Int. J. Chem. Sci.: 9(1), 2011, 255-264
ISSN 0972-768X

NOVEL VISIBLE SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF FEW SELECTED DRUGS USING COBALT THIOCYANATE AS CHROMOGENIC REAGENT

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ABSTRACT

A new, simple, accurate and economical spectrophotometric method for the determination of benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride, and drotaverine hydrochloride by using cobalt thiocyanate has been developed. The colored complexes are formed by coordination of secondary/tertiary amine group of drug with metal of cobalt thiocyanate that is extractable into nitrobenzene from aqueous solution. All the chromogens exhibit maximum absorption at 626 nm and obey Beer's law in the concentration range of 100-500, 10-50, 25-175 and 50-300 µg/mL for benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride and drotaverine hydrochloride, respectively. The method was validated in terms of accuracy, precision, and specificity and can be used for routine analysis of these drugs in bulk and pharmaceutical dosage forms.

Key words: Spectrophotometric, Benzapril hydrochloride, Quinapril hydrochloride, Ranitidine hydrochloride, Drotaverine hydrochloride, Cobalt thiocyanate.

INTRODUCTION

Chemical name of benzapril hydrochloride[1] (BH) is 3-[[1-(ethoxy-carbonyl)-3-phenyl-(1S)-propyl] amino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3S)-benzazapine-1-acetic acid monohydrochloride (Fig. 1). Its molecular formula is $C_{24}H_{28}N_2O_5$.HCl. Benazapril hydrochloride is an ACE (angiotensin converting enzyme) inhibitor. ACE is an enzyme in the

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body that is important for the formation of angiotensin II. Angiotensin II causes constriction of arteries in the body; thereby, elevating blood pressure. ACE inhibitors such as benazapril lower blood pressure by inhibiting the formation of angiotensin II; thus, relaxing the arteries. Relaxing the arteries not only lowers blood pressure, but also improves the pumping efficiency of a failing heart and improves cardiac output in patients with heart failure.

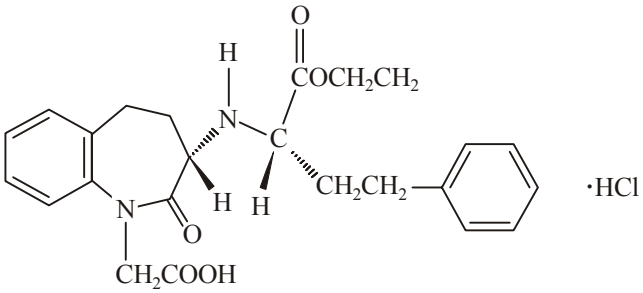

Fig. 1: Structure of benzapril hydrochloride

Quinapril hydrochloride[2] (QH) is used in the treatment of hypertension and congestive heart failure. Quinapril hydrochloride is actually a prodrug. It is converted to its active metabolite, quinaprilat, in the liver. The chemical name of quinapril hydrochloride is 2-(2-((1-(ethoxy carbonyl)-3-phenyl propyl) amino)-1-oxopropyl)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid mono hydrochloride (Fig. 2).

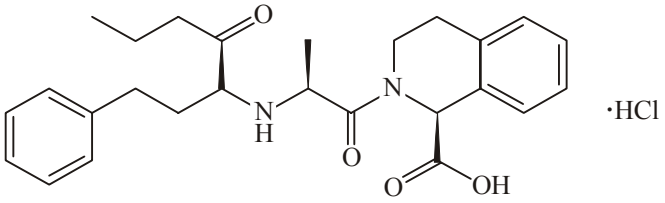

Fig. 2: Structure of quinapril hydrochloride

Ranitidine hydrochloride[3] (RH) chemically is *N*- (2-[(5-(dimethylaminomethyl) furan- 2-yl) methylthio] ethyl)- *N*-methyl- 2-nitroethene- 1,1-diamine hydrochloride (Fig. 1). Ranitidine hydrochloride is a histamine H_2- receptor antagonist that inhibits stomach acid production. It is commonly used in treatment of peptic ulcer.

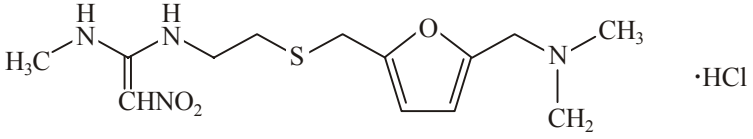

Fig. 3: Structure of ranitidine hydrochloride

Chemically, drotaverine hydrochloride[4] (DH) is 1,2,3,4-tetrahydro-6, 7-diethoxy-1-((3,4-diethoxyphenyl) methylene)-isoquinoline hydrochloride (Fig. 4). Drotaverine hydrochloride is an analogue of papaverine with smooth muscle relaxant properties. It is a non-anticholinergic antispasmodic, which selectively inhibits phosphodiesterase IV and is accompanied by a mild calcium channel-blocking effect

