ISSN 0975-6299 Vol 3/Issue 2/April – June 2012

International Journal of Pharma and Bio Sciences

RESEARCH ARTICLE ANALYTICAL CHEMISTRY

A SIMPLE EXTRACTIVE SPECTROPHOTOMETRICDETERMINATION OF LORATADINE, DESLORATADINE AND RUPATADINE FROM PHARMACEUTICAL FORMULATIONS

*** RELE RAJAN. V. AND GURAV PANKAJ .J.**

D.G. RUPAREL COLLEGE, MAHIM, MUMBAI 400 016.

RELE RAJAN. V.
D.G. RUPAREL COLLEGE, MAHIM, MUMBAI 400 016.

ABSTRACT

Simple sensitive and accurate extractive spectrophotometric method was developed for the estimation of loratadine, desloratadine and rupatadine in pharmaceutical dosage forms. The method was based on the formation of colored ion pair complexes by the drugs with thiocynate ions. These ion pair complexes were quantitatively extracted under the experimental condition in chloroform. The absorbance values were measured at 618 nm,614 nm and 616 nm respectively. The proposed method was validated statistically.Recoveries of method was carried out by standard addition methods. The Beer's lawranges were found to be 1-12 µg/ml, 0.5-3 µg/ml and 0.5-8 µg/ml for loratadine, desloratadine and rupatadine respectively. The low values of standard deviation and percentage RSDindicate high precision of method. Hence the method is useful for routine estimation of loratadine, desloratadine and rupatadine in tablets respectively.

KEYWORDS

Loratadine,Desloratadine,Rupatadine fumarate ,Cobalt nitrate,Ammonium thiocynate,Chloroform

INTRODUCTION

Loratadine is Ethyl 4-(8-chloro-5, 6-dihydro-11 H-benzo [1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate. It shows molecular formula as $C_{22}H_{23}ClN_2O_2$ with molecular weight 382.9. It is official in USP[1], BP[2], IP[3] . It is non sedating peripheral histamine H_1 receptor antagonist. A literature survey reveals spectrophotometric[(4-5)] and HPLC[(6-13)] methods.

Desloratadine is 8-chloro-6,1 dihydro-11(4 piperidinylidine) -5-H- benzo [1,2-b]pyridine, descarboethoxyloratadine. It shows molecular formula as $C_{19}H_{19}ClN_2$ with molecular weight 310.82. It is not yet official in any pharmacopeias. It is non sedatingperipheral histamine H_1 receptor antagonist, active metabolite of loratadine. A literaturesurvey reveals a spectrophotometric[14- 16] and HPLC[17-21] methods.Rupatadine is 8-chloro-6,11-dihydro-11-[1-(5-methyl-3-pyridinyl) methyl-4-pipe-ridinyllidene] 5H-benzo [5,6]-cyclohepta-[1,2-b] pyridine.It shows molecular formula as $C_{26}H_{26}N_3Cl$ with molecular weight 415.96. It is not yet official in any pharmacopeias.It is non sedating peripheral histamine H_1 receptor antagonist. A literature survey reveals HPLC[22-23],HPTLC[24], MEKC[25],spectrophotometric[26] and aqueous titration[27] methods.

MATERIAL AND METHODS

A SHIMADZU -160 A double beam UV-VISIBLE recording spectrophotometer with pair of 10 mm matched quartz cell was used to measure absorbance of solutions.
A SHIMADZU analytical balance was used.
Ammonium thyocinate, cobalt nitrate and chloroform of A.R. grade were used in the study.

PREPRATION OF STANDARD SOLUTION:

Stock solutions of loratadine, desloratadine and rupatadine (100 µg/ml) were prepared in ethanol. From these stock solutions, working standard solutions (10 µg/ ml) were prepared by diluting 10 ml stock solution to 100 ml with ethanol. .

Prepartion of reagents*:*

Cobalt thiocyanate was prepared by dissolving cobalt nitrate and ammonium thiocyanate in 1:2 molar proportion in distilled water.

EXPERIMENTAL

For loratadine*:* Into a series of separating funnels appropriate amount of the working standard drug solutions were pipetted out. To each funnel 2 ml of cobalt thiocynatatecomplex solution was added. A 10 ml of chloroform was added to each funnel. The solutions were shaken for thorough mixing of the two phases and were allowed to stand for separation of the layers. The absorbance value of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 618 nm).

