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Simultaneous Estimation of Naproxen and Ranitidine HCl by Using UV Spectrophotometer

Tasnuva Haque[1], Md. Mesbah Uddin Talukder[3], Susmita Laila[2], Kanij Fatema[1] , Abul Kalam Lutful Kabir
Department of Pharmacy, Stamford University Bangladesh[1]
51 Siddeswari Road, Dhaka-1217.
Department of Pharmaceutical Technology, Faculty of Pharmacy[2]
University of Dhaka, Dhaka-1000, Bangladesh.
Department of Pharmacy, The University of Asia Pacific[3]
Dhaka-1209, Bangladesh.

Corresponding Author
Tasnuva Haque
Tel: 01712-130454
E-mail: Shoume_du@yahoo.com

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ABSTRACT

The development of a UV Spectrophotometric method for simultaneous estimation of Ranitidine HCl and Naproxen involves absorbance measurement of Ranitidine HCl at 313 nm in pH 7.4 phosphate buffer and 314 nm in both 0.1N HCl and in water and that of Naproxen at 229 nm in pH 7.4 phosphate buffer and 232 nm in both 0.1N HCl and in water corresponding to the respective absorption maxima. Both the drugs obey Beer- Lambert's law in the range of 5-25 µg/ml for Ranitidine HCl and 0.2-1.25 µg/ml for Naproxen. The method developed was validated to determine its linearity, precision, reproducibility and sensitivity. The tablet formulations were evaluated for the percent content of both the drugs at the selected wavelengths and the percent potency were 98.83 and 99.15 for Naproxen and Ranitidine HCl respectively.

Key words: Naproxen, Ranitidine HCl, Ultraviolet spectroscopy, marketed products.

INTRODUCTION

Naproxen (NAP) is chemically 2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, (s)-(+)-(s)-6-Methoxy-α-methyl-2-naphthaleneacetic acid (USP, 2004). Ranitidine (RAN) is chemically *N*-[2-[[[5-[(Dimethylamino) methyl] furan-2-yl]methyl]sulphanyl]ethyl]-*N*¢-methyl-2-nitroethene-1,1-diamine hydrochloride (IP, 1996). It is official in IP-2 and USP-3. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain, fever, inflammation and stiffness. It works by inhibiting both the COX-1 and COX-2 enzymes. Like other NSAIDs, naproxen is capable of producing disturbances in the gastrointestinal tract (MIMS Bangladesh, 2002). Ranitidine is a H_2-receptor antagonist. It is a classification of drugs used to block the action of histamine on parietal cells in the stomach, decreasing acid production by these cells. These drugs are used in the treatment of dyspepsia (MIMS Bangladesh, 2002).

Naproxen and Ranitidine combination is widely prescribed by the physicians in order to avoid NSAID induced ulcers. This paper describes a simple UV Spectrophotometric method for the estimation of Naproxen and Ranitidine in a new combined formulation.

EXPERIMENTAL

Materials and Methods

Naproxen and Ranitidine HCl were gift samples from Eskayef Bangladesh Ltd. Methanol was obtained from Merck, Germany. Distilled water was prepared by Aquatron deionizing water system. Hydrochloric acid and tribasic sodium phosphate were purchased from Merck (Germany) and orthophosphoric acid from (Sigma- Aldrich, Switzerland). Tablets of Naproxen and Ranitidine were purchased from the local market.

Equipments

UV- visible spectrophotometer used in this experiment was a HACH DR/4000U spectrophotometer, USA with 1 cm matched quartz cells.

Preparation of 0.1N HCl and pH 7.4 phosphate buffer

At first 50 ml water was taken in a 1000 ml volumetric flask. 10 ml of 37% (w/v) solution of HCl was added to it. Then it was shaken and required amount of water was added to make it up to 1000 ml. Thus 1000 ml of 0.1N HCl was prepared. In a beaker 750 ml 0.1 N HCl was taken and 180 ml of previously prepared 0.3 M tribasic sodium phosphate was added and rest amount of water was added upto 1000 ml. The pH was checked 7.4 with pH meter.

Preparation of single separate and combined stock solutions of Naproxen and Ranitidine HCl in pH 7.4 phosphate buffer

At first 5 mg Ranitidine equivalent to 5.567 mg Ranitidine HCl was weighed out using an electronic balance (sensitivity 0.001) and was taken in a 50 ml volumetric flask, pH 7.4 Phosphate buffer was added to dissolve it and the volume was made upto the volume. Now it is considered as a standard solution A of concentration of 100 µg/ml. In another 50 ml volumetric flask 5 mg of Naproxen was taken and the concentration was 100 µg/ml. Now the solution was diluted 10 times with buffer. Thus its final concentration was 10 µg/ml and it was the stock solution B. Stock solution A and B were mixed in 1:1 ratio by mixing 10 ml of Stock solution A by 10 ml of stock solution B. This mixture was considered as the combined stock solution C, having the concentration of Ranitidine HCl as 50 µg/ml and Naproxen of 5 µg/ml.