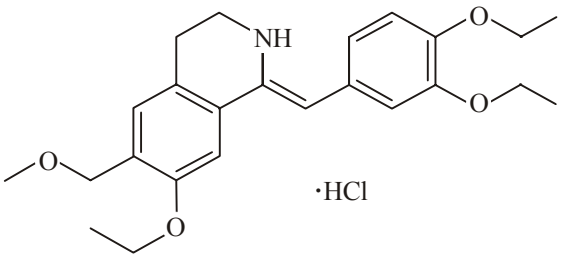

Fig. 4: Structure of drotaverine hydrochloride

There are number of methods reported for the determination of benzapril hydrochloride[5-12], for quinapril hrdrochloride[13-18], for ranitidine hydrochloride[19-24] and for drotaverine hydrochloride[25-29]. The common feature of all the above drugs is the presence of an amino function, which forms a coordination complex with the central atom of cobalt thiocyanate. The complexes formed are extractable into nitrobenzene and exhibit maximum absorbance at 626 nm. The existing spectrophotometric methods do not appear to have adequately exploited the chemical properties of benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride and drotaverine hydrochloride for designing sensitive procedures. In the present investigation, the authors have developed a sensitive visible spectrophotometric method for the determination of these drugs utilizing secondary amine group. The proposed method is applicable for the determination of these drugs in bulk and pharmaceutical dosage formulations

EXPERIMENTAL

Materials and method

Instrument

A Shimadzu UV-1800 double beam UV-Visible spectrophotometer with 10 mm matched quartz cells was used to carry out spectral analysis. Metler electronic balance was used to weigh the samples.

Reagents

All the chemicals used were of analytical grade and the solutions were freshly

prepared. Pharmaceutical grade benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride and drotaverine hydrochloride were kindly provided by M/s Aurobindo Pharmaceuticals Ltd., Hyderabad, India. All other chemicals used were of analytical grade; procured from S. D. Fine Chemicals Ltd., Mumbai, and distilled water was used through out the analysis. For the present work, commercial tablets benzapril hydrochloride-BENACE 5 and 10 mg (Novartis), quinapril hydrochloride -ACCUPRIL 5 mg (Park Devis), ranitidine hydrochloride- ACIBLOC and 150 mg & 300 mg (Marc lab), drotaverine hydrochloride-DOTRA 80 mg (Dynamic lab) were procured from the local drug store.

Aqueous solution of cobalt thiocyanate

Cobalt thiocyanate solution was prepared by dissolving 7.25 g of cobalt nitrate and 3.8 g of ammonium thiocyanate in 100 mL of distilled water.

Buffer solution (pH 2.0)

Buffer was prepared by mixing 25 mL of potassium chloride (0.2 M) and 13 mL of hydrochloric acid (0.2 M) and made up to 100 mL with distilled water and pH was adjusted to 2.0.

Analytical grade of nitrobenzene was used to extract the colored complex.

Preparation of standard stock solutions

1 mg/mL solutions of benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride and drotaverine hydrochloride were prepared separately by using distilled water.

Procedure for calibration curve

Aliquots of standard stock solution (1.0- 5.0 mL) of BH or (0.1-0.5 mL) of QH or (0.25-1.75 mL) of RH or (0.5-3.0 mL) of DH were transferred to a series of 60 mL separating funnel. To each separating funnel, measured volume of pH 2.0 buffer and cobalt thiocyanate solutions were added (Table 1). The total volume of aqueous phase in each separating funnel was adjusted to 10 mL with distilled water. To each separating funnel, 10 mL of nitrobenzene was added and the contents were shaken for 2 min. Two phases were allowed to separate and the absorbance of nitrobenzene layer was measured at 626 nm against reagent blank. The colored species was stable for 1 hour. The Beer's plot of absorbance against concentration was plotted. A linear correlation was obtained between absorbance and concentration over a range of 100-500 μg/mL for BH, 10-50 μg/mL for QH, 25 –175 μg/mL for RH and 50-300 μg/mL for DH.

Table 1: Optimum conditions and results of the proposed method

Reagent	Benzapril hydrochloride	Quinapril hydrochloride	Ranitidine hydrochloride	Drotaverine hydrochloride
Conc. of drug (μg/mL)	100-500	10-50	25 -175	50-300
Volume of pH 2 buffer (mL)	2.5	2.0	0.5	1.5
Volume of reagent (mL)	2.0	2.5	3.5	3.0
λ max (nm)	626	626	626	626

Preparation for analysis of tablet dosage formulations

Twenty tablets of each drug were weighed and powdered separately. A quantity of tablet powder equivalent to about 25 mg of each drug was weighed accurately and transferred to 25 mL volumetric flasks. The drug in each flask was dissolved with 10 mL distilled water and made up to the mark. Each sample was filtered through Whatmann filter paper and appropriate dilutions of sample solutions were made and assayed as given earlier. The drug contents of the preparations were calculated using the standard curve.

