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SPCTROPHOTOMETRIC DETERMINATION OF DRUGS IN BULK AND PHARMACEUTICAL DOSAGE FORM BY USING P-CHLORANILIC ACID

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Abstract: Simple, sensitive and accurate UV-Visible Spectrophotometric methods have been developed for the determination of following drugs *viz.*, Vilazodone hydrochloride (VLZ), Dronedarone hydrochloride(DND), Brinzolamide(BNZ), Donepezile hydrochloride(DPZ) and Fexofenadine methyl ester(FME) in bulk and their dosage forms using *p*-Chloranilic acid as analytical reagent. The methods have been developed based on the formation of charge transfer complex of drugs as *n*-electron donor with *p*-Chloranilic acid as π acceptor. The selected drugs turned the pale yellow color of reagent *viz.*, *p*-chloranilic acid in acetonitrile, to purple and exhibited a band at 515nm due to anion of the reagent whose intensity increased with increase in the concentration of the drugs. Under the optimized experimental conditions, Beer's law is obeyed over the concentration range of, 15-75 μ g/ml, 5-25 μ g/ml, 5-25 μ g/ml, 5-25 μ g/ml and 10-50 μ g/ml for, VLZ, DND, BNZ, DPZ and FME respectively. The effect of reagent concentrations, polarity of solvents and effect of reaction time have been studied and optimized. The composition of each complex is found to be 1:1. These methods have been validated in terms of ICH guidelines and applied to the quantification of selected drugs in bulk and dosage forms.

Keywords: Drugs, Spectrophotometry, *p*-Chloraniliac acid, Quantification, Validation.



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INTRODUCTION

Vilazodone hydrochloride: Vilazodone, 5-{4-[4-(5-cyano-1H-indol-3-yl)butyl]piperazin-1-yl}benzofuran-2-carboxamide, is a new antidepressant that was developed for the treatment of major depressive disorder [1]. It is a selective serotonin reuptake inhibitor (SSRI) and a 5-HT_{1A} receptor partial agonist used for the treatment of major depressive disorder [2].

Literature search reveals that there are a few analytical methods have been developed for the determination of Vilazodone hydrochloride like spectrophotometry, RP-HPLC, Stability indicating RP-HPLC, Isolation and structure elucidation by HPLC, RP-HPLC with Fluorimetric Detection and LC-MS/MS [3].

Dronedarone hydrochloride: Dronedarone chemically known as N-{2-butyl-3-[4-(3-dibutylaminopropoxy) benzoyl]-benzofuran-5-yl} methanesulfonamide, is a potent drug mainly used for the indication of cardiac arrhythmias [4]. Dronedarone is a multi-ion channel blocker, inhibiting the potassium currents involved in cardiac re-polarization including I_{Kr}, I_{Ks}, I_{Kur}, and I_K (A_{Ch}) and has been shown to be effective in the treatment of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL) [5-8].

A literature survey revealed that there are a few analytical methods were available for the investigation of pharmacokinetics of dronedarone like liquid chromatography-tandem mass spectrometry [9], HPLC-UV [10], Stability indicating HPLC [11], UV spectrophotometry [12].

Brinzolamide: Brinzolamide (BRZ), [(R)-(+)-4-Ethylamino-2-(3-methoxypropyl)-3, 4-dihydro-2H thieno [3,2-e]-1,2-thiazine-6-sulfonamide-1,1-dioxide], is a new active substance which is useful only for topical use in the treatment of glaucoma [13]. BRZ has been marketed in combination with TM in eye drops for treatment of glaucoma, which have lesser side effects and patient specificity compared to previous eye drops, DORZOX-T (dorzolamide and timolol maleate) [14].

Literature search reveals that there are a few analytical methods have been developed for the determination of Brinzolamide like Stereo-Selective HPLC [15], Spectrophotometry [16].

Donepezil hydrochloride:

Donepezil hydrochloride chemically known as (±)-2,3-dihydro-5,6-dimethoxy 2-[[1-(phenyl methyl)-4-piperidiny]methyl]-1H-inden-1-one hydrochloride [17]. Donepezil hydrochloride (DH) is a specific and reversible inhibitor of acetyl cholinesterase, and used in the treatment of Alzheimer's disease [18].

Through Survey of Literature reveals that a few methods were reported for the determination of Donepezil like ultraviolet (UV) visible spectrophotometry, HPLC, (LC-MS)-MS, HPTLC [19].

Fexofenadine methyl ester: Fexofenadine α , α -dimethyl-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidiny] butyl]-benzene acetic acid [20], is the active carboxylic acid analogue of the antihistamine terfenadine. It shares the histamine H1 receptor antagonist and non-sedative properties of the parent compound. This could be attributed to its capability to exist in zwitterionic form so it cannot pass through blood-brain barrier and therefore does not cause sedation [21, 22].

