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Research Article

New Spectrophotometric Methods for the Quantification of Bumetanide Tablets

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Abstract

Four new spectrophotometric methods have been proposed for the determination of Bumetanide tablets using phosphate buffer pH 3.6, phosphate buffer pH 2.0, hydrochloric acid and distilled water. Shimadzu UV-1800 Model UV-VIS spectrophotometer double beam was used for the study. Bumetanide has shown linearity 1-60 µg/ml in all the reagents. The linear regression equations were found to be y = 0.012x - 0.010 (R^2 = 0.999), y = 0.063x + 0.028 (R^2 = 0.999), y = 0.061x + 0.047 (R^2 = 0.999) and y = 0.012x - 0.003 (R^2 = 0.999) respectively in phosphate buffer pH 3.6, phosphate buffer pH 2.0, hydrochloric acid and distilled water and all the methods were validated as per ICH guidelines. The methods were found to be precise, simple, and accurate and can be applied successfully for the determination of Bumetanide in tablets.

Keywords: Zero order spectroscopy (D0); Bumetanide, phosphate buffer; Hydrochloric acid; Validation; ICH guidelines

Introduction

Bumetanide (Figure 1) is used to reduce extra fluid (edema) in the body caused by conditions such as heart failure, liver disease, and kidney disease [1]. Bumetanide was patented in 1968 and came into medical use in 1972 and it is also available as a generic medication. Bumetanide was determined by different analytical methods such as HPLC [2-3], HPTLC (4), LC-MS [5], UPLC [6], spectrophotometry [7], automated flow injection with fluorimetric detection [8], amperometric detection [9] and also in biological fluids [10-11] and with and where as a very few methods were developed for its assay in pharmaceuticals using. In the present study the authors have developed a robust and economic stability indicating method for the quantification of Bumetanide in tablets. The method was validated as per ICH guidelines [12].

Materials and Method

Shimadzu double beam UV-VIS spectrophotometer (Model No. UV-1800) with quartz cells was used for the study and the solutions were scanned (200-400 nm). Bumetanide is available as tables with brand names Bumex (Validus pharmaceuticals LLC) (Genentech, Inc.) (Labelled claim: 1 and 0.5 mg), Burinex (Labelled claim: 2 mg/mL) (Leo pharma).

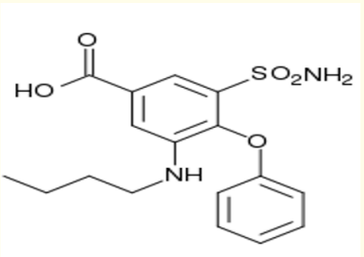

Figure 1: Chemical structure of Bumetanide

Preparation of solutions

Solutions such as phosphate pH 3.6, phosphate pH 2.0 and 0.1 N hydrochloric acid were prepared as per IP 2010. Stock solution of Bumetanide was prepared by dissolving 25 mg of Bumetanide in 25 ml volumetric flask with methanol (1000 µg/ml) and further working standard solutions (100 µg/ml) were prepared by diluting the stock solution with phosphate pH 3.6, phosphate pH 2.0, 0.1 N hydrochloric acid and distilled water for Method A, B, C and D respectively. Bumetanide tablets of two different brands were procured and extracted with methanol followed by dilutions and assay was performed.

Method validation

Linearity

A series of Bumetanide solutions 1-60 µg/ml were prepared in phosphate pH 3.6, phosphate pH 2.0, 0.1 N hydrochloric acid and distilled water from the stock solution and scanned (200-400 nm) against reagent blank. The absorption spectrum has shown maximum absorbance (λ_{max}) at 336.21, 346.19, 345.02 and 345.13 nm in phosphate pH 3.6, phosphate pH 2.0, 0.1 N hydrochloric acid and distilled water for Method A, B, C and D respectively. The absorbance of all the solutions were noted at their λ_{max} and calibration curves were drawn taking concentration on the x-axis and the corresponding absorbance on the y-axis for Method A, B, C and D respectively.

Precision and accuracy studies

The intra-day and inter-day precision studies were executed at three different concentration levels and accuracy studies were carried out by standard addition method (50%, 100%, and 150%). The % recovery was calculated for all techniques Method A, B, C and D.

Assay of Bumetanide tablets

Twenty Bumetanide tablets were weighed accurately, powdered and powder equivalent to 25 mg of Bumetanide was extracted with methanol in a 25 ml volumetric flask and dilutions were made using phosphate pH 3.6, phosphate pH 2.0, 0.1 N hydrochloric acid and distilled water. The assay was carried out using the above analytical techniques and the percentage recovery was calculated.