For desloratadine : Into a series of separating funnels appropriate amount of the working standard drug solutions were pipetted out. To each funnel 2.0 ml of cobalt thiocynatate complex solution was added. A 10 ml of chloroform was added to each funnel. The solutions were shaken for thorough mixing of the two phases and were allowed to stand for separation of the layers. The absorbance value of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 614 nm).

For rupatadine : Into a series of separating funnels appropriate amount of the working

standard drug solutions were pipetted out. To each funnel 2ml of cobalt thiocynatate complex solution was added. A 10 ml of chloroform was added to each funnel. The solutions were shaken for thorough mixing of the two phases and were allowed to stand for separation of the layers.

The absorbance value of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 616 nm.)

Estimation from tablets

Twenty tablets of labelled claim 10 mg of loratadine / 5 mg of desloratadine / 10 mg of rupatadine were weighed accurately. Average weight of each tablet of loratadine /desloratadine / rupatadine was determined. Tablets were crushed into fine powder. An accurately weighed quantity of powder equivalent to 10 mg of loratadine /desloratadine /rupatadine was transferred into a beaker and it was shaken with 50 ml of ethanol and filtered. The filtrate and the washing were collected in a 100.0 ml volumetric flask. This filtrate and the washing were diluted up to the mark with ethanol to obtain final concentration as 100 µg /ml. A 10 ml. of this solution was further diluted to give 10 µg /ml. Such solutions were further used for estimation of loratadine, desloratadine and rupatadine respectively.

Appropriate aliquots of drug solution were taken. The individual assay procedures were carried out for the estimation of drug contents in tablets. The concentration of the drug in the tablets was calculated using calibration curve. The recovery experiment was carried out by standard addition method. The values of optical and regression terms of analysis are given in table no 1.

RESULT AND DISCUSSION

The extractive spectrophotometric methods are popular due to their sensitivity in assay of the drug and hence ion pair extractive spectrophotometric methods have gain considerable attention for quantitative determination of many pharmaceutical preparations. These proposed methods are extractive spectrophotometric methods for the determination of loratadine/desloratadine/rupatadine by using chloroform as solventfrom its formulations i.e.tablets.

The colour ion –pair complexes are formed and are very stable. The working conditions of these methods were established by varying one parameter at time and keeping the other parameters fixed by observing the effect produced on the absorbance of the colour species. The various parameters involved for maximum colour development for these methods were optimized.

The proposed methods were validated statistically and by recovery studies .The molar absorptivity and Sandell's sensitivity values (Table no. 1) show the sensitivity of methods while the precision was confirmed by % RSD (relative standard deviation). The optical characteristics such as absorption maxima (nm), molar absorptivity (Lit- $mole^{-1}$ cm^{-1}), correlation coefficient (r) and sandell sensitivity ($\mu g/cm^2/0.001$) were calculated and are also summarized in table I. Assay results of recovery studies are given in table no. II, III, IV. Results are in good in agreement with labelled value. The percent recovery obtained indicates non interference from the common excipients used in the formulation.

The reproducibility, repeatability and accuracy of these methods were found to be good, which is evidenced by low values of standard deviations. Spectrophotometric methods suggested in literature were applied in UV region, need costly reagents for development of chromogen and useful in higher concentration. The proposed methods are simple, sensitive, accurate, precise, and reproducible applicable to even very low concentration as compare to previous methods suggested in literature. They are directly applied to drug to form chromogen. Hence they can be successfully applied for the routine estimation of

loratadine/desloratadine/rupatadine in bulk and pharmaceutical dosage form even at very low concentration in formulation such as tablets.

The strong recommendation is made here for the proposed methods for determination of loratadine/desloratadine/rupatadine from its formulation i.e. tablets.