Table 1: Linearity of Ranitidine HCl in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U Spectrophotometer.

Media	λ_{max}	**Equation	R^2	% RSD of slope	*% RSD of R^2
Buffer (pH7.4)	313 nm	y = 0.039x + 0.004	0.997	2.398	0.302
		y = 0.041x + 0.004	0.993		
		y = 0.039x + 0.015	0.999		
0.1N HCl	314 nm	y = 0.015x - 0.003	0.996	2.518	0.061
		y = 0.016x - 0.013	0.995		
		y = 0.016x - 0.008	0.996		
Water	314 nm	y = 0.039x + 0.039	0.991	0.2564	0.172
		y = 0.039x + 0.034	0.994		
		y = 0.039x + 0.029	0.995		

*%RSD (Relative Standard Deviation) = SD (Standard Deviation) X 100/mean; **y=mx +C, where, y = absorbance, x =concentration (µg/ml), m = slope and C = intercept.

Table 2: Linearity of Naproxen in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U Spectrophotometer.

Media	λ_{max}	Equation	R^2	% RSD of slope	% RSD of R^2
Buffer (pH 7.4)	229 nm	y = 0.755x - 0.021	0.998	1.549	0.143
		y = 0.697x - 0.010	0.998		
		y = 0.760x - 0.035	0.995		
0.1N HCl	232 nm	y = 0.483x - 0.014	0.999	1.470	0.110
		y = 0.498x - 0.027	0.997		
		y = 0.487x - 0.013	0.998		
Water	232 nm	y = 0.352x + 0.005	0.999	1.830	0.135
		y = 0.349x + 0.004	0.997		
		y = 0.361x - 0.010	0.999		

Scanning of wave lengths of Naproxen and Ranitidine HCl in pH 7.4 phosphate buffer

The stock solution A and B separately was scanned over a range of 200-400 nm, two peaks were observed for A at 236 and 314 nm, using buffer as blank, whereas peak at 314 nm was the most sharp and four peaks were found for B at 232, 262,270 and at 328 nm and peak at 232 nm was the most sharp one. The combined solution was then scanned in the similar way and four peaks were found at 229, 272, 313 and 382 nm. Now, taking 229 nm λ_{max} for Naproxen and 313 nm for ranitidine HCl, the stock solution A was diluted to produce a concentration of 20, 10 and 5 µg/ml

and their absorbance was 0.868, 0.461 and 0.215 respectively. Stock solution B was diluted to produce Naproxen concentration of 1 µg/ml and 0.5 µg/ml, having absorbance of 0.467 and 0.217.

Again Stock solution C was diluted 5 and 10 times. Now the diluted solutions contained Ranitidine HCl of 10 µg/ml and 5 µg/ml respectively and Naproxen of 1 µg/ml and 0.5 µg/ml respectively. At λ_{max} of 313 nm for Ranitidine, the concentrations had given the absorbance of 0.429 and 0.201 and λ_{max} of 229 nm for naproxen the concentrations gave the absorbance of 0.479 and 0.251 respectively.
This has shown that though slight shifting of λ_{max} of single drugs occurred after mixing together, but at that shifted λ_{max}, the same concentration of single drug and combined drug had given almost same absorbance.

Preparation of stock and standard solutions of combined Naproxen and Ranitidine HCl in 0.1N HCl

At first 2 mg Naproxen was taken in a 100 ml volumetric flask, 3 ml methanol was added to dissolve it. Then 5 mg Ranitidine equivalent to 5.57 mg of Ranitidine HCl was added to it. Sufficient amount of 0.1N HCl was added to dissolve it. Finally the volume was made up to 100 ml with 0.1N HCl. Now, combined stock solution of Naproxen and Ranitidine HCl having concentrations of 20 µg/ml and 50 µg/ml respectively was prepared. Required dilution was done with 0.1N HCl.

Preparation of stock and standard solutions of combined Naproxen and Ranitidine HCl in water

Like the method mentioned above, a combined stock solution of Naproxen and Ranitidine HCl having concentrations of 100 µg/ml and 100 µg/ml respectively were prepared in water using small amount of methanol as co-solvent for Naproxen. Further dilution was carried out by water.

Scanning of wave lengths in 0.1N HCl and in Water

Combined stock solution of Naproxen and Ranitidine HCl in 0.1N HCl and in water was scanned within 200-400 nm wave lengths. For both cases two peaks were observed at 232 and at 314 nm. At first single solution of Naproxen and Ranitidine HCl were prepared in both 0.1N HCl and in water. They were sufficiently diluted and their single absorbance at 314 nm (for Ranitidine HCl) and at 232 nm (for Naproxen) were measured. Then combined solution was diluted and at those same concentrations of single Naproxen and Ranitidine, their absorbance was measured. The absorbance of single Naproxen and Ranitidine HCl were same with the combined ones.

