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# Simultaneous Estimation of Valdecoxib and Tizanidine by Vierodt's and Q-Analysis UV Spectrophotometric Method

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**The simple, accurate and precise Vierodt's and Q-analysis UV Spectrophotometric method has been developed for the simultaneous determination of valdecoxib and tizanidine in combined tablet dosage form. Shimadzu UV-1601 instrument was used and the λmax of valdecoxib and tizanidine was found to be 237 nm and 319 nm, respectively. In Q-analysis, the isoabsorptive point for both the drugs was found at 289.5 nm. The linearity range lies between 5-30 µg/ml for valdecoxib and 0.5-3 µg/ml for tizanidine at their respective wavelengths.**

Valdecoxib, a new COX-2 inhibitor, an antiinflammatory drug is chemically, 4,5,(5-methyl-3-phenyl isoxazol-4-yl) benzene sulfonamide[1]. It is yet not official in any pharmacopoeia. Tizanidine is a muscle relaxant, official in Martindale[2]. Chemically, it is 5-chloro-N-(2-imidazolin-2-yl)-2,1,3-benzothiadiazol-4-yl amine hydrochloride. Both the drugs in combination are used in the treatment of painful muscle spasm and disc prolapse. Literature survey reveals that various methods have been developed for the determination of tizanidine alone as well as when in combination with other drugs[3-6] but no method was found to be developed for it's estimation with valdecoxib in combined dosage forms. The authors have hence developed the Vierodt's[7] and Q-analysis method[8] for the estimation of valdecoxib and tizanidine in tablet dosage form.

Methanol (Qualigens Fine Chemicals Ltd. Mumbai) and double distilled water were used for the present study. Tablets were procured from a local pharmacy. Spectral absorbance measurements were made on Shimadzu UV-1601 with 10 mm matched quartz cells.

The stock solutions having 1 mg/ml solutions of both valdecoxib and tizanidine were prepared in methanol. Aliquots of both the stock solutions were diluted further with

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TABLE 1: THE RESULTS OF THE ANALYSIS OF COMMERCIAL FORMULATIONS AND THE RECOVERY STUDIES.

| Drug | Label claim (mg/tab) | Amount found (mg/tab) | % label claim | Standard deviation | % recovery |
|---|---|---|---|---|---|
| Vierodt's method | | | | | |
| Grandix-Nizox-MR | | | | | |
| Valdecoxib | 20 | 19.97 | 99.88 | ±0.68 | 99.16 |
| Tizanidine | 2 | 2.03 | 101.7 | ±1.52 | 101.48 |
| Valoflam-TZ | | | | | |
| Valdecoxib | 20 | 20.05 | 100.25 | ±0.44 | 99.70 |
| Tizanidine | 2 | 2.02 | 101.02 | ±0.83 | 100.3 |
| Q-analysis method: | | | | | |
| Grandix-Nizox-MR | | | | | |
| Valdecoxib | 20 | 19.96 | 99.84 | ±0.03 | 99.86 |
| Tizanidine | 2 | 1.99 | 99.91 | ±0.02 | 100.01 |
| Valoflam-TZ | | | | | |
| Valdecoxib | 20 | 19.95 | 99.76 | ±0.02 | 99.90 |
| Tizanidine | 2 | 1.996 | 99.83 | ±0.02 | 99.87 |

*All the values are the mean of five readings.

distilled water to get the concentration of valdecoxib as 5, 10, 15, 20, 25 and 30 µg/ml and that of tizanidine as 0.5, 1, 1.5, 2, 2.5 and 3 µg/ml, respectively to study the verification of Beer's law by both the methods. For simultaneous study according to Vierodt's method, the absorbance values were recorded at the 237 nm for valdecoxib and at 319 nm for tizanidine. For study according to Q-analysis method, the absorbance values were taken at 289.5 nm (isoabsorptive point) and 319 nm from the overlain spectra of both the drugs.

Drug concentrations of 10 µg/ml (valdecoxib), 1 µg/ml (tizanidine) and a mixture containing the same concentration of both the drugs were analyzed by Vierodt's method. For Q-analysis, 20 µg/ml of valdecoxib, 2 µg/ml of tizanidine and their mixture were estimated.