Table I
Optical and regression of drugs

Parameter	Drugs		
	Loratadine	**Desloratadine**	**Rupatadine**
λ max (nm)	618	614	616
Beer Law Limits (mcg/mL)	1-12	0.5- 3	0.5 -6
Molar absorptivity(L/mol.cm)	2.68 x 10^4	9.2 x10^4	5.781 x 10^4
Sandell's sensitivity	.0 x10^{-5}	3.0 x10^{-4}	1.4 x10^{-4}
Correlation coefficient(r^2)	0.9999	0.999	0.9999
Regression equation (y=b+ac)			
Slope (a)	0.070	0.296	0.139
Intercept(b)	-0.002	0.004	0. 001

Table II
Results of recovery of drug (Loratadine)

Amount of drug added µg/ml	Amount of standard added µg/ml.	Total amount recovered	Percent recovery (%)	Standard deviation	Percentage of relative standard deviation C.O.V.	Mean standard deviation	Mean of C.O.V.
1	0	1.0184	101.84	0.03636	3.5707		
1	1	2.0204	101.02	0.05397	2.6714	0.0535	2.4396
1	2	3.0204	100.68	0.05397	1.7869		
1	3	4.03061	100.76	0.06970	1.7294		
Mean of percent (%) recovery = 101.075							

Table III
Results of recovery of drug (desloratadine)

Amount of drug added µg/ml	Amount of standard added µg/ml.	Total amount recovered	Percent recovery (%)	Standard deviation	Percentage of relative standard deviation C.O.V.	Mean standard deviation	Mean of C.O.V.
0.5	0	0.4999	99.98	0.01375	2.750		
0.5	0.5	1.0001	100.01	0.01359	1.3594	0.009641	1.3085
0.5	1.0	1.4999	99.999	0.009461	0.6427		
0.5	1.5	2.0001	00.01	0.009641	0.4820		
Mean of percent (%) recovery = 99.9999							

Table IV
Results of recovery of drug (Rupatadine)

Amount of drug added µg/ml	*Amount of standard added µg/ml.*	*Total amount recovered*	*Percent recovery (%)*	*Standard deviation*	*Percentage of relative standard deviation C.O.V.*	*Mean standard deviation*	*Mean of C.O.V.*
0.5	0	0.4969	99.38	0.03121	6.2814		
0.5	0.5	1.0051	100.51	0.03212	3.1957	0.030407	3.2194
0.5	1.0	1.4999	99.993	0.02914	1.9432		
0.5	1.5	2.0001	100.05	0.02914	1.4574		
Mean of percent (%) recovery = 99.98							

ACKNOWLEDGEMENT

Authors express sincere thanks to the Principal, D. G. Ruparel College for providing necessary facilities and encouragement for research work.

REFERENCES

1. United States Pharmacopoeia, US Pharmaceutical Convention Inc., Rockville, Volume I, II, III(2010) .
2. British Pharmacopoeia, Her Majesty's Stationary Office, London, Volume I, II, and III. (2010).
3. Indian Pharmacopoeia, Controller of Publication, Delhi, volume I, II, III.
4) Georgeta Pavalach, Vasile Dorneanu, Antoanela Popescu; UV molecular absorption spectrophotometric method for determination of loratadine ; Ovidius University Anals of Chemistry, 21(2), 157-162, (2010).
5) N. Harikrishnan, Deepthi R., Manjusha V., P. Satya Vani, M.V. Asha Jyothi, C. Roosewelt ; UV spectrophotometric method for estimation of loratadine in bulk and pharmaceutical dosage form; Asian Journal of Research in Chemistry, 3(2), 302-304,(2010).
6) Georgeta Pavalache, Vasile Dorneanu ; HPLC method for determination of loratadine in pharmaceutical dosage form ; Farmacia, 59(02), 200-208(2011).
7) G. Pavalache, V. Dorneanu, A. Popescu ; HPLC method for determination of loratadine in dosage form ; AMT,2(4),276-278 (2010).
8) Lu J., Wei Y.C., Markovich R.J., Rustum A.M. ; a novel stability-indicating gradient ion-pair RP-HPLC method for assay loratadine ; Journal of Analytical Chemistry,93(3), 891-903 (2010).
9) Jun Lu, Yu Chien Wei, Robert J. Markovichm, Abu M. Rustum ; ion-pair RP-HPLC method for retension behavior of loratadine ; Journal of Liquid Chromatography & Related Compounds, 33(05), 603-614(2010).
10) Diana T.El-Sherbiny, Naned El-Enany, Fathalla F.Belal, Steen H.Hansen ; a rapid HPLC procedure for analytical quality control of pharmaceutical preparation containing loratadine and/or its anolog desloratadine using a microemulsion as the eluent; Journal of