Results and Discussion

Four new spectrophotometric methods have been developed for the assay of Bumetanide tablets. The previously published analytical methods were compared with the present proposed methods in (Table 1). The absorption spectra obtained (Figure 2) for Bumetanide has shown λmax at 336.21, 346.19, 345.02 and 345.13 nm in phosphate pH 3.6 (Method A), phosphate pH 2.0 (Method B), 0.1 N hydrochloric acid (Method C) and distilled water (Method D) respectively. Bumetanide obeys Beer-Lambert's law (Figure 3) over the concentration range 1-60 µg/ml in Method A, B, C and D (Table 2) and the linear regression equations were found to be y = 0.012x - 0.010 (R^2 = 0.999), y = 0.063x + 0.028 (R^2 = 0.999), y = 0.061x + 0.047 (R^2 = 0.999) and y = 0.012x - 0.003 (R^2 = 0.999) respectively. The percentage RSD in precision and accuracy studies in all the four methods was found to be less than 2 indicating that the methods are precise (Table 3) and accurate (Table 4). The optical characteristics and the assay results of Bumetanide in all the four methods were given in (Table 5).

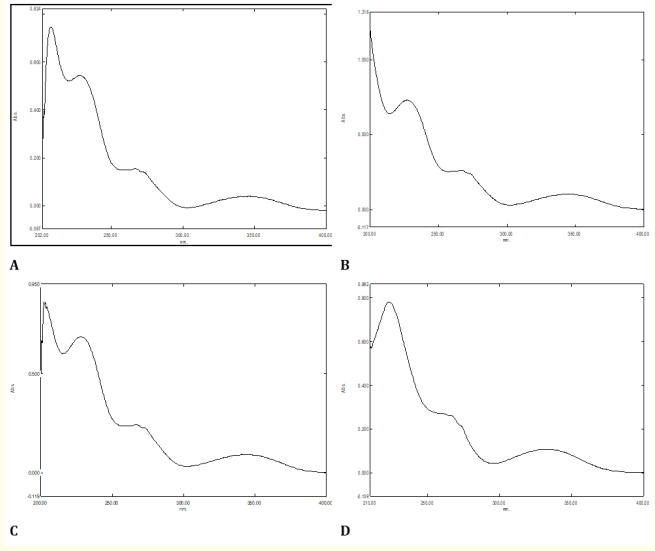

Figure 2: Absorption spectra of Bumetanide
(A) Phosphate buffer pH 3.6 (B) Phosphate buffer pH 2.0
(C) 0.1N HCl (D) Water

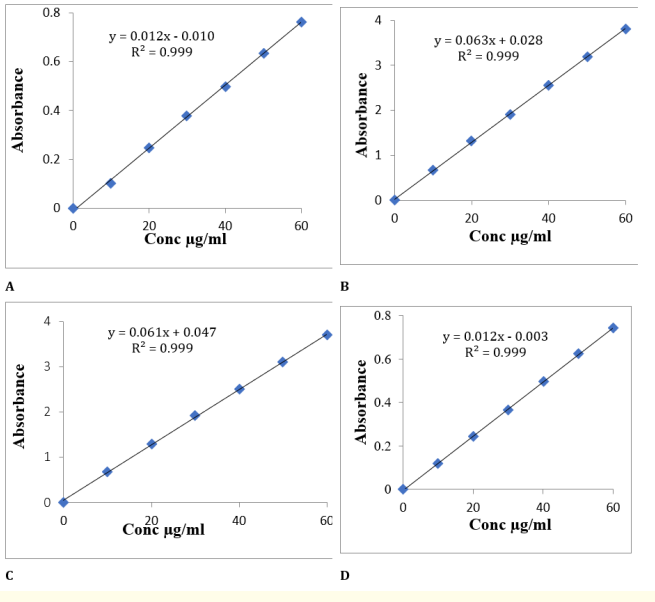

Figure 3: Calibration curves of of Bumetanide
(A) Phosphate buffer pH 3.6 (B) Phosphate buffer pH 2.0
(C) 0.1N HCl (D) Water

Reagent	λ (nm)	Linearity (µg/ml)	Reference
Borate buffer (pH 9.0) Phosphate buffer (pH 7.0)	252	5.0-75	7
Phosphate buffer pH 3.6 Phosphate buffer pH 2.0 Hydrochloric acid Water	336.21 346.19 345.02 345.13	1-60	Present method

Table 1: Literature survey of spectrophotometric methods for Bumetanide.

Conc. (µg/ml)	Absorbance at λ_{max}			
	A	B	C	D
0	0	0	0	0
10	0.105	0.669	0.68	0.121
20	0.245	1.321	1.3	0.242
30	0.381	1.92	1.91	0.366
40	0.5	2.57	2.5	0.497
50	0.636	3.2	3.1	0.625
60	0.763	3.8	3.7	0.741

Table 2: Linearity of Bumetanide.

