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Simultaneous Determination of Tizanidine and Ibuprofen in Tablets

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Abstract: A simple, specific, accurate and precise reverse phase high pressure liquid chromatographic method has been developed for the simultaneous determination of tizanidine and ibuprofen from tablets. The sample was analyzed using methanol: water in the ratio of 60:40, pH adjusted to 4.20 with orthophosphoric acid on an octadecylsilane C_{18} column. The effluent was monitored at 1.2 ml/min flow rate using 305 nm as detecting wavelength. The linear dynamic ranges for ibuprofen and tizanidine 0.2-1.0µg/ml and 10-40µg/ml respectively. Coefficients of correlation observed for ibuprofen and tizanidine were 0.999 and 0.998 respectively.
Key words: RP-HPLC, Ibuprofen, Tizanidine, Validation

Introduction

Ibuprofen is chemically 2[4-(2-methyl propyl) phenyl] propanoic acid. The structural formula is $C_{13}H_{18}O_2$, and molecular weight is 206. It is non-steroidal anti inflammatory drug (NSAID). It is used for relief of symptoms of arthritis, primary dysmenorrheal, and fever and as an analgesic. Ibuprofen is known to have an ant platelet (blood-thinning effect).Paracetamol is chemically N-(4-hydroxyphenyl) acetamide. It is a centrally and peripherally acting non-opioid analgesic and antipyretic. Many methods have been described in the literature for the determination of paracetamol with other drugs individually and in combination[1-11].

Tizanidine 5-chloro-4-(2-imidazolin-2-ylamino)-2, 1, 3-benzothiadiazole is a 2 – adrenergic agonist and centrally active myotonolytic skeletal muscle relaxant with a chemical structure unrelated to other muscle relaxants[12-14]. In the literature, a radioimmunoassay method for the quantification of tizanidine hydrochloride has been widely used[15] .Also determination of tizanidine in human plasma by gas chromatography–mass spectrometry has been reported [16, 17] .There are very few reports on analytical methods for estimation of tizanidine in bulk and its dosage form.

Experimental

Ibuprofen and tizanidine tablets (TIZAFEN, Sun Pharma) were procured from the market. They had labeled content of 400 mg and 2 mg of Ibuprofen and tizanidine, respectively. Water and methanol HPLC grade, orthophosphoric acid reagents were used. A High Performance Liquid Chromatograph system, with LC solutions data handling system (Shimadzu-LC2010) with an auto sampler was used for the analysis. The data was recorded using LC 2010 solutions software. The purity determination performed on a stainless steel column 150 mm long, 4.6 mm internal diameter filled with Octadecyl silane chemically bonded to porous silica particles of 5µm diameter (Inertsil C_{18}, 5µ , 150 mm x 4.6 mm, make: Shimadzu ltd, Japan). A water-methanol mixture was prepared by mixing 400 ml of water with 600 ml of methanol and its pH was adjusted to 4.20 with orthophosphoric acid at ambient temperature. Flow rate was kept at 1.2ml/min and the elution was monitored at 305 nm.

About 500 mg Ibuprofen and 10 mg tizanidine were accurately weighed, transferred to 100 ml volumetric flask and dissolved in methanol. The volume was made up to the mark. An aliquot 0.02 ml of this solution was diluted to 10 ml with mobile phase to get the working standard solution (10 µg/ml for ibuprofen and 0.2 µg/ml for tizanidine).

Twenty tablets were accurately weighed and finely powdered. Accurately weighed quantity of powder equivalent to 100 mg of ibuprofen and 2 mg of tizanidine was transferred in 100 ml volumetric flask and dissolved in methanol and volume was adjusted to 100 ml with methanol and the solution was shaken for 10 min, filtered through grade-I filter paper and finally through 0.45 µm membrane filter paper. A 0.02 ml of aliquot filtrate

solution was taken in 10 ml volumetric flask and diluted upto the mark with mobile phase. The mobile phase consisting of methanol: water (60:40), pH adjusted to 4.20 with orthophosphoric acid showed symmetric, sharp, reproducible peaks with good resolution. The flow rate was kept at 1.2 ml/min and 305 nm was selected as the wavelength for determination of eluted components. Several aliquots of standard ibuprofen and tizanidine stock solution were taken in different 100 ml volumetric flasks and diluted upto the mark with mobile phase so that the final concentrations of tizanidine and ibuprofen were in the range of 10-40 µg/ml and 0.2-10 µg/ml, respectively. The plots of peak area of each component against respective concentration of each corresponding drug were found to be linear in the range of 10-40 µg /ml and 0.2-10 µg /ml for tizanidine and ibuprofen, respectively. Evaluation of two drugs was performed with UV detector at 305 nm. Peak areas were recorded for all the peaks. The coefficients of correlation were found to be 0.999 and 0.998 for ibuprofen and tizanidine (Fig-1, Fig-2), respectively.