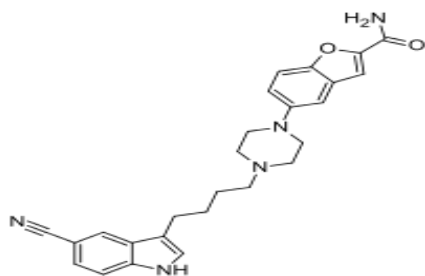
Literature search reveals that there are a few methods reported like LC-MS/MS [23], ultraviolet detection [24] and fluorescence detection [25]. Spectrophotometry [26], LC methods with ultraviolet detection [27-29], capillary electrophoresis [30, 31].

Thorough survey of literature on the selected drugs revealed that quantification using *p*-CA as analytical reagent has not been reported yet. This paper reports simple, direct, and sensitive spectrophotometric method for determination of selected drugs using *p*-CA as π -acceptor based on the formation of charge transfer complex.

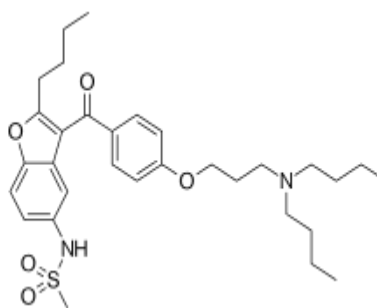
EXPERIMENTAL

Instrument: Shimadzu 2600 double beam UV-Visible spectrophotometer, UV-3600 Shimadzu UV-VIS-NIR Spectrophotometer & Elico 159 UV-Visible single beam spectrophotometers were used to record the spectra of individual components as well as the charge transfer complexes, using matched pair of Quartz cells of 10mm path length.

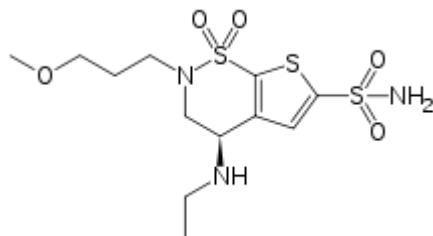
Materials: The *p*-Chloranilic acid was supplied by sigma Aldrich. The AR grade solvents *viz.*, acetonitrile, methanol and chloroform are supplied by SD Fine chem. Ltd. Mumbai, India. The drugs used in present study were procured from Hetero drugs pvt.ltd. Hyderabad and the pharmaceutical dosage forms of drugs were purchased from the local market.