Pharmaceutical and Biomedical Analysis, 43(4),1236-1242,(2007).
11) M. Nogowska, M. Zajac, I. Muszalska ; spectrophotometric (UV) and chromatographic (HPLC) methods for deternination of loratadine hydrochloride in tablets andin suspension; Chemia Analityczna, 45,(5), 681-688(2000).
12) Noqueria,Nayane M., Alves,Jouo M.P., Santoro, Maria Ines Rocha Miritello, Singh,Anil K. ; spectrophotometric (UVDS) and a stability indicating high performance liquid chromatographic (HPLC) methods for analysis of loratadine in tablets and syrups ; Latin American Journal of Pharmacy, 29(3), 325-332 (2010).
13) Diana T. El. Sherbiny, Naned El -Enany, Fathalla F.Belal, Steen H.Hansen ; four-stability indicating procedures for determination of loratadine ; Journal of Pharmaceutical and Biomedical Analysis, 43(04), 1236-1242,(2007).
14) Patel J. M. J.M. Talele G.S. Fursule R.A. Spectrophotometric determination of desloratidine in bulk and tablets form. Asian J. of chemistry.2004 ;16(2): 1220.
15) Patel J.M., Talele G.S., Furule R.A. and Surana S.J. Extractive spectrophotometric determination of desloratadine from its bulk and pharmaceutical dosage form. Indian Drugs. June 2006; 43(6) : 507
16) Caglar S.,Oztune A. A sensitive spectrophotometric determination of desloradine in tablets. J. AOAC, Int. 2007; 90 (2) :372-375.
17) NahedEl-Enany, Dina El-Sherbiny, Fathalla Belel .Spectrophotmetric, spectrofluorometric and HPLC determination of Desloratadine in dosage form and plasma. Chem. Pharm. Bull.2007; 55(12) :1662.
18) Liu L.H., Qi M .L., Wang P ,Li H.Z. HPLC method for the bioequivalence evaluation of desloratadine for tablets in dogs. J. pharm biomed, Anal 2004; 34(5):1013.
19) More A.R. Vaidya A.J., Vaidya V.V. and Deshmukh R.G. Determination of loratadine and active metabolites from plasma by HPLC for bioequivalence studies. Indian Drugs. 2005; 42(8): 525.
20) Dina T. El-Sherbiny, Nahed El-Enany, Fathalla F. Belal and Steen H. Hansen.Simultaneous determination of loratadine and Desloratadine in pharmaceutical preparation, J. of pharm. and Biomed. Analysis.2007; 43(4):1236.
21) Sutherland F.C.W., De Janger A.D., Hundt A.F. Sensitive liquid chromatography – tadem mass spectrophotometric method for determination of loratadine and its active metabolites descarboehoxy – loratadine in human plasma, J. Chromatogr. A. 2001; 914 (12): 37.
22) Nogueria D.R., D' Avila Felipe, Rolim Clarice, Dalmora Sergo L. Development and validation of a stability indicating liquid chromatographic method for determination of rupatadine in pharmaceutical formulations. Chromatographia 2007; 66: 915-919
23) Yuan Tain, Jingjing Zhang, Hui Lin, Jiabi Lang, Zanjian Zhang, Yun Chen. High performance liquid chromatography – tadem mass spectrometric determination of rupatadine in human plasma and its pharmacokinetics. J. of pharmaceutical and biomedical analysis 2008; 47 (4-5): 899-906
24) A.A Shirkhendar, R.R. Thorve, R. A Fursule, S.j. Surana. Development and validation of stability indicating HPTLC method for analysis of rupatadine fumarate in bulk and tablets form. Act Chromatographica. 2008; 20: 423-437
25) Noqueria D.R., da silva L.M., Todeschini V. and Dalmora S. L. Determination of rupatadine

in pharmaceutical formulation by a validated stability indicating MEKC method. J. of
separation science. 2008; 31 (16-17): 3098-3105

26) R.V. Rele, S.A Sawant and P.D. Desai ; Simple extractive spectrophotomeric determination of rupatadine as rupatadine fumarate from pharmaceutical formulation., Analytical chemistry
An Indian journal,8(2):165-167 (2009).

27) R.V. Rele, S.A. Sawant and S.A. Mahimkar, A validated simple titrimetric method for the quantitative determination of rupatadine as rupatadine fumarate from pharmaceutical dosages.,Analytical chemistry An Indian journal,8(4): 561-564 (2009).