Conc. g/ml	Inter day precision			
	* Mean ± Standard deviation (% RSD)			
	A	B	C	D
10	0.106 ± 0.001 (0.943)	0.66 ± 0.001 (0.149)	0.67 ± 0.001 (0.149)	0.122 ± 0.001 (0.819)
20	0.24 6 ± 0.002 (0.609)	1.32 ± 0.001 (0.075)	1.31 ± 0.01 (0.763)	0.243 ± 0.001 (0.411)
60	0.764 ± 0.001 (0.130)	3.81± 0.01 (0.262)	3.71 ±0.01 (0.269)	0.742 ± 0.002 (0.202)
Intraday precision				
10 (Day 1)	0.106 ± 0.001 (0.943)	0.668 ± 0.001 (0.149)	0.67 ± 0.001 (0.149)	0.122 ± 0.001 (0.819)
10 (Day 2)	0.107 ± 0.001 (0.934)	0.670 ± 0.001 (0.142)	0.68 ± 0.001 (0.147)	0.123 ± 0.001 (0.813)
10 (Day 3)	0.105 ± 0.001 (0.952)	0.669 ± 0.001 (0.149)	0.69 ± 0.001 (0.144)	0.124 ± 0.001 (0.806)
20 (Day 1)	0.246 ± 0.002 (0.609)	1.322 ± 0.001 (0.075)	1.31 ± 0.01 (0.763)	0.243 ± 0.001 (0.411)
20 (Day 2)	0.245 ± 0.002 (0.612)	1.342 ± 0.001 (0.074)	1.33 ± 0.01 (0.751)	0.244 ± 0.001 (0.409)
20 (Day 3)	0.248 ± 0.002 (0.604)	1.332 ± 0.001 (0.075)	1.32 ± 0.01 (0.757)	0.242 ± 0.001 (0.413)
60 (Day 1)	0.764 ± 0.001 (0.130)	3.8 ± 0.01 (0.262)	3.71 ± 0.01 (0.269)	0.742 ± 0.002 (0.202)
60 (Day 2)	0.763 ± 0.001 (0.131)	3.83 ± 0.01 (0.261)	3.73 ± 0.01 (0.268)	0.743 ± 0.002 (0.201)
60 (Day 3)	0.765 ± 0.001 (0.130)	3.84 ± 0.01 (0.260)	3.74 ± 0.01 (0.267)	0.744 ± 0.002 (0.201)

Table 3: Precision studies of Bumetanide.

Spiked Conc. (µg/ml)	Formu lation (µg/ml)	Total Conc. (µg/ml)	*Conc. obtained (µg/ml) [% Recovery]			
			A	B	C	D
10 (50%)	20 20 20	30 30 30	29.86 (99.53)	29.86 (99.53)	29.86 (99.53)	29.86 (99.53)
20 (100%)	20 20 20	40 40 40	39.87 (99.67)	39.87 (99.67)	39.87 (99.67)	39.87 (99.67)
30 (150%)	20 20 20	50 50 50	50.03 (100.06)	49.97 (99.94)	49.73 (99.46)	49.82 (99.64)

Table 4: Accuracy studies of Bumetanide.

Parameters	A	B	C	D
Linearity range (µg /ml)	1-60	1-60	1-60	1-60
λ_{max} (nm)	336.21	346.19	345.02	345.13
Molar extinction coefficient (Litre/mole/cm)	3826.3785	24379.4973	24780.356	4409.4457
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	0.09524	0.01495	0.01471	0.08265
Slope	0.012	0.063	0.061	0.012
Intercept	- 0.010	0.028	0.047	- 0.003
Correlation coefficient	0.999	0.999	0.999	0.999
Inter day Precision (%RSD) Intraday Precision (%RSD)	0.13-0.943 0.13-0.952	0.075-0.262 0.074-0.202	0.149-0.763 0.144-0.757	0.202-0.819 0.201-0.806
Accuracy (%RSD)	99.53-100.06	99.53-99.94	99.46-99.67	99.53-99.67
Assay (%)	99.83-99.91	99.78-99.89	99.81-99.93	99.59-99.98

Table 5: Optical characteristics of Bumetanide.

Assay of Bumetanide tablets

Assay was performed by extracting the Bumetanide with methanol from two different brands and it was found that Bumetanide was 99.45-99.72 in the two marketed formulations selected in all the spectrophotometric techniques.

Conclusion

The spectrophotometric techniques were validated as per ICH guidelines and found to be simple, precise, accurate and economical for the routine analysis of Bumetanide tablets.

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