Recovery studies

To study the accuracy, reproducible and precision of the proposed method, recovery experiments were carried out. Recovery studies were carried out by adding known amount of pure drug to the pre-analyzed formulations and the proposed method was followed. The total amount of the drug present in the sample was determined and the percentage recovery was then calculated.

RESULTS AND DISCUSSION

The four drugs BH, QH, RH and DH selected for the present investigation form coordination complexes with the metal of cobalt thiocyanate. The optimum conditions were so selected that the maximum sensitivity, largest linear range and low blank readings with the maximum correlation coefficient and precision were obtained. Beer's law limits and molar absorptivity, Sandell's sensitivity and regression characteristics of the proposed method are presented in Table 2. The % RSD and range of error at 95% confidence level of the proposed method are also summarized in Table 2.

Table 2: Optical characteristics and precision of the proposed method

Parameter	Benzapril hydrochloride	Quinapril hydrochloride	Ranitidine hydrochloride	Drotaverine hydrochloride
λ max	626	626	626	626
Beer's law limits (mcg/mL)	100-500	10-50	25-175	50-300
Sandell's sensitivity ($mcg/cm^2/0.001A.U$)	0.4645	0.0759	0.2118	0.3960
Molar absorptivity ($L\ mol^{-1}cm^{-1}$)	9.14×10^3	6.25×10^4	1.65×10^4	1.09×10^4
Correlation coefficient (r^2)	0.999	0.998	0.999	0.999
Regression equation (y = mx + c)**	0.00214x + 0.01058	0.01623x-0.08420	0.00319x + 0.15940	0.00184x + 0.14185
Slope (a)	0.00214	0.01623	0.00319	0.00184
Intercept (b)	0.01058	-0.08420	0.15940	0.14185
Range of errors*				
Confidence limit with 0.05 level	0.1460	0.3596	0.4436	0.4311
Confidence limit with 0.01 level	0.2159	0.5319	0.6562	0.6377
% Relative standard deviation*	0.1746	0.4300	0.5305	0.5156

** y is the absorbance and x is the concentration in µg/mL

*Average of six determinations

The recovery experiments were also carried out by adding known amount of standard drug to the pre-analyzed tablet formulation. The % recovery values, which are close to 100%, indicate the reproducibility of the proposed method and absence of interference of the excipients present in the formulation. The accuracy of the method was ascertained by comparing the results of proposed and reference methods (UV methods) statistically by the t- test and F- test. This comparison showed that there is no significant difference between the

results of proposed methods and those of reference ones. The assay results obtained by the proposed method were found to be in good agreement with labeled amount Table 3.

Table 3: Assay and recovery studies of proposed method

Name of the dosage form	Labeled amount (mg)	Content of the drug found [a] ± S.D		% Recovery by the proposed method [b]
		Proposed method	Reference method	
Benzapril hydrochloride Tablet 1	5.0	5.03 ± 0.0719	4.98 ± 0.0390	100.4
	10	F = 0.2050		
		T = 3738		
Tablet 2		10.04 ± 0.0804	9.91 ± 0.0318	100.6
		F = 0.6309		
		T = 0.1959		
Quinapril hydrochloride Tablet 1	5.0	4.99 ± 0.02266	4.98 ± 0.5785	99.80
		T = 0.8546		
		F = 0.3709		
Ranitidine hydrochloride Tablet 1	150	150.05 ± 0.2629	149.9 ± 0.2768	
		F = 0.9128		100.03
		T = 0.3427		
Tablet 2	300	299.98 ± 0.3287	299.9 ± 0.3464	
		F = 0.9112		99.96
		T = 0.7911		
Drotaverine hydrochloride Tablet 1	80	79.94 ± 0.0731	79.86 ± 0.3272	99.81
		F = 0.0051		
		T = 0.6455		

[a]Average ± standard deviation of eight determinations, the t and F-values refer to comparison of proposed method with reference method. Theoretical values at 95% confidence limits t = 2.365 and F = 4.88.

[b]Recovery of 10 mg added to the pre-analyzed pharmaceutical formulations (average of three determinations).

For reference UV methods of benzapril hydrochloride, quinapril hydrochloride and drotaverine hydrochloride, methanol was used as solvent while for ranitidine hydrochloride, water was used.

CONCLUSION

From the study of validation parameters namely accuracy, precision, specificity, linearity and range, it was observed that the method is convenient, specific, accurate, precise and reproducible. This method can be used for the routine analysis of these drugs in bulk and pharmaceutical dosage forms.

ACKNOWLEDGEMENTS

The authors are thankful to the M/s Aurobindo Pharmaceuticals Ltd., Hyderabad, India for providing benzapril hydrochloride, quinapril hydrochloride, ranitidine hydrochloride, and drotaverine hydrochloride as gift samples and to the Principal, S. K. Gulati, HOD, K. Ram Subha Reddy and the Management of the Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya, Hyderabad, for providing the laboratory facilities and their constant encouragement for carrying out the research work.

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Revised : 12.11.2010 *Accepted : 16.11.2010*