Int. J. Chem. Sci.: 11(1), 2013, 257-264
ISSN 0972-768X
www.sadgurupublications.com

VISIBLE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF ALFUZOCIN HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS THROUGH SCHIFF'S BASE FORMATION

CH. V. R. MURTHY[a], M. L. N. ACHARYULU[*], M. GANESH and T. S. REDDY[b]

VITAM College of Engineering, Mindivanipalem, Ananadapuram Mandal,
VISAKHAPATNAM – 531173 (A.P.) INDIA
[a]Department of Chemical Engg, AUCE (A), A.U. College of Engineering,
VISAKHAPATNAM (A.P.) INDIA
[b]DLR College (Degree & P.G. Courses), GOLLALAMAMIDADA – 533344,
Dist.: E.G. (A.P.) INDIA

ABSTRACT

Two new simple spectrophotometric methods for the assay of alfuzocin hydrochloride (ALF) has been described in pure form or in pharmaceutical formulations based on the reaction of the drug with aromatic aldehydes, p-dimethylamino cinnamaldehyde (PDAC) and vanillin (VN) in acidic medium producing colored Schiff's base having λ_{max} 660 nm, 680 nm, respectively. The obtained results are in good agreement with Beer's law in the range of 10-50 µg/mL (Method A), 4-24 µg/mL (Method B), respectively. The proposed method is selective, simple and accurate with a recovery of 99.60-100.28%. The results obtained are reproducible and statistically validated.

Key words: Spectrophotometric, Alfuzocin hydrochloride (ALF), Schiff's Base, PDAC, VN.

INTRODUCTION

Alfuzocinhydrochloride[1-6] is (R, S)-N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl) ethylamino] propyl] tetrahydro-2-furancarboxamide hydrochloride. The empirical formula of ALF is $C_{19}H_{27}N_5O_4HCl$. ALF exhibits selectivity for apha$_1$-adrenergic receptors in the lower urinary tract. Blockade of these adrenoreceptors can cause smooth muscle in the bladder neck and prostate to relax, resulting in an improvement in urine flow and a reduction

[*]Author for correspondence; E-mail: vasudevamln12@rediffmail.com

in symptoms of BPH. Literature cites only a very few physico-chemical methods for the determination of ALF in pharmaceutical formulations less and more for plasma samples like Spectrophotometeric (visible or colorimetry)[7-14], HPLC[15-23], RPLC[24] and conductivity[25]. The analytically useful functional groups are aryl alkoxy, hetero nitrogen, tertiary nitrogen and aliphatic primary amine after hydrolysis (Fig. 1**)**. From the literature, it is clear that no attempt has been made to develop a method for the drug chosen by the authors using the reagents as mentioned.

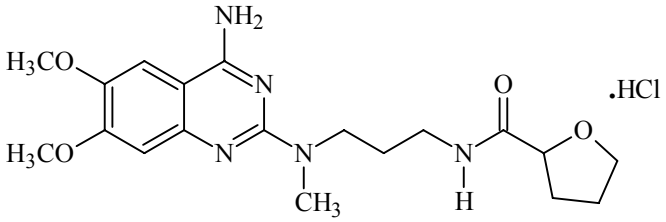

Fig. 1: Chemical structure of ALF

Hence the authors tried to develop a method to determine the selected drug by making use of Schiff base formation between primary amine and PDAC (Method A) and VN (Method B), respectively. The methods are simple, sensitive and reproducible for not only in pure form but also in formulations.

EXPERIMENTAL

Materials and methods

Instrument and reagents

A UV – 1601, Shimadzu digital spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. Systronics digital pH meter 361 was used for pH measurements. PDAC solution (BDH, 0.4%) and VN (CDH, 0.4%) were prepared by dissolving specific quantities of reagents in in 100 mL of methanol. Concentrated sulphuric acid and methanol were obtained from Qualigens and were used as such. ALF formulations were obtained from the local market.

Preparation of standard drug solution

A 1 mg/mL stock solution of ALF was prepared by dissolving 100 mg of the drug in aldehyde free 100 mL methanol. This stock solution was further diluted with appropriate

solvent to get the working standard solutions 500 µg/mL (Method A) and 150 µg/mL (Method B), respectively.

Pharmaceutical formulation solution

Tablets (Alfu, Fual, Xelflo, Alfusin) from local markets were mixed thoroughly and 20 tablets were selected at random and grinded to a fine powder. A portion of the mixed powder, equivalent to 100 mg of ALF was dissolved in methanol and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved in 100 mL methanol to achieve a concentration of 1 mg/mL. This solution was further processed as required for analysis.