Sample preparation

20 tablets of marketed brands of Naproxen and Ranitidine were weighed separately. Their average weights were determined. Powder of tablets equivalent to 25 mg of Ranitidine and 20 mg of Naproxen were weighed and taken in a 50 ml volumetric flask. 20 ml of water was and 10 ml methanol was added. It was sonicated for 30 min for dissolve it. It was filtered through Whitman filter paper no. 41 and made 50 ml with water. Further dilution was carried out by water.

RESULT AND DISCUSSION

Specificity

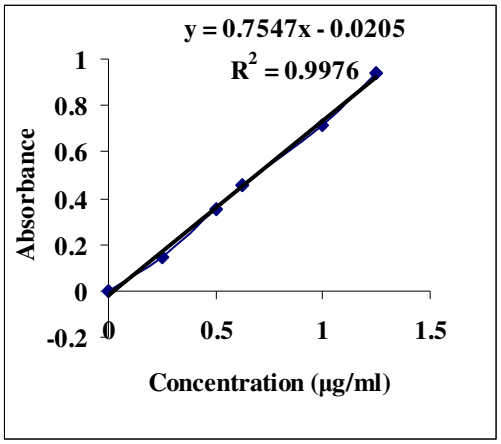
From the scanning result, it can be said that this method is very specific for simultaneous estimation of Naproxen and Ranitidine HCl.

Linearity

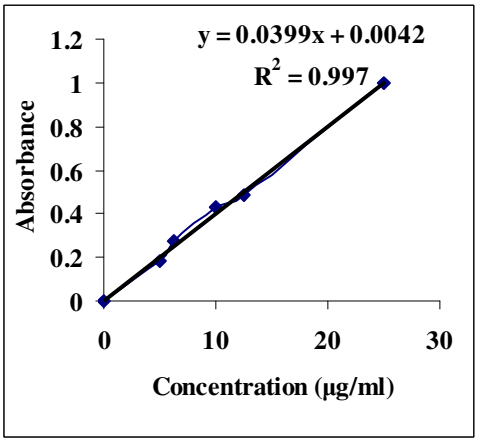
Figure 1 (a) and 1 (b) and Table- 1and 2 represents the equation of the regression line, correlation coefficient (R^2), relative standard deviation (RSD %) values of the slopes and R^2. Excellent linearity was obtained for Naproxen between 0.2- 1.25 µg/ml and for Ranitidine HCl linearity was observed between 1.5-12 µg/ml (Sharma et al., 2003).

Precision

The precision of the method {intraday and interday (5 days) variation of replicate determination} was checked by preparing one concentration of combined Naproxen (1.0 µg/ml) and Ranitidine HCl (10 µg/ml) for 3 times. The precision of the method, expressed as the RSD % of intraday and interday variation is given in Table 3 and 4.



(a)



(b)

Figure 1: Standard curve of (a) Naproxen in combination with Ranitidine and (b) Ranitidine in combination with Naproxen in pH 7.4 phosphate buffer.

Table 3: Intraday and Interday precision of Ranitidine HCl in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U Spectrophotometer.

Media	Conc. (µg/ml)	Absorbance (intraday)	Absorbance (mean±SD)	RSD%	Absorbance (interday)	Absorbance (mean±SD)	RSD%
Buffer (pH 7.4)	10	0.429 0.412 0.425	0.422±0.009	2.106	0.417 0.421 0.424	0.421±0.004	0.835
0.1N HCl	10	0.125 0.118 0.125	0.123±0.004	3.295	0.121 0.119 0.118	0.119±0.002	1.280
Water	10	0.41 0.42 0.412	0.414±0.002	1.278	0.430 0.420 0.410	0.42±0.010	2.381

Table 4: Intraday and Interday precision of Naproxen in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U spectrophotometer.

Media	Conc. (µg/ml)	Absorbance (intraday)	Absorbance (mean±SD)	RSD%	Absorbance (interday)	Absorbance (mean±SD)	RSD%
Buffer (pH 7.4)	1	0.719 0.717 0.720	0.718±0.002	0.213	0.730 0.720 0.710	0.720±0.010	1.389
0.1N HCl	1	0.467 0.455 0.445	0.455±0.011	2.410	0.454 0.459 0.449	0.454±0.005	1.100
Water	1	0.351 0.331 0.341	0.341±0.010	2.933	0.348 0.351 0.350	0.350±0.002	0.437

Reproducibility

Three different standard working solution-containing combined Naproxen and Ranitidine HCl was prepared. The absorbance of prepared mixture of standard solutions was measured 3 times as a test sample. From the respective absorbance counts, the concentrations of Naproxen and Ranitidine HCl were calculated (Table- 5 and 6).