Twenty microlitres each of the working standard solution and sample solution were injected separately into the column. The detector responses were recorded for the same and the amounts of the drugs were calculated. The precision of the method was established by replicate analysis of the analyte (five times) using the proposed method. The low value of relative standared deviation (RSD) shows that the method is precise. The values are given in table-1. To study the accuracy, reproducibility and precision of the proposed method, recovery experiments were carried out and results were obtained. The concentrations were found to be within 99-101% of the true concentrations of each drug, which indicates the accuracy of the method

Analysis of tablets containing nimesulide and tizanidine was carried out by using optimized mobile phase containing methanol and water (60:40), pH adjusted to 4.20 with orthophosphoric acid, and detection was done at 305 nm. The retention time for ibuprofen was 6.73 min and for tizanidine was 2.56 min. The average content of ibuprofen and tizanidine found were 100.14 mg/tab and 2.028 mg/tab, respectively. As per USP-XXIV, system suitability tests were carried out on freshly prepared solution of ibuprofen and tizanidine and parameters obtained with 20 ml solution are shown in table-2. The percentage recoveries of ibuprofen (100.25%) and tizanidine (101%) reveal no interference of excipients. Ruggedness and robustness studies were carried out, as they are the measures to indicate the degree of reproducibility. It was observed that the method was rugged and robust as after carrying out the analysis by different analysts and on different days the results showed RSD well within permissible limits.

Table-1: Results of HPLC Assay

Expt. No.	Ibuprofen		Tizanidine	
	Assay	Recovery	Assay	Recovery
1	99.97	100.22	1.9867	2.0042
2	100.25	100.24	2.0891	2.0865
3	100.36	100.12	2.0825	2.0105
4	99.98	100.43	2.0658	2.0108
Mean	**100.14**	**100.2525**	**2.056025**	**2.028**
SD	**0.195789**	**0.129454**	**0.047245**	**0.039119**
%RSD	**0.0489**	**0.0323**	**2.292**	**1.928**

Table-2: Summary of results of system suitability

Parameter	**Ibuprofen**	**Tizanidine**
%RSD	0.0038	0.036
Resolution	15.568	
Capacity factor	5.04	1.29
Asymmetry	1.5	1.6
Theoretical plates per meter	62465	26345

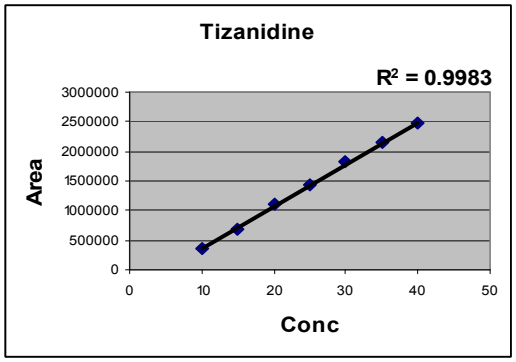

Fig-1: Calibration curve of Tizanidine by HPLC

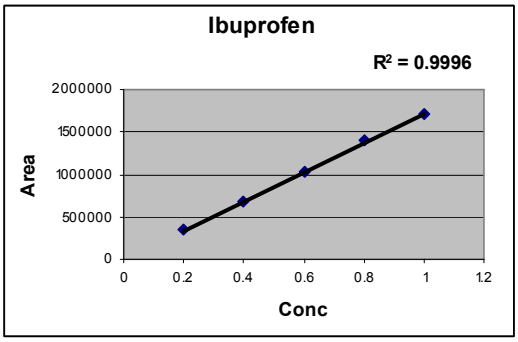

Fig-2: Calibration curve of Ibuprofen by HPLC

References

1. British pharmacopoeia, Vol II, London: Her mejesty's Stationary office 1998, p. 1854
2. Indian pharmacopoeis Vol II, New Delhi, The controller of Publications. Govt of India, 1996, p. 554.
3. Hasan, N.Y., Abdel-Elkawy, M., Elzeany, B.E. and Wagieh, N.E., Farmaco., 2003, 58, 91.
4. EI-Saharty, Y.S., Refaat, M. and EI-Khateeb, S.Z., Drug. Develop. Ind. Pharm., 2002, 28, 571.
5. Zawilla, N.H., Mohammad, M.A., EI-Kousy, N.M. and EI-Moghazy Aly, S.M., J.Pharma. Biomed. Anal., 2002, 27, 243.
6. Hinz, B., Auge, D., Rau, T., Rietbrock, S., Brune, K. And Werner, U., Biomed. Chromatogr., 2003, 17, 268.
7. Liu, XQ., Chen, X.J., Zhao, L. H. And Peng, J.H., Yao Xue Ba., 1997, 32, 546.
8. Lee, H.S., Jeong, C.K., Choi, S.J. Kim, S.B., Lee, M.H., Ko, G.I, and Sohn, D.H., J. Pharm. Biomed. Anal., 2000, 23, 775.
9. EI-Kousy, N.M., J. Pharm. Biomed. Anal., 1999, 20, 185.
10. Jensen, L.S., Valentine, J., Milne, R.W. and Shimada, K., J. Pharm. Biomed. Anal., 2004, 34, 585.
11. Ohta, M., Kawakami, N., Yamato, S. and Shimada, K. J.Pharm Biomed. Anal., 2003, 15, 1759.
12. P. Koch, D.R. Hirst and B.R. von Wartburg, Xenobiotica ,1989,19 , 1255–1260.
13. F.L.S. Tse, J.M. Jaffe and S. Bhuta, Fundam. Clin. Pharmacol., 1987,1 ,479–485.
14. M.K. Shellenberger, L. Groves, J. Shah and G.D. Novak, Drug Metab.Dispos.,1999, 27, 201–205.
15. V. Healzlewood, P. Symoniw, P. Maruff and M.J. Eadie, Eur. J. Clin.Pharmacol.,1983, 25, 65–72.
16. J. Lee, J.H. Seo and D.H. Kim, Analyst, 2002,127 , 917–920.
17. L.J. Jackman and T. Jen, J. Am. Chem. Soc.,1975, 97 ,2818.

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