SD/ $(n)^{1/2}$	Confidence limit (µg/ml)	Recovery R(%)
3.3	3.31	0058	1.74	0.0257	3.31 ± 0.0713	100.3
16.54	16.38	0.156	0.95	0.0696	16.38 ± 0.1932	99.03
33.07	33.18	0.258	0.78	0.1156	33.18 ± 0.3209	100.33

49.61	49.6	0.274	0.55	0.1225	49.6 ± 0.3401	99.98
66.15	66.18	0.126	0.19	0.0563	66.18 ± 0.0563	100.05
82.69	82.89	0.149	0.18	0.0668	82.89 ± 0.1854	100.24
99.22	99.03	0.136	0.14	0.0608	99.03 ± 0.1688	99.8
115.76	115.93	0.131	0.11	0.0585	115.93 ± 0.1624	100.15
132.29	132.22	0.109	0.08	0.0487	132.22 ± 0.1352	99.94
148.84	148.93	0.123	0.08	0.0885	148.93±0.1537	100.06

*Five independent analyses

Table 3:Result of the estimation FUR in tablets.

Formulation	Lable claim (mg)	FUR taken µg mL^{-1}	FUR found µg mL^{-1}	Stander deviation SD	Content Determined* (mg)	Relative Stander deviation R.S.D %	Relative Recovery R(%)
UNI LASIX	40	40	39.76	0.09	39.76	0.04	99.4

IV. CONCLUSION

The proposed method for the estimation of FUR using DHBA is advantages over many of the reported methods. The methods are rapid, simple and have good sensitivity and accuracy. Proposed method makes use of simple reagent, which an ordinary analytical laboratory can afford. The high recovery percentage and low relative Standard deviations reflect the high accuracy and precision of the proposed method. The method are easy, applicable to a wide range of concentration, besides being less time consuming and depend on simple reagent which are available, thus offering economic and acceptable method for the routine determination of FUR in its formulations.

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