Sensitivity

The sensitivity (Sathe et al., 2007) of measurement of Naproxen and Ranitidine HCl was estimated in terms of the limit of quantification (LOQ). The smallest amounts detected under the UV conditions used were estimated in terms of the limit of detection (LOD). LOQ and LOD were calculated by use of the equations LOD = 3 × N/B and LOQ = 10 × N/B, where N is the standard deviation of the absorbance of the drugs, taken as a measure of noise, and B is the slope of the corresponding calibration plot. Results are shown in Table 7 and 8.

Table 5: Reproducibility of Ranitidine HCl in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U spectrophotometer.

Media	Concentration (µg/ml)	Absorbance (mean±SD)	Equation	Measured conc. µg/ml, n=3 (Mean±SD)	RSD %	Deviation%
Buffer (pH 7.4)	5	0.181±0.003	y = 0.755x - 0.021	4.439±0.063	1.420	11.220
	10	0.422±0.009		10.470±0.220	2.130	-4.700
	25	0.997±0.002		24.899±0.038	0.154	-0.404
0.1N HCl	5	0.080±0.003	y = 0.015x - 0.003	5.760±0.170	2.990	-15.200
	10	0.143±0.002		10.005±0.014	1.430	-0.050
	25	0.360±0.005		24.93±0.105	0.420	0.280
Water	5	0.237±0.004	y = 0.039x + 0.039	5.070±0.102	2.020	-1.400
	10	0.414±0.005		9.600±0.140	1.410	4
	20	0.817±0.004		19.920±0.103	0.519	0.400

Potency determination

The potency was determined for two different marketed brands of Naproxen and Ranitidine tablets shown in Table-9. The potencies were found 99.148 % for Ranitidine HCl and 98.83 % for Naproxen respectively.

Table 6: Reproducibility of Naproxen in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U spectrophotometer.

Media	Conc. (µg/ml)	Absorbance (mean±SD)	Equation	Measured conc. µg/ml, n=3 (mean±SD)	RSD %	Deviation %
Buffer (pH 7.4)	0.500	0.351±0.003	y = 0.755x - 0.021	0.490±0.004	0.810	2
	1	0.719±0.002		0.980±0.002	0.210	2
	1.250	0.940±0.004		1.270±0.005	0.370	-1.600
0.1N HCl	0.500	0.230±0.003	y = 0.487x - 0.013	0.500±0.005	1.020	0
	1	0.460±0.010		0.960±0.020	2.350	4
	1.250	0.590±0.010		1.230±0.020	1.660	1.600
Water	0.500	0.177±0.002	y = 0.352x +0.005	0.490±0.006	1.170	2
	1	0.341±0.010		0.950±0.030	2.980	5
	2	0.710±0.003		1.990±0.009	0.460	0.500

Deviation % = (Theoretical concentration – measured concentration) x 100/ measured concentration

Table 7: Sensitivity of Ranitidine HCl in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U spectrophotometer.

Media	Conc. (µg/ml)	Absorbance	Equation	SD	LOD	LOQ
buffer (pH 7.4)	5	0.184	y = 0.039x + 0.004	0.342	25.714	85.714
	10	0.429				
	22	0.859				
0.1N HCl	5	0.081	y = 0.015x - 0.003	0.366	75.205	250.685
	10	0.125				
	50	0.736				
Water	5	0.243	y = 0.039x + 0.039	0.280	21.460	71.535
	10	0.460				
	20	0.798				

Table 8: Sensitivity of Naproxen in pH 7.4 phosphate buffer, in 0.1 N HCl and in water using HACH DR/4000U spectrophotometer.

Media	Conc. (µg/ml)	Absorbance	Equation	SD	LOD	LOQ
Buffer (pH 7.4)	0.250	0.146	y = 0.755x - 0.021	0.290	1.153	3.843
	0.500	0.351				
	1	0.719				
0.1N HCl	0.500	0.232	y = 0.487x - 0.013	0.229	1.411	4.702
	1	0.467				
	1.5	0.689				
Water	0.500	0.177	y = 0.352x + 0.005	0.270	2.301	7.670
	1	0.351				
	2	0.706				

Table 9: Assay result of two marketed brands of Naproxen and Ranitidine HCl using HACH DR/4000U spectrophotometer.

Compound	Dilution factor	Absorbance	Equation	Conc. (µg/ml)	Amount (mg) in 50 ml	Claimed amount (mg) in 50 ml	% potency
Naproxen	300	0.974	y = 0.755x -0.021	395.323	19.766	20	98.830
Ranitidine HCl	100	0.202	y = 0.039x + 0.004	495.739	24.787	25	99.148

% Potency = Measured amount X 100/ Claimed amount.

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