Assay procedure

To each of 10 mL calibrated tubes, aliquots (1.0-3.0 mL, 50 µg/mL for Method A, 0.5-2.5 mL, 200 µg/mL for Method B) of standard ALF solution, 2.0 mL of vanillin and 3.0 mL of concentrated sulphuric acid were added successively and the total volume in each flask was brought to nine mL by the addition of methanol and placed in heating water bath for 15 min (Method A), and 25 min (Method B). Then the flasks were cooled and made up to the mark with methanol and the absorbances were measured after 5 min at 660 nm (Method A, Fig. 2) against reagent blank prepared in a similar way and 680 nm (Method B, Fig. 3), respectively. The concentration of drug in the samples was computed from Beer's plots (Fig. 4, Fig. 5).

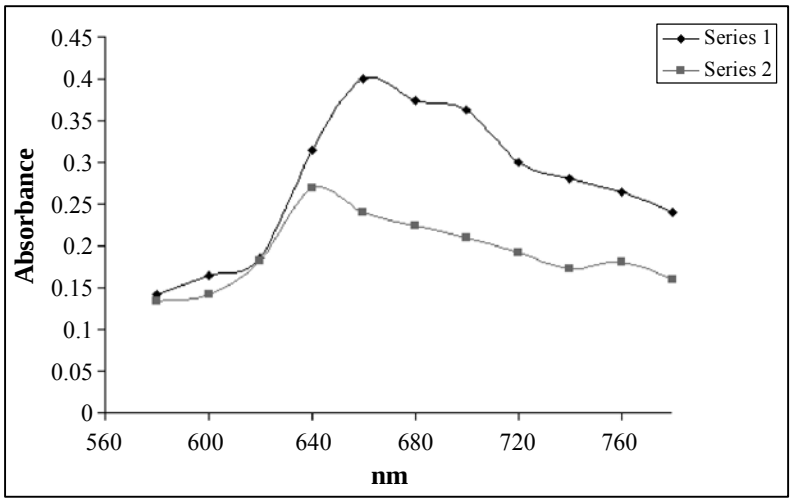

Fig. 2: Absorption spectra of ALF-PDAC

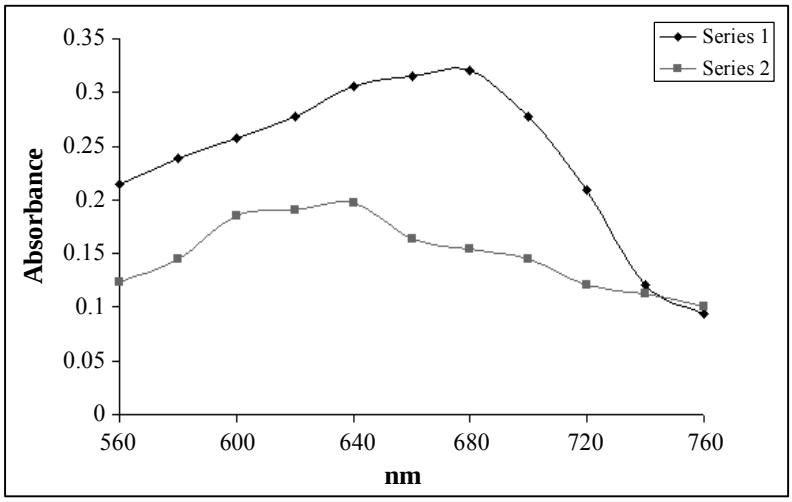

Fig. 3: Absorption spectra of ALF-VN

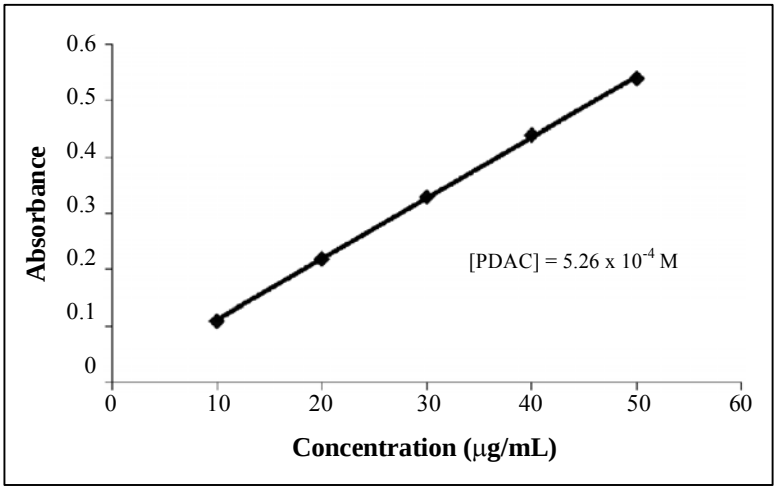

Fig. 4: Beer's plot of ALF-PDAC

RESULTS AND DISCUSSION

The optimum conditions for this method were established by varying one parameter at a time (OVAT) method and keeping the others fixed and observing the effect produced on the absorbance of the coloured species. Beer's law limits, molar extinction coefficient, Sandell's sensitivity, regression characteristics of the method, the relative standard deviation and % range of error are presented in Table 1.

Table 1: Optical characteristics, precision, accuracy of the methods proposed in the determination of ALF

S. No.	Optical characteristics	Method A	Method B
1	λ_{max} (nm)	660	680
2	Beer's law limits (µg/mL)	10-50	4-24
3	Molar absorptivity (l mol^{-1} cm^{-1})	5.79 x 10^4	2.97 x 10^4