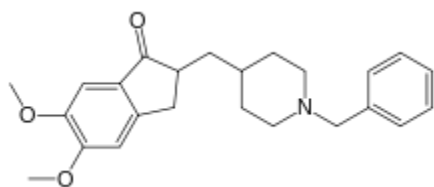
Vilazodone hydrochloride



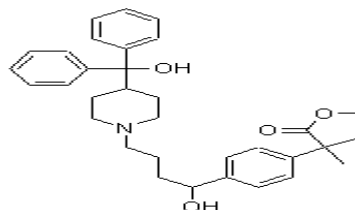
Dronedarone hydrochloride



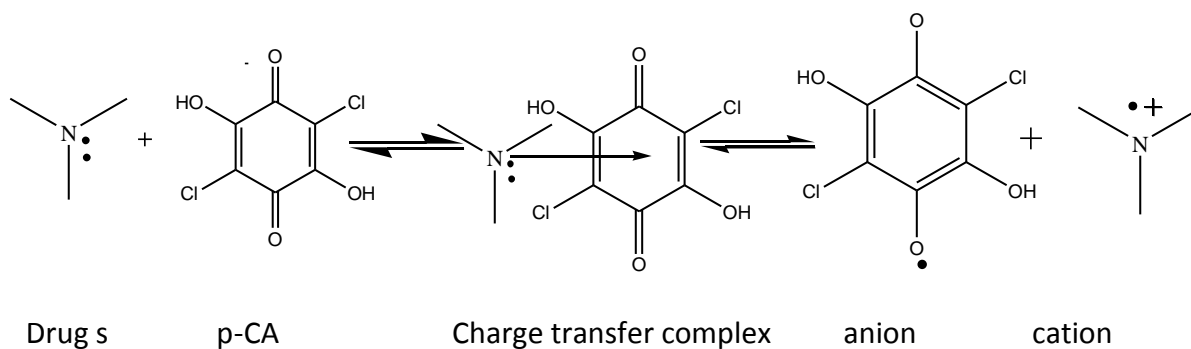
Brinzolamide



Donepezile hydrochloride



Fexofenadine methyl ester



Drug s

p-CA

Charge transfer complex

anion

cation

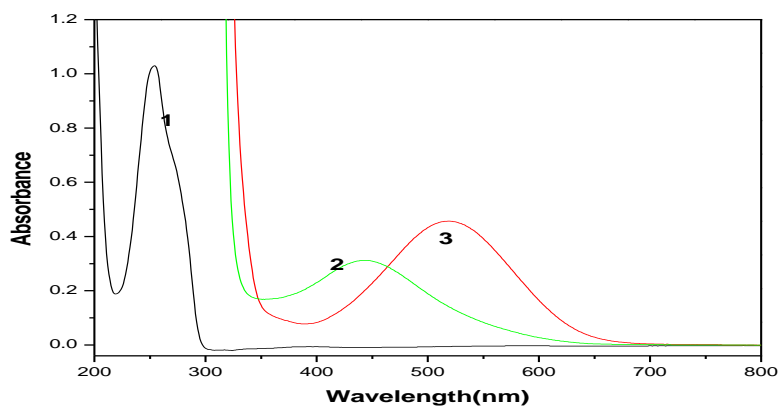


Fig. (1): Vilazodone hydrochloride in acetonitrile, (2) p-Chloranilic acid in acetonitrile & (3) Charge transfer complex spectra of Vilazodone with p-CA.

PREPARATION OF STANDARD STOCK SOLUTION

For VLZ, DND & DPZ: An accurate weight of drugs (100mg) were weighed and dissolved in distilled water in a 100ml of standard flask and transferred into a 125ml separating funnel, where 15 ml of 0.1N NaOH solution were added. The mixture was mixed and extracted three times with 20ml of CHCl_3 each, then the chloroform layer was separated and evaporated to dryness where the obtained residue was dissolved quantitatively in 100ml of acetonitrile (final conc. 1mg/ml).

For BNZ & FME: An accurate weight of drug (100mg) was dissolved in 100ml of acetonitrile to give a concentration of 1000 $\mu\text{g/ml}$. The prepared standard stock solutions were further diluted according to the requirement for their analysis.

DETERMINATION OF DRUGS IN DOSAGE FORM

Vilazodone hydrochloride (Viibryd): Fifteen tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets equivalent to 50mg of Vilazodone hydrochloride was dissolved in 50ml of distilled water in a 50ml calibration flask and transferred into a 125ml separating funnel, where 10ml of 0.1N NaOH solution were added. The mixture was mixed and extracted three times with 15ml of CHCl_3 each, and then the chloroform layer was separated and evaporated to dryness where the obtained residue was dissolved and then diluted to obtain a concentration in the range of linearity previously determined with pure drug.

Dronedarone hydrochloride (Multaq): Ten tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets equivalent to 50mg of Dronedarone hydrochloride was dissolved in 50ml of distilled water in a 50ml calibration flask and transferred into a 125ml separating funnel, where 10ml of 0.1N NaOH solution were added. The mixture was mixed and extracted three times with 15ml of CHCl_3 each, and then the chloroform layer was separated and evaporated to dryness where the obtained residue was dissolved and then diluted to obtain a concentration in the range of linearity previously determined with pure drug.

Brinzolamide (Befardin): Ten tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets equivalent to 50mg of Brinzolamide was transferred into 50ml validation flask and dissolved in about 50ml of methanol. The contents of flask were sonicated for 10 minutes. The mixture was filtered through Whitman filter paper and evaporated to dryness. Residue was dissolved in acetonitrile and then diluted to obtain a concentration in the range of linearity previously determined with pure drug.

Donepezile hydrochloride (Aricept): Twenty tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets equivalent to 50mg of Donepezile hydrochloride was dissolved in 50ml of distilled water in a 50ml calibration flask and transferred into a 125ml separating funnel, where 10ml of 0.1N NaOH solution were added. The mixture was mixed and extracted three times with 15ml of CHCl_3 each, and then the chloroform layer was separated and evaporated to dryness where the obtained residue was dissolved and then diluted to obtain a concentration in the range of linearity previously determined with pure drug.

Fexofenadine methyl ester (Allegra): Fifteen tablets were weighed, finely powdered and an accurately weighed sample of powdered tablets equivalent to 50mg of Fexofenadine methyl ester was transferred into 50ml validation flask and dissolved in about 50ml of methanol. The contents of flask were sonicated for 10 minutes. The mixture was filtered and evaporated to dryness. Residue was dissolved in acetonitrile and then diluted to obtain a concentration in the range of linearity previously determined with pure drug.