Twenty tablets containing 20 mg valdecoxib and 2 mg tizanidine (Grandix-Nizox-MR, Grandix Pharmaceuticals Pvt. Ltd. Chennai and Valoflam-TZ, Sigma Laboratories Pvt. Ltd. Mumbai) were weighed and finely powdered. A quantity of powder equivalent to 10 mg valdecoxib and 1 mg tizanidine was accurately weighed and transferred to a 50 ml volumetric flask, dissolved in methanol, filtered through Whatman filter paper No.1 and the volume was made up to 50 ml with the same solvent. Aliquots of this solution were diluted with distilled water to get the working standards of 10 µg/ml valdecoxib (~1 µg/ml tizanidine) and also 20 µg/ml valdecoxib (~2 µg/ml tizanidine). The sample solutions were scanned over the range of 190-400 nm. Absorbance of the sample solutions at 237 nm and 319 nm and at 289.5 nm and 319 nm (overlain spectra) were measured and from the absorbance values, the concentration of drugs in the sample solution was determined by Vierodt's and Q-analysis method.

For determining the concentration of drugs by Vierodt's method, following equation was used. $Cx=(A_2a_{y1}-A_1a_{y2})/(a_{x2}a_{y1}-a_{x1}a_{y2})$. $Cy=(A_1a_{x2}-A_2a_{x1})/(a_{x2}a_{y1}-a_{x1}a_{y2})$ where, Cx and Cy are concentration of valdecoxib and tizanidine, respectively, $a_{x1}$ and $a_{x2}$ are the absorptivity values of valdecoxib at 237 nm and at 319 nm, respectively, $a_{y1}$ and $a_{y2}$ are the absorptivity values of tizanidine at 237 nm and at 319 nm, respectively and $A_1$ and $A_2$ are the absorbances of the diluted sample at 237 nm and at 319 nm, respectively.

For estimating the concentration of valdecoxib and tizanidine by Q-analysis method, the absorbance and the

TABLE 2: THE ABSORPTIVITY VALUES OF VALDECOXIB AND TIZANIDINE THE PROPOSED METHODS.

| Absorptivity values | Vierodt's method | | Q-analysis method | |
|---|---|---|---|---|
| Wavelength (nm) | 237 | 319 | 289.5 | 319 |
| $ax_1$ | 540 | - | 18.5 | - |
| $ax_2$ | - | 3 | - | 1.5 |
| $ay_1$ | 790 | - | 190 | - |
| $ay_2$ | - | 570 | - | 570 |

$ax_1$ and $ax_2$ are the absorptivity values of valdecoxib at the respective wavelengths. $ay_1$ and $ay_2$ are the absorptivity values of tizanidine at the respective wavelengths.

TABLE 3: REGRESSION ANALYSIS OF CALIBRATION CURVES AND SUMMARY OF VALIDATION PARAMETERS.

| Parameters | Valdecoxib | Tizanidine | Valdecoxib | Tizanidine |
|---|---|---|---|---|
| Wavelength (nm) | 237 | 289.5 | 289.5 | 319 |
| Beer's law limit (μg/ml) | 5-30 | 0.5-3.0 | 5-30 | 0.5-3.0 |
| ε-Molar absorptivity (l/mol/cm) | $1.7030 \times 10^4$ | $0.5513 \times 10^4$ | $0.0583 \times 10^4$ | $1.6541 \times 10^4$ |
| Limit of detection (μg/ml) | 0.5 | 0.1 | 0.5 | 0.1 |
| Limit of Quantitation (μg/ml) | 1 | 0.5 | 1 | 0.5 |
| Sandell's sensitivity (μg/cm²) | 0.01851 | 0.05263 | 0.54054 | 0.01754 |
| Regression equation* | | | | |
| Intercept (α) | -0.00164 | 0.00021 | 0.00021 | 0.00007 |
| Slope (β) | 0.05404 | 0.019 | 0.00187 | 0.05643 |
| Correlation coefficient ($r^2$) | 0.9999 | 0.9997 | 0.9987 | 0.9998 |

