Simultaneous Spectrophotometric Estimation of Valdecoxib and Tizanidine HCl in Mixture

A. S. K. SANKAR*, K. ANANDAKUMAR, D. NAGAVALLI, M. SENTHIL PALANIAPPAN, T. VETRICHELVAN AND K. NITHYANANDHAM

Department of pharmaceutical Analysis, Adhiparasakthi College of Pharmacy, Melmaruvathur-603 319, India.

***For correspondence**

E-mail: asksankar@yahoo.com

Two simple, rapid, accurate and economical methods have been developed for the estimation of valdecoxib and tizanidine HCl in the mixture. Valdecoxib has an absorbance maximum at 243 nm and tizanidine HCl has two absorbance maxima at 228 nm and 320 nm in methanol:0.1 M HCl (1:1) mixture. The linearity was observed in the concentration range 5-30 µg/ml for valdecoxib and 2-20 µg/ml for tizanidine. First method is based on the simultaneous equations and second method is based on Q absorbance ratio. Absorbances at 243 nm and 228 nm were selected for simultaneous equations method. Absorbance at isoabsorptive point 280.4 nm and at 243 nm, the λ_{max} of valdecoxib were selected for absorbance ratio method. These methods were validated statistically. The recovery studies confirmed the accuracy of the proposed methods.

Valdecoxib (VAL)[1] is chemically 4-(5-methyl-3-phenyl-4-isoxazolyl) benzene sulfonamide and has been used as a non-steroidal antiinflammatory drug (NSAID) for pain relief in rheumatoid arthritis. Tizanidine HCl (TZH)[1] chemically, 5-chloro-4-(2-imidazolin-2-ylamino)-2,1,3-benzothiadiazole hydrochloride, is a centrally acting muscle relaxant and an alpha-2-adrenergic agonist that acts mainly at the level of spinal cord.

VAL and TZH are available in combined dosage forms. VAL and TZH are not official in any pharmacopoeia. The reported methods for analysis are HPLC[2], spectrophotometry[3], and LC-MS[4] for VAL alone and in combinations. HPTLC[5], GC-MS[6], spectrophotometry[7,8] methods are available for TZH alone and RP-HPLC[9-12], spectrophotometric[13] methods are available for combination of TZH with other drugs. However, there are no methods currently available for the estimation of VAL and TZH in combination from its pharmaceutical dosage forms. The present study discusses two simple, rapid, accurate and economical methods developed for simultaneous estimation of VAL and TZH combined dosage forms.

VAL (100 mg) and TZH (100 mg), gifted by M/S A TO Z Analytical Labs, Chennai, were accurately weighed and dissolved in a mixture of methanol:0.1 M HCl (1:1) to give stock solutions containing 1000 µg/ml. From these stock solutions, working standard solutions of the concentration 100 µg/ml each were prepared by appropriate dilutions. Working standard solutions were scanned in the entire UV range to determine the $\lambda_{max.}$ The λ_{max} of VAL and TZH were found to be 243 nm, and 228 nm and 320 nm, respectively. For better results, 228 nm was selected for TZH. Six standard dilutions of each drugs were prepared having concentrations of 5, 10, 15, 20, 25 and 30 µg/ml for VAL and 2, 4, 8, 12, 16 and 20 µg/ml for TZH separately. The absorbances of these standard solutions were measured at 228 nm and 243 nm and calibration curves were plotted at these wavelengths. The absorptivity coefficients of these two drugs were determined using calibration curves. Two simultaneous equations were formed using these absorptivity coefficient values. $A_1 = 583XC_V + 752XC_T$, $A2 = 610XC_V + 174XC_T$, where C_V and C_T are concentrations of VAL and TZH, respectively in g/100 ml in the sample solution. A_1 and A_2 are absorbances of the mixture at 228 nm and 243 nm, respectively. Solving these two equations, the concentrations of C_V and C_T can be readily found out.

Absorbance ratio method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and the other being λ_{max} of one of two components. From the overlain spectra of two drugs, it is evident that VAL and TZH have isoabsorptive point at 280.4 nm and λ_{max} of VAL is at 243 nm. Six standard solutions of each pair having concentration 5, 10, 15, 20, 25 and 30 µg/ml were prepared separately in methanol:0.1 M HCl (1:1) and the absorbances at 280.4 nm (isoabsorptive point) and at 243 nm (λ_{max} of VAL) were measured, and absorptivity coefficients were calculated using calibration curve. The concentration of two drugs in the mixture can be calculated using equations[14], $C_V = Q_M - Q_Y/Q_X - Q_Y X A_1/aV_1$, $C_T = A_1/aT_1 - C_V$, where, A_1 and A_2 are absorbance of mixture at 280.4 nm and 243 nm, and aV_1 and aT_1 are absorptivity of VAL and TZH respectively at 280.4 nm, aV_2 and aT_2 are absorptivity values of VAL and TZH, respectively, at 243 nm and $Q_M = A_2/A_1$, $Q_Y = aT_2/aT_1$, $Q_X = aV_2/aV_1$.