RESULTS AND DISCUSSION

The p-Chloranilic acid solution of $4.78 \times 10^{-3}\text{M}$ in acetonitrile was freshly prepared. Aliquots of drugs (0.5-2.5ml) were transferred into a series of 10ml calibrated flasks, to each flask, 1 ml of p-CA solution in acetonitrile was added and remaining volume was made up by acetonitrile. The absorbance of purple colored solution was recorded after 5min of mixing against reagent blank at 585nm was plotted against the corresponding concentrations ($\mu\text{g/ml}$) of the drug to construct the calibration curve.

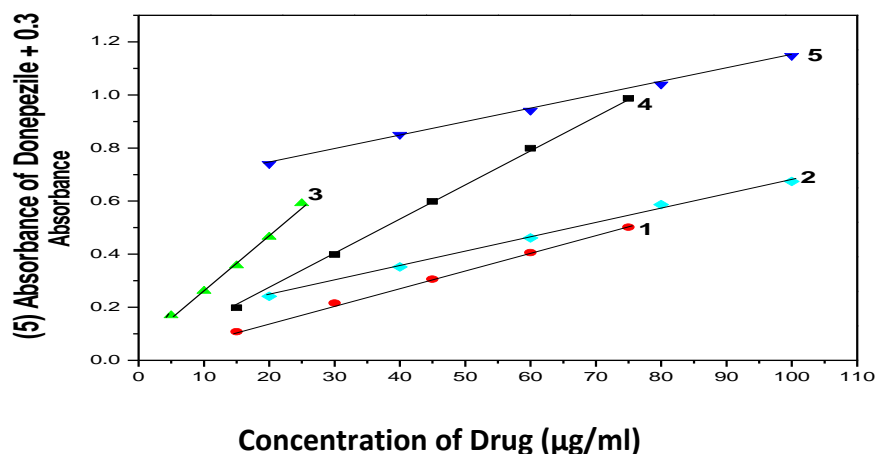


Fig. (2): Calibration curves of p-CA with (1) Dronedarone, (2) Fexofenadine methyl ester, (3) Brizolamide, (4) Vilazodone & (5) Donepezile.

EFFECT OF SOLVENT

Both polar and non-polar solvents such as methanol, acetone, chloroform, 1, 2-dichloroethane and acetonitrile were used to select elegant solvent for the analysis of drugs. Acetonitrile is found to be suitable solvent for p-CA it produces maximum absorbance with a fixed concentration of drugs, while other solvents produced lower absorbance due to incomplete dissociation of complex.

EFFECT OF CONCENTRATION OF ACCEPTOR

To establish the optimum concentration of reagent, Vilazodone hydrochloride 45 µg/ml, Dronedarone hydrochloride 25 µg/ml, Brizolamide 25µg/ml, Donepezile hydrochloride 20 µg/ml and Fexofenadine methyl ester 50 µg/ml were react with different volumes of p-CA ($4.78 \times 10^{-3}M$). The results showed that the highest absorbance was obtained with 1ml. Hence 1ml of reagent was used for the determination of drugs.

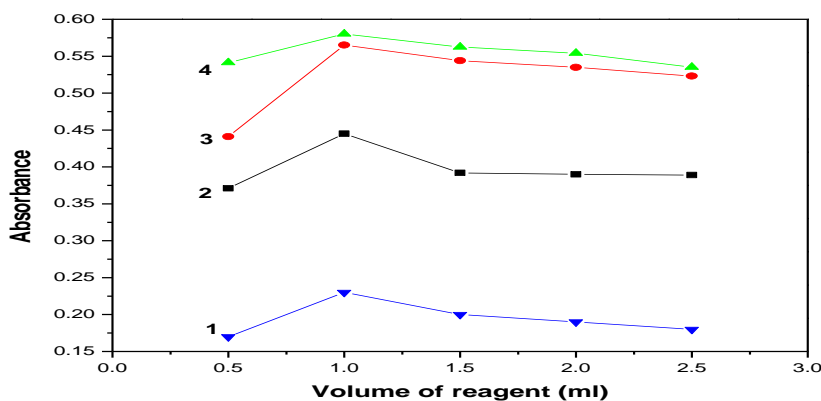


Fig. (3).Effect of volume of reagent on the optical density of the CT complex of p-CA with (1) Vilazodone, 2) Brinzolamide, 3) Dronedarone & 4) Donepezile.

EFFECT OF REACTION TIME

The interaction of p-CA with drugs resulted in the formation of Charge transfer complexes which stabilized with in 6 min of mixing. The developed color remained stable at room temperature for about an hour. After a day all solutions are decolorized.