Where,*$y = \alpha + \beta x$, x is the concentration of the analyte and y is the absorbance value.

absorptivity values at the particular wavelengths were calculated and substituted in the following equation: $Cx=(Q_0-Q_2)xA_1/(Q_1-Q_2)xa_1$, $Cy=(Q_0-Q_1)xA_1/Q_2-Q_1)xa_2$, where Cx and Cy are concentration of valdecoxib and tizanidine, respectively. $A_1$ is the absorbance of sample at 289.5 nm, $a_1$ and $a_2$ are the absorptivity values of valdecoxib and tizanidine at 289.5 nm, respectively, $Q_0$ was obtained by using the equation, (absorbance of sample at 319 nm)/(absorbance of sample at 289.5 nm), $Q_1$ was obtained from (absorptivity of valdecoxib at 319 nm)/(absorptivity of valdecoxib at 289.5 nm), and $Q_2$ was obtained from (absorptivity of tizanidine at 319 nm)/(absorptivity of tizanidine at 289.5 nm). The amount and % claim calculated for both the drugs are shown in Table 1. The absorptivity values of valdecoxib and tizanidine at various wavelengths are given in Table 2.

To study the linearity, accuracy and precision of the proposed method, the recovery studies were carried out by adding a known quantity of standard to the pre analyzed sample and the % recovery was calculated and shown in Table 1. The regression analysis of the calibration curves and the optical characteristics such as Beer's law limits, detection limit, molar absorptivities and sandell's sensitivities are presented in Table 3.

The proposed Vierodt's and Q-analysis are simple, accurate and economical for routine analysis of two drugs without prior separation. The amount found was in good agreement with the label claim of the formulation. The value of the standard deviation was satisfactorily low indicating the reproducibility and accuracy of the proposed methods.

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# Simultaneous Spectrophotometric Determination of Pioglitazone Hydrochloride and Glimepiride in Tablets

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**Two simple, accurate and precise methods for simultaneous estimation of pioglitazone hydrochloride and glimepiride in combined dosage form have been described. First method employs formation and solving of simultaneous equation using 268.6 nm and 227.6 nm as two analytical wavelengths. Second method is absorbance ratio method, 268.6 nm for estimation of pioglitazone hydrochloride and 251.5 nm, isobestic point, where two drugs shows equal absorptivity, for the estimation of glimepiride. Both the methods allow the simultaneous determination of pioglitazone hydrochloride and glimepiride in the concentration ranges employed for this purpose. The result of analysis has been validated statistically and by recovery studies and assay of tablets with standard deviation < 1.0 % was found.**

Pioglitazone hydrochloride[1] (PIO-H), a thiazolidinedione antidiabetic drug and chemically it is (±)-5(4-(2-(5-ethyl-2-pyridinyl)ethoxy phenyl) methyl)-2,4-thiazolidinedione HCl. Glimepiride[2] (GLIM) is a sulphonylurea antidiabetic drug and chemically it is trans-3-ethyl-2,5-dihydro-4-methyl-N-(2-(-(((4methyl cyclohexylamino)carbonyl)amino)sulfonyl)phenyl)ethyl-1,2-oxo-IH pyrrole)-carboxamide. The combination of pioglitazone hydrochloride (PIO-H) and glimepiride (GLIM) is newly introduced in market and used in the treatment of Type II DM (NIDDM). Both the drugs are non-official, reports are available for estimation of PIO-H by HPLC[3-6] and GLIM by HPLC[7-9] and derivative UV spectrophotometry[10]. But there is no evidence in literature for simultaneous estimation of these drugs in combination products. Hence, in the present investigation, a simple rapid and reproducible method was developed for simultaneous estimation of PIO-H and GLIM from their combined dosage forms.

UV/Vis double beam spectrophotometer, model SHIMADZU UV-2401 with 1 cm UV matched quartz cells were used. Gift samples of PIO-H were obtained from Wockhardt Research Centre, Aurangabad and GLIM from Glenmark Pharmaceuticals, Nashik. Tablet of brand

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