4	Correlation coefficient (r)	0.9985	0.9999
5	Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	4.32 x 10^{-4}	1.0 x 10^{-3}
6	Regression equation (y = a + bc)		
	(i) Slope (b)	0.0165	0.02741
	(ii) Standard deviation on intercept (S_b)	0.00623	5.76 x 10^{-5}
	(iii) Intercept (a)	0.08343	-0.2686
	(iv) Standard deviation (S_a)	0.2030	8.97 x 10^{-4}
	(v) Standard error of estimation (S_e)	0.1967	9.65 x 10^{-4}
7	Optimum photometric range (µg/mL)	19.9-49.9	11.9-23.9
8	Relative standard deviation*	0.3634	0.7012
9	Detection limit	0.2313	0.2320
10	% of range of error (confidence limit) (i) 0.05 level	0.3815	0.7347
	(ii) 0.01 level	0.6279	1.209

Recovery studies were carried out in commercial formulations by addition of known standard drug solution to pre-analyzed sample solution. Results of recovery studies are presented in Table 2. The results obtained were in good agreement with the labeled amount. The interference studies in the determination of ALF in pharmaceutical formulations revealed that the normally existing excipients and additives were found not to interfere even when present in excess. The effect of various parameters, such as concentration and volume of PDAC, vanillin, nature and strength of acid, order of addition of reagents, solvent for final dilution were studied and the optimum conditions developed and actual conditions chosen for the procedure were studied. The aromatic aldehydes have lead to numerous applications as analytical reagents. Aldehydes were applied to the colorimetric determination of primary alkyl amines[26] in acid medium. The condensation of derivatives in acid medium gives the coloured product[27].