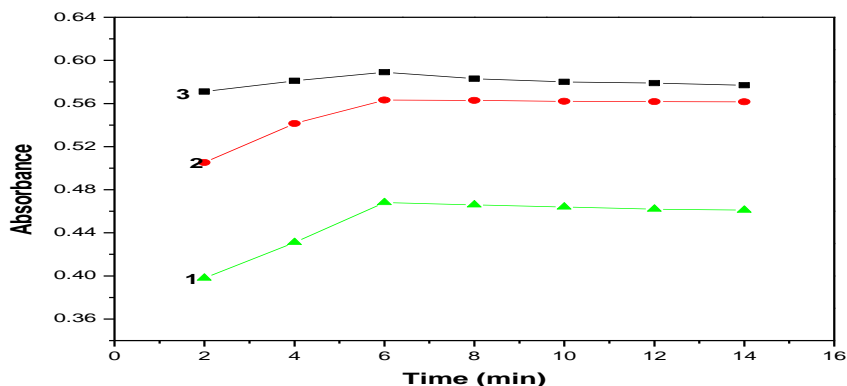


Fig (4): Effect of reaction time on formation of charge transfer complex of p-CA with (1) Donedarone, 2) Donepezile & 3) Brinzolamide.

VALIDATION OF THE PROPOSED METHODS

The methods developed have been validated in terms of guidelines of international conference of harmonization viz., selectivity, sensitivity, precision, accuracy, linearity, LOD, LOQ. Sandell's sensitivity and robustness. The methods are selective and can differentiate the analyte from the excipients. The precision is tested by repeating each experiment at least 6 times while the accuracy has been tested by taking known weight of sample and performing recovery experiments. The values %RSD are in the permissible range of experimental errors. (Table 2). Sandell's sensitivity (ss), LOD and LOQ have been calculated by using the following equations.

$$\text{Sandell's sensitivity (ss)} = 0.001/S$$

$$\text{LOD} = 3.3s/S$$

$$\text{LOQ} = 10s/S.$$

Where s = standard deviation of the intercept (n = 6)

S = slope of Calibration plot.

The robustness of the methods is examined by performing the experiments on three different Spectrophotometers with excellent tally of absorbance values.

The methods developed have also been applied for the analysis of pharmaceuticals. The recovery experiments performed show high accuracy and precision and the results are compared with the available validated reported methods on each drug. The values %RSD and t- and F tests are in the permissible range of experimental errors (Table 3), and show that the methods can be used in both pharmaceutical and drug industries.

STABILITY CONSTANTS OF CHARGE TRANSFER COMPLEX

Benesi - Hildebrand method (BH) is used for determination of stability constant K and molar absorption coefficient of the charge transfer complexes

$$A_0/d = 1/K (D_0) \epsilon + 1/\epsilon$$

Where A_0 = conc. of acceptor, d = optical density, D_0 = conc. of drug, ϵ = Molar absorption coefficient and K = stability constant.

A plot of A_0/d Vs $1/D_0$ is a straight line from whose slope and intercept the K and ϵ are determined. Benesi – Hildebrand plot of selected drugs with p-CA is presented in (Fig-5).

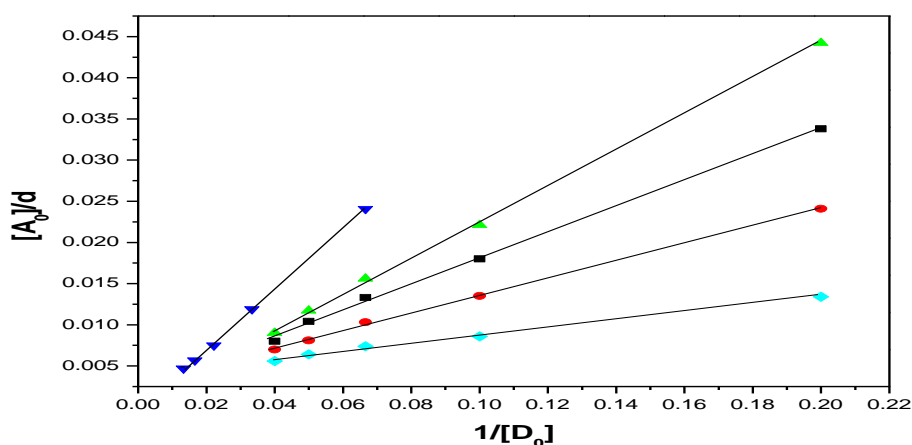


Fig (5): Benesi-Hildebrand plot of p-CA with (1) Brizolamide, 2) Fexofenadine methyl ester, 3) Dronedarone, 4) Vilazodone & 5) Donepezile.