The synthetic mixtures of the combination of both the drugs were prepared in the ratio of 10:1 (VAL:TZH) considering the dosage strength of formulations available in the market. From the synthetic mixture, a stock solution containing VAL (100 µg/ml) and TZH (20 µg/ml) was prepared. Appropriate dilutions of the stock were prepared and the concentration of VAL and TZH were determined. Absorbance at selected wavelengths in both proposed method were recorded. The concentration of VAL and TZH were worked out utilizing the equations developed. The diluted solutions were also used for the recovery studies.

TABLE 1: ANALYSIS OF VALDECOXIB AND TIZANIDINE IN FORMULATION BY PROPOSED METHODS

Drug	Label amount	Method I n=6		% CV	Method II n=6		% CV
	mg/tab	% Found±SD*	% Recovery±SD*		% Found±SD*	% Recovery±SD*	
VAL[a]	20	99.99±0.103	100.50±0.434	0.75	101±0.792	98.5±0.792	1.415
TZH[a]	2	100.1±0.75	103.76±0.861	1.022	99.6±0.98	100±0.33	0.491
VAL[b]	20	100.29 ± 0.271	100.05±0.142	0.667	102±0.232	102±0.96	0.971
TZH[b]	2	99.95 ± 0.426	100.1±0.634	0.875	101±0.862	102±0.90	0.347

*Mean±SD of six observations, a: formulation 1, b: formulation 2

In method I, two wavelengths of respective absorbance maxima i.e., 243 nm and 228 nm for VAL and TZH, respectively, were used for the analysis of the drugs. In absorbance ratio method (method II) the primary requirement for developing a method for analysis is that the entire spectra should follow the Beer's law at all wavelengths. This requirement was fulfilled in the case of both these drugs. The two wavelengths used for the analysis of both the drugs were 280.4 nm (iso absorptive point) and 243 nm (the λ_{max} of VAL).

Two formulations were selected, Velycox-MR, (Fine cure, Formulation 1), Vabra-TZ (Intra labs, Formulation 2). Twenty tablets were weighed accurately and powdered. Weighed quantity equivalent to 20 mg of VAL, extracted with methanol and suitably diluted with the same solvent to get the concentration equivalent to 15 µg/ml. This solution was analysed as described above for method I and method II.

The validation parameters were studied at all the three wavelengths for both the methods. Accuracy was determined by calculating the recovery and the mean was determined. Precision was calculated as a repeatability (standard deviation and relative standard deviation) and inter and intra day variation (% CV) for both the drugs. Both the methods were successfully used to estimate the amount of VAL and TZH present in the synthetic mixture that was prepared. The results obtained were in well agreement with the corresponding label amount (Table 1). By observing the validation parameters, both the methods were found to be specific, accurate and precise. Hence both the methods can be employed for routine analysis of these two drugs in combinations.

REFERENCES

1. Anonymous, Physician's Desk Reference, 57th Edn, Thomson Publishers, 2003, 2578, 1274.
2. Ramakrishna, N.V.S, Vishwotham, K.N., Wishu, S. and Koteshwara, M., **J. Chromatogr. B. Analyte Technol. Biomed. Life. Sci.,** 2004, 802, 271.
3. Zhang, J.Y., Fast, D.M. and Breau, A.P., **J. Pharm. Biomed. Anal,** 2003, 33, 61.
4. Werner, U., Werner, D., Hinz, B., Lambrecht, L. and Brune, K., **Biomed. Chromatogr.** 2005, 19, 113.
5. Mahadik, K.R., Paradkar, A.R., Agarwal, H., and Kaul, N., **J. Pharm. Biomed. Anal.,** 2003, 33, 545.
6. Lee, J., Seo. J.H and Kim, D.H., **Analyst,** 2002, 127, 917.
7. Rao, K.K.V., Satish Kumar, M., Mathivanan, N., Kiran Kumar, M. and Rao, M.E.B., **Indian Drugs**, 2004, 4, 583.
8. Sujatha, K., Chitra, K., Dhanushka, S.H., Krishnan, M.V. and Janardhan, V., **Indian Drugs**, 2002, 39, 548.
9. Subramanian, G., Musmade, P., Agarwal, S. and Udupa, N., **Indian J. Pharm. Sci.,** 2004, 66, 694.
10. Subramanian, G., Pandey, S. and Udupa, N., **Indian J. Pharm. Sci.,** 2004, 66, 699.
11. Shingare, M.S., Naidu, K.R and Kale., **Indian J. Pharm. Sci,** 2003, 65, 315.
12. Raman, B. and Patil, D., **Indian Drugs,** 2002, 39, 392.
13. Amin, A .S., Elkousu, N., Dessouki, H.A. and Sultan, M., **Egypt. J. Pharm. Sci.,** 1998, 39, 463.
14. Beckett, A.H. and Stenlake, J.B., Eds., Practical Pharmaceutical chemistry, 4th Edn, Part Two, CBS Publisher, New Delhi, 1997, 286.

Accepted 12 February 2007
Revised 19 June 2006
Received 5 December 2005
Indian J. Pharm. Sci., 2007, 69 (1): 132-134