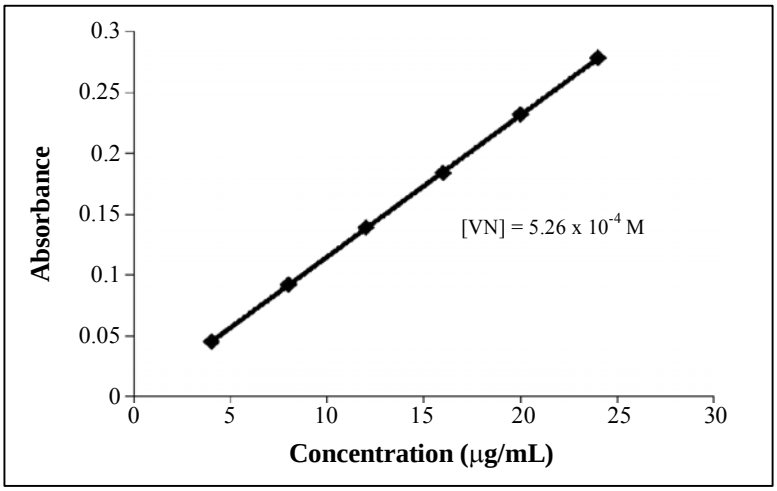

Fig. 5: Beer's plot of ALF-VN

Table 2: Determination of ALF in pharmaceutical formulations

Pharmaceutical formulation	Labelled amount	%Recovery proposed methods		% Recovery
		PDAC/H_2SO_4	**VN/H_2SO_4**	**Reference method**
Tablets – T_1	100 mg	99.60 ± 0.70 t = 0.50 F = 1.50	100.28 ± 0.58 t = 0.01 F = 2.27	99.3 ± 0.43
Tablets – T_2	100 mg	99.72 ± 0.72 t = 0.30 F = 2.28	99.97 ± 0.27 t = 0.62 F = 1.31	99.6 ± 0.21
Tablets – T_3	100 mg	99.66 ± 0.37 t = 0.35 F = 1.20	99.61 ± 0.48 t = 0.90 F = 2.76	99.4 ± 0.18
Tablets – T_4	100 mg	99.70 ± 0.28 t = 1.21 F = 3.18	99.76± 0.61 t = 0.93 F = 2.50	99.2 ± 0.33

*Tablets from four different pharmaceutical companies.

**Average ± standard deviation of six determinations, the t-and F-test values refer to comparison of the proposed method with the reference method. Theoretical values at 95 % confidence limit

CONCLUSION

The proposed methods have higher λ_{max} (nm) values and sensitivity. They are simple, rapid and have reasonable precision and accuracy. The methods are useful for the determination of ALF in pure state and pharmaceutical formulations.

ACKNOWLEDGEMENTS

The authors, expresses their deep sense of gratitude to UGC, SAP, Phase-III, for assistance.

REFERENCES

1. British Phamacopeia, **Vol. II,** HMSO, London (2007).
2. European Pharmacopeia, 5th Edn. Council of Europe, Strasbourg (1997) and Supplement (1999).
3. Martinadale, The Complete Drug Reference, (Extra Phamacopeia) 30th Edn. (1993).
4. The Merck Index, 13th Edn. Merck & Co Inc, New York (1996).
5. Physicien Desk Reference (PDR) 60th Edn. (2006).
6. CIMS-97 April (2007).
7. B. Mohammed Ishaq, J. Pharm. Res., **4**, 1 (2011).
8. A. S. Fayed, M. A. Shehata, N. Y. Hassan, S. A. Weshahy, Pharmazie., **62(11)**, 830-835 (2007).
9. Safwan Ashour et al., Int. J. Biomed. Sci., **2(3)**, 273-278, 15 (2006).
10. Vamsi Krishna and D. Gowri Sankar**,** Pharma. Review-Articles Archive, July (2007).
11. M. Vamsi Krishna and D. Gowri Sankar, E-J. Chem., **4(3)**, 397-407 (2007).
12. M. Vamsikrishna and D. Gowrisankar, E-J. Chem., e-journals.net, **4**, 496 (2007).
13. Ragaa, El Sheikh et al., Chem. Ind. Chem. Engg., **18(2)**, 179-191 (2012).
14. S. Ashour, C. M. Fawaz and R. Bayramet**,** Int. J. Biomed. Sci.**, 2(3)**, 273-278 (2006).
15. Dipti B. Patel and J. Patel, Int. J. Chem. Tech. Res., **1(4)**, 985-990 (2009).
16. R. Cirillia and La Torre, F. J, Chromatogr. A, **818(1)**, 53 (1998).

17. I. E. Ponderi, J. Pharma. Biomed. Anal., **21(2)**, 257 (1999).
18. N. F. Erk, Oncer, Analysis, **25(5)**, 161 (1997).
19. Gumieniczek, Anna, Pryborowski Lech. Acta. Pol. Pharm., **54(1)**, 13 (1997).
20. Erk, Nevin, J. Pharma. Biomed. Anal., **20(1-2)**, 155 (1999).
21. D. L. Massart et al., Chemometrics, A Text Book, Elsevier, Amstendam., 293 (1988).
22. V. Arregunine, Anales Asoc. Quim. Aregentina, **31**, 38 (1943).
23. L. Vignoli, B. Cristau and J. P. Defretin, Ann. Pham. Fr., **23**, 715 (1965).
24. R. Dhaneshwar et al., Der Pharmacia Lett., **2(6)**, 342-349 (2010).
25. M. Mona et al., J. Chem. Pharmaceut. Res., **4(7)**, 3740-3748 (2012).
26. E. Sawiki and Johnson, Chemist-Analyst., **101** (1966),
27. P. Byrun and H. Turnball, Talanta, **10**, 1217 (1963).

Revised : 27.11.2012 *Accepted : 30.11.2012*