STOICHIOMETRY

The stoichiometry of each of the complex has been determined from Job's continuous variation method and found to be 1:1 in each case. A typical Job's plot of selected drugs with p-CA is presented in (Fig-6).

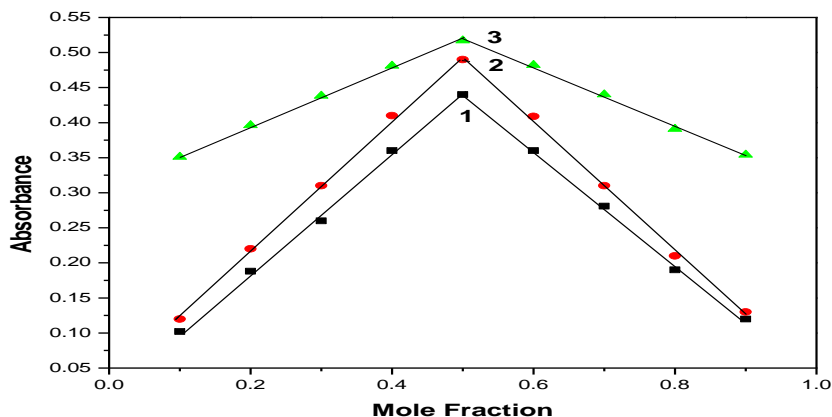


Fig (6): Job's continuous variation plot of p-CA with (1) Vilazodone, (2) Dronedarone & (3) Brinzolamide

CONCLUSION

p-CA forms charge transfer complexes with selected drugs and exhibits band at 585nm. The interaction enabled the quantitative determination of these drugs. This method is validated in terms of precision, accuracy, linearity and robustness. This method relies on the use of simple and inexpensive chemicals and techniques but provide sensitivity comparable to that achieved by sophisticated and expensive techniques like HPLC and LC-MS. Thus, they can be used as alternatives for rapid and routine determination of bulk sample and tablets.

13. ACKNOWLEDGEMENT

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Table [1]: Spectral, analytical and statistical parameters of charge transfer complexes of drugs with p-CA.

Parameters	VZL	DND	BNZ	DPZ	FME
λ max, nm	515	515	515	515	515
Beer's law limit ($\mu\text{g/ml}$)	15-75	15-75	5-25	20-100	20-100
Molar absorptivity($\text{L mol}^{-1} \text{cm}^{-1}$)	1.32×10^4	2.16×10^4	2.61×10^4	9.14×10^4	1.76×10^4
Slope(specific absorptivity),b	0.0287	0.0197	0.0219	0.0196	0.0155
Intercept, a	0.0243	0.0127	0.0406	0.3555	0.0132

Correlation coefficient, r	0.9979	0.9994	0.9998	0.9992	0.9976
Sandell's sensitivity(μgcm^{-2})	0.1149	0.0507	0.0456	0.0510	0.1818
Formation constant, $K(\text{M}^{-1})$	680	514	1818	724	320
SD of intercepts (n=6)	0.0068	0.0072	0.0023	0.0122	0.0015
LOD ($\mu\text{g/ml}$)	0.7818	1.2060	0.3465	0.1132	3.3212
LOQ($\mu\text{g/ml}$)	2.3693	3.6548	1.0502	0.3431	0.9677
Regression equation $y=a+bx$; $x=\text{concentration of drug}(\mu\text{g/ml})$	0.0243 + 0.0087x	0.0127 + 0.0197x	0.0406 + 0.0219x	0.3555 + 0.0196x	0.0132 + 0.0055x

Table 2 Determination of accuracy and precision of the methods on pure drug Samples

Drug	Amount taken ($\mu\text{g/ml}$)	Amount Found ($\mu\text{g/ml}$)	%Recovery	% RSD	Proposed Mean \pm SD
VLZ	15	14.97	99.80	0.2367	100.07
	30	30.06	100.20		\pm
	45	45.10	100.22		0.2369
DND	30	29.89	99.63	0.1612	99.69
	45	44.95	99.88		\pm
	60	59.75	99.58		0.1607
BNZ	5	5.02	100.4	0.3884	100.24
	10	9.98	99.80		\pm
	15	15.08	100.53		0.3894
	20	20.09	100.45		0.6059

DPZ	40	39.84	99.60	±	0.6046
	60	59.57	99.28		
FME	40	39.87	99.67	0.3056	99.81
	60	59.76	99.60		±
	80	80.13	100.16		0.3051

Table 3 Results of assay of tablets by the proposed methods and statistical evaluation and recovery experiments by standard addition method.

