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Spectrophotometric determination of Furosimide in pharmaceutical formulations by charge transfer complex method

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Abstract : The simple and sensitive spectrophotometric method for the determination of furosimide reacts with 1ml of DDQ (2, 3 –dichloro -5, 6-dicylano-1, 4-benzoquinone) by charge –transfer complex method. In this method the drug furosimide as n-electron donors with acceptor 2, 3 dichloro-5, 6- dicyano 1,4- benzoquinone (DDQ) to form reddish pink color charge-transfer complexes. This reaction is instantaneous and quantitative. The drug maximum absorbance at 450 nm and Beer's law limit was obeyed at 20-160 µg/ml.The optical characteristics of the proposed method such as molar absorptivity, sandell's sensitivity, slope and intercept were 2.0847 $L.mole^{-1}cm^{-1}$, 0.00208 $\mu g.cm^{-2}$,0.0059 and 0.0061 for furosimide respectively.The developed method was found to be simple, specific, robust, accurate and precise for the determination of furosimide.
Key words : furosimide, chloroform, methanol, DDQ and UV-Spectrophotometric method.

1. Introduction

Furosimide, chemically known as 5-(aminosulfonyl-4-chloro-2-[(2-furanylmethyl) amino] benzoic acid, is structurally a sulfonamide, an antibacterial agent. Furosimide is an anthracitic acid derivative extensively used for its diuretic effect in the treatment of edema associated with pulmonary, cardiac, hepatic and renal disease[1], and of hypertension accompanied by fluid retention or impaired renal failure[2]. Because of its predominant action on the loop of Hanley and the marked dieresis it can produce, this compound is often designated as a loop diuretic and high ceiling diuretic. The adverse effects of furosimide are hypertension, congestive heart failure[3, 4], and cirrhosis of the liver.

Numerous methods have been reported for the determination of furosimide in pharmaceutical samples. Most of the methods developed are based on different spectrophotometric methods[5-8],HPLC[9], rapid titrimetric and spectrophotometric[10],spectrophotometric – partial least squares (PLS-1)[11], diffuse reflectance spectroscopy[12], developments in analytical method[13], first digital derivative spectrophotometry[14], ratio spectra derivative spectrophotometry[15]. Second order derivative spectroscopy and area under curve (AUC) [16]. These methods are available for the determination of furosimide.

2. Experimental

2.1 Instrumentation

A Shimadzu UV-visible double beam spectrophotometer (model 2450) with 1 cm matched quartz cells was used for the spectral measurements.

2.2 Chemicals and reagents

All the chemicals used were of analytical grade. Double distilled water was used for all the experimental studies.

2.3 DDQ solution(1% w/v)

DDQ (2,3-dichloro5,6-dicyano-p-benzoqunone) (Loba Chem.,India) solution is prepared by dissolving 100 mg in 100 ml of distilled water.

2.4 Furosemide solution

An accurately weighed 50 mg of furosemide is dissolved in methanol and the volume was adjusted to 50 ml with methanol. Further dilution is made to obtain the working concentration of 100 μg /ml.

2.5 Spectrum of furosimide treated with DDQ

1.0ml of furosimide standard solutions was taken into a standard flask. To this solution 1ml of DDQ reagent is added to form a pale reddish pink colored solution. The final volume was brought to 10ml with methanol. The solution was taken in 125 ml separating funnel and extracted with 5ml chloroform twice by shaking for two minutes and allowed to stand for clear separation of two phases. The resultant solution is well mixed and allowed to stand for 5 minutes for completion of the reaction. The absorbance of the reddish pink colored solution is measured in the wavelength range of 400 to 700 nm against the reagent blank. The spectrum is given in fig.1.from figure the drug treated with DDQ solution has maximum absorbance at 450 nm. Hence, all further studies are made at 450 nm.

2.6 Assay procedures

Sample solutions ranging from 0.2-1.6 ml were transferred into a series of standard flaks and solution of DDQ (1 ml) is added to produce a reddish pink color. The final volume is brought to 10 ml with methanol. The tubes were taken thoroughly and placed in a boiling water bath for about 30 minutes. The reaction mixture in each tube was called, transferred quantitatively into a 125ml calibrated flask and diluted to the mark with distilled water. The absorbance of the reddish pink color solution was measured at 450 nm against the reagent blank prepared in similar manner omitting drug solution. Calibration graph is obtained by plotting absorbance values against the concentration of furosimide solution. The calibration curve is found to be linear over a concentration range of 20 to 160μg/ml of furosimide. The amount of furosimide drug present in the sample is readfrom the calibration graph. The results are presented in fig 2.

2. 7 Effect of interferences

In order to apply the proposed method to the analysis of pharmaceutical formulations, the influence of commonly used excipients starch, lactose, glucose, Dextrose sugar, and talc and additives was studied by preparing solutions containing $2.0x10^{-3}$M furosimide and increasing concentrations of the potential interference up to $1.0x10^{-3}$M.The results are shown in table .3

2.8 Assay in serum and urine samples

To apply the proposed method for biological samples, blood and urine samples were collected from donors, and centrifuged at 3000 rpm for nearly 10 min. The resulted solutions were filtered and preserved in the absence of light at a temperature of 4^{o}C. From these solutions, various concentrations of the drug furosimide were analyzed with the help of proposed analytical method and these results were recorded in table 4. Hence, the proposed method can be successfully applied to recover furosimide in biological samples, viz. urine and serum due to its high accuracy and good recoveries.