Tablets	Drug in tablet (µg/ml)	Drug added (µg/ml)	Total Found (µg/ml)	% Recovery	% RSD	Proposed Mean ± SD	Ref Mean ± SD	t-test	F-test
Viibryd (VLZ)	0.50	2.0	2.48	99.20	0.4544	100.03 ± 0.66	100.01 ± 0.4545	0.485 (3.18)	0.474 (5.28)
	0.50	4.0	4.51	100.22					
	0.50	6.0	6.49	99.84					
	15.0	0.0	15.08	100.53					
	30.0	0.0	30.03	100.10					
	45.0	0.0	45.08	100.17					
Multaq (DND)	0.50	6.0	6.48	99.69	0.1966	99.74 ± 0.389	99.96 ± 0.1966	1.082 (2.44)	0.255 (3.05)
	0.50	8.0	8.50	100.00					
	0.50	10.0	10.03	100.30					
	30	0.0	29.99	99.96					
	45	0.0	44.97	99.93					
	60	0.0	59.95	99.91					
	0.50	1.0	1.50	100.00					

	0.50	2.0	2.49	99.60	0.1898	100.8	99.92	1.863	0.024
Befardin	0.50	3.0	3.50	100.00		±	±		
(BNZ)	5.0	0.0	5.00	100.00		1.20	0.1897	(2.57)	(3.40)
	10.0	0.0	9.98	99.80					
	15.0	0.0	15.02	100.13					
	0.50	4.0	4.46	99.11	0.4592				
Aricept	0.50	8.0	8.50	100.00		100.8	99.94	1.096	0.121
(DPZ)	0.50	12.0	12.52	100.16		±	±		
	20	0.0	20.10	100.50		1.32	0.4593	(3.18)	(5.28)
	40	0.0	39.99	99.97					
	60	0.0	59.97	99.95					
	0.50	9.0	9.50	100.00					
Allegra	0.50	12.0	12.49	99.92		101.5	99.97	1.580	0.007
(FME)	0.50	15.0	15.49	99.93	0.0760	±	±		
	40	0.0	39.96	99.90		0.89	0.0769	(3.18)	(5.28)
	60	0.0	59.98	99.96					
	80	0.0	80.09	100.11					

REFERENCES:

1. Ling-ling Zenga, Li-li Suna, Qiaogen Zoub*, Fan Zhoua, Ping Weia and Ping-kai Ouyanga, Biomed. Chromatogr. 2014; 28: 1738–1743.
2. Laughren T. P, Gobburu J, Vilazodone: clinical basis for the US Food and Drug Administration's approval of a new antidepressant, The Journal of Clinical Psychiatry, 2011, 72(9), 1166–73.

3. Damle Mrinalini C.*, Agrawal Anshu A. International Journal for Pharmaceutical Research Scholars (IJPRS).
4. Shashikant B. Landge, Sanjay A. Jadhav, Kapil P. Nimbalkara, Anil C. Mali, Vijayavithal T. Mathad* American Journal of Analytical Chemistry, 2013, 4, 323-335.
5. "Australian Public Assessment Report for Dronedarone Hydrochloride," Submission No: PM-2008-3045-3, 2010. <http://www.tga.gov.au/pdf/auspar/auspar-multaq.pdf>
6. Assessment Report for Multaq, "Evaluation of Medicines for Human Use," European Medicines Agency, Procedure No. EMEA/H/C/001043, 2009. http://www.ema.europa.eu/docs/enGB/document_library/EPAR_Public_assessment_report/human/001043/WC500044538.pdf.
7. Center for Drug Evaluation and Research, "Chemistry Review(s)," Application Number: 22425,2009.http://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/022425s000ChemR.
8. FDA, "FDA Approves Multaq to Treat Heart Rhythm Disorder," 2009.
9. C. Xie, S. L. Yang, D. F. Zhong, X. J. Dai and X. Y. Chen, "Simultaneous Determination of Dronedarone and Its Active Metabolite Debutyl-dronedarone in Human Plasma by Liquid Chromatography-Tandem Mass Spectrometry: Application to a Pharmacokinetic Study," *Journal of Chromatography B*, Vol. 879, No. 28, 2011, pp. 3071-3075.
10. D. Patel and A. Choudhury, "Development and Validation of Dronedarone HCl In Plasma by RP-HPLC Method Coupled with UV-Detector," *Inventi Impact: Biomedical Analysis*, Vol. 2012, 2012, Article ID: Inventi: pba/47/12. <http://www.inventi.in/Article/pba/47/12.aspx>
11. N. Tondepu¹, S. S. Sait, K. V. Surendranath, R. K. Kaja¹ and S. Kumar, "A Stability Indicating HPLC Method for Dronedarone in Bulk Drugs and Pharmaceutical Dosage Forms," *American Journal of Analytical Chemistry*, Vol. 3, 2012, pp. 544-551. [doi:10.4236/ajac.2012.38072](https://doi.org/10.4236/ajac.2012.38072).
12. Kishore Konam¹ & Dharmeshwar Jadhav². International Journal of Pharmacy and Biological Sciences (e-ISSN: 2230-7605).
13. USP-35, NF-30, USP monographs, Volume-II, 2012, pp 2385-2386, 4871-4872.
14. Sezgin Akçay Bİ, Güney E, Bozkurt KT, Unlü C, Akçali G, (The safety and efficacy of brinzolamide 1%/timolol 0.5% fixed combination versus dorzolamide 2%/timolol 0.5% in patients with open-angle glaucoma or ocular hypertension). *J Ocul Pharmacol Ther*, 2013; 29(10): 882-6.