3.Results and discussion

The UV spectrum of furosimide is presented in fig 1. The absorption maximum was observed at 450nm for furosimide abeyance to Beer's law was confirmed by the linear of the calibration curve of furosimide, which

are presented in fig 2.The molar absorptivity and sandell's sensitivity values show that method is sensitivity. The regression analysis using method of least squares was made for the slope (b) intercept (a) and correlation (r) obtained from different concentrations and results are summarized in the table 1. The value of correlation coefficient (r) was 0.999 which indicated the good linearity of calibration lines.

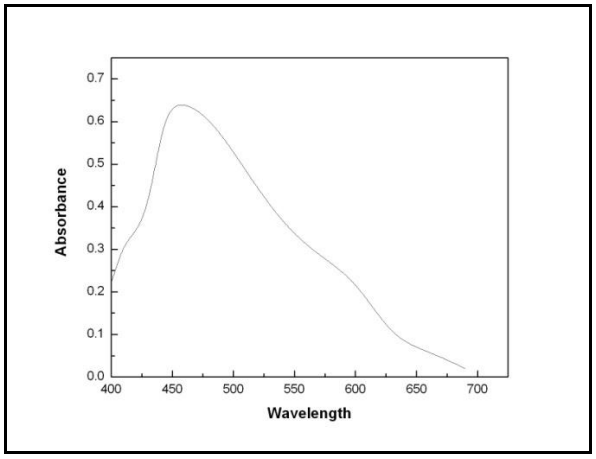

Fig.1 Spectrum of furosimide react with DDQ

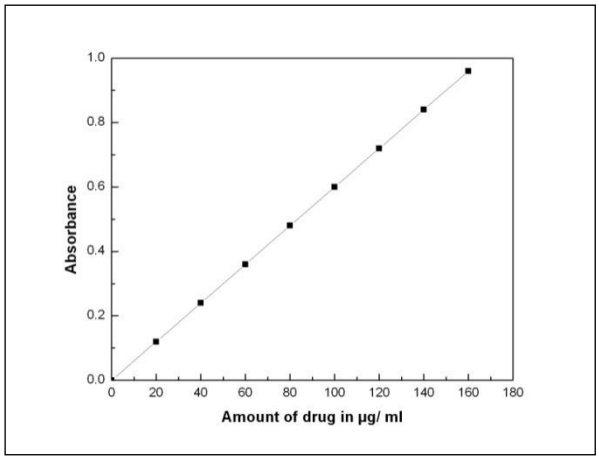

Fig.2 Calibration Curve of Furosimide

Table .1 Optical characteristics of the proposed methods

Parameters	Proposed method
λ max(nm)	450
Beer's law limit(µg/ml)	20-160
Molar absorptivity (L.mole^{-1} cm^{-1})	2.0847
Sandal's sensitivity (µg.cm^{-2}/0.001 A.U)	0.00208
Slope(b)	0.0059
Intercept(a)	0.00619
Correlation coefficient(r^2)	0.9997
Relative standered deviation(RSD)%	0.20833
LOD (µg/ml)	0.50480
LOQ (µg/ml)	1.68101
Color	Reddish pink

Table .2 Assay of furosimide in tablet formulations

Tablets	Labelled amount mg/ml	Amount found mg/ml	%Recovery	±SD	% RSD
Frusemene	250	249.53	99.81	0.3511	0.1407
Frusenes	250	249.53	99.81	0.3511	0.1407
Diucontin	250	249.43	99.77	0.8082	0.3240

***Average of five determinations**

Table .3 Determination offurosimide in presence of excipients

Excipients	Amount taken mg/ml	*Found mg/ml	Recovery %	±SD	RSD %
Glucose	5	4.98	99.73	0.0152	0.3060
Sucrose	10	9.98	99.86	0.0152	0.1520
Lactose	15	14.96	99.77	0.0115	0.0770
Dextrose	20	19.97	99.88	0.0020	0.0458
Talc	30	29.96	99.87	0.0152	0.0501
Starch	20	19.97	99.89	0.0036	0.1018

Table .4 Method accuracy from recovery assay

Sample	Added mg/ml	*Found mg/ml	Recovery %	±SD	RSD%
Serum samples	0.5	0.49	99.66	0.001	0.2317
	0.7	0.69	99.71	0.001	0.1432
	0.9	0.89	99.66	0.002	0.2229
	1.1	1.09	99.75	0.002	0.1897
Urine samples	2	1.98	99.26	0.006	0.3238
	2.2	2.19	99.81	0.001	0.0788
	2.4	2.39	99.88	0.002	0.0868
	2.6	2.59	99.88	0.002	0.1018

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