15. Airy S, Chiou J, Nguyen H, Stafford G, Gan O, Jani R, Marsh D, (Development of Stereo-Selective HPLC Method for the Analysis of Brinzolamide (AL4862) Predevelopment/Pharmaceutics, Alcon Research, Ltd.
16. Purvi A. Shah*, Ankita S. Kadikar, Riddhi M. Katira, Kalpana G. Patel, Tejal R. Gandhi, World Journal of Pharmacy and Pharmaceutical Sciences, Volume 3, Issue 2, 1955-1967. ISSN 2278 – 4357.
17. Stella Kafkala *, Stella Matthaiou, Pandora Alexaki, Morfis Abatzis, Antonios Bartzeliotis, Maria Katsiabani.
18. Sweetman S. Marindale: The Complete Drug Reference. 36th ed. USA: Pharmaceutical Press; 2009. p. 362-7.
19. Chintan Patel, Nrupesh Patel, Charmy Kothari*, Journal of Young Pharmacists Vol 6 • Issue 4 • Oct-Dec 2014.
20. Hadir M Maher¹, 2*, Maha A Sultan¹ and Ileana V Olah¹, Maher et al. Chemistry Central Journal 2011, 5:76.
21. Simpson K, Jarvis B: Fexofenadine: a review of its use in the management of seasonal allergic rhinitis and chronic idiopathic urticaria. Drugs 2000,59:301-321.
22. Meeves SG, Appajosyula S: Efficacy and safety profile of fexofenadine HCL: A unique therapeutic option in H1-receptor antagonist treatment. J Allergy Clin Immunol 2003, 112:S69S77.
23. Guo D, Zou J, Zhu Y, Lou S, Fan H, Qin Q: Measurement of fexofenadine concentration in micro-sample human plasma by a rapid and sensitive LC-MS/MS employing protein precipitation: application to a clinical pharmacokinetic study. Biomed Chromatogr 2010, 24:335-341.
24. Arayne MS, Sultana N, and Shehnaz H, Haider A: RP-HPLC method for the quantitative determination of fexofenadine hydrochloride in coated tablets and human serum. Med Chem Res 2011, 20:55-61.
25. Konieczna L, Plenis A, Oledzka I, Kowalski P, Baczek T: Rapid RP-LC method with fluorescence detection for analysis of fexofenadine in human plasma. Chromatographia 2010, 71:1081-1086.
26. Gazy AA, Mahgoub H, El-Yazbi FA, El-Said MA, and Youssef RM: Determination of some histamine H1-receptor antagonists in dosage forms. J Pharm Biomed Anal 2002, 30:859-867.

27. Ulavapalli KR, Sriramulu J, Mallu UR, Bobbarala V: Simultaneous determination of psuedoephedrine, fexofenadine and loratadine in pharmaceutical products using high resolution RP-HPLC method. J Pharm Res 2011, 4:1219-1221.
28. Breier AR, Menegola J, Paim CS, Steppe M, Schapoval EES: Development and Validation of a Liquid Chromatographic Method for Fexofenadine Hydrochloride in Capsules. J AOA Int 2004, 87:1093-1097.
29. Karakuş S, Küçükgülzel I, Küçükgülzel SG: Development and validation of a rapid RP-HPLC method for the determination of cetirizine or fexofenadine with pseudoephedrine in binary pharmaceutical dosage forms. J Pharm Biomed Anal 2008, 46:295-302.
30. Breier AR, Garcia SS, Jablonski A, Steppe M, Schapoval EES: Capillary electrophoresis method for fexofenadine hydrochloride in capsules. J AOAC Int 2005, 88:1059-1063.
31. Mikus P, Valášková I, Havránek E: Determination of fexofenadine in tablets by capillary electrophoresis in free solution and in solution with cyclodextrins as analyte carriers. Drug Dev Ind Pharm 2005, 31:795-801.