# Simultaneous Spectrophotometric Estimation of Famotidine and Domperidone in Combined Tablet Dosage Form

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Two simple, accurate, precise and economical procedures for simultaneous estimation of famotidine and domperidone in two component tablet dosage form have been developed utilizing concept of standard addition. Both the methods utilize DMF/0.1N HCl (1:3) as solvent. Famotidine and domperidone at their respective $\lambda_{max}$ 267 nm and 285 nm shows linearity in the concentration range of 10-60 μg/ml. Wavelengths selected for estimation of famotidine and domperidone in simultaneous equation methods were 267 nm and 285 nm, respectively and for dual wavelength method were 275 nm, 291.1 nm and 275 nm, 257.9 nm, respectively. The result of analysis have been validated statistically, standard deviation lies in the range from 0.600-1.187, recovery studies range from 98.4-101.4% confirmed the accuracy of the proposed methods.

The combination of famotidine (FAM) {3-[[[2-[diaminomethylene) amino] thiazole-4-yl] methyl] sulphanyl]-N'sulphamoyl propanimidamide} and domperidone (DOM) {5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazole-1-yl)propyl]piperidine-4-yl]]-1,3-dihydro-2H-benzimidazole-2-one} is used in gastro oesophageal reflux disorder and peptic acid disorders. An extensive literature survey revealed titrimetry[1,2], HPLC[3,5], HPTLC[6] and Spectrophotometric[7,8] methods for the analysis of FAM in bulk and in formulations. Similarly for estimation of DOM titrimetry[9], HPLC[10,11], HPTLC[12] and Spectrophotometric[13,14] methods are reported. Not a single method has been yet reported for the simultaneous estimation of both the drugs. The objective of the work was to report a method for simultaneous estimation of FAM and DOM in tablet dosage form.

An UV/Vis double beam double detector spectrophotometer of the make Shimadzu UV-1700 and Citizen balance were used for the experimental purpose. Analytical grade DMF and HCl (Merck) were used. FAM and DOM were provided by Bal Pharma, Indore and Aristo Pharma, Mandideep, respectively.

Accurately weighed 20 mg of FAM was transferred to a 25 ml Volumetric flask and volume was made up with the solvent to get a solution of concentration 1250 μg/ml (stock-A). 4 ml of stock-A was diluted to 10 ml to get a concentration of 500 μg/ml (stock-B). Finally 5 ml of stock-B was transferred to 25 ml volumetric flask and volume was made up with solvent to get a concentration of 100 μg/ml (stock-C). Standard stock solution of DOM was also prepared separately in the same manner. Stock-C of both the drugs were further diluted separately to get concentration of 30 μg/ml of each drug and were scanned in the spectrum mode over the range of 250-330 nm. FAM showed an absorbance peak at 267 nm, where as DOM at 285 nm. They also showed an iso-absorptive point at 277.9 nm. FAM and DOM follow Beer-Lambert's law in the range 10-60 μg/ml. By considering the overlain spectra (fig. 1) of both the drugs, two methods were developed, namely simultaneous equation and dual wavelength method.

Two wavelengths selected for the method are 267 nm and 185 nm, which are $\lambda_{max}$ of FAM and DOM respectively. Both the drugs individually in the range 10-60 μg/ml were scanned over 250-330 nm. The absorbances were measured at the selected wavelengths (Table 1) and absorptivities (A 1%, 1 cm) for both the drugs were determined. It was found to be 311 and 127 for FAM, 93 and 270 for DOM at 267 nm and 285 nm respectively. These calculated values were the mean of six independent determinations. Concentrations in the sample were obtained by using following equations, $C_x = A_2.a_{y1} - A_1.a_{y2}/a_{x2}.a_{y1} - a_{x1}.a_{y2}$ (1), $C_y = A_1.a_{x2} - A_2.a_{x1}/a_{x2}.a_{y1} - a_{x1}.a_{y2}$ (2), where $A_1$, $A_2$ are absorbances of mixture at 267 nm ($\lambda_1$) and 285 nm ($\lambda_2$), respectively $a_{x1}$ and $a_{x2}$ are absorptivities of FAM at $\lambda_1$ and $\lambda_2$, respectively, $a_{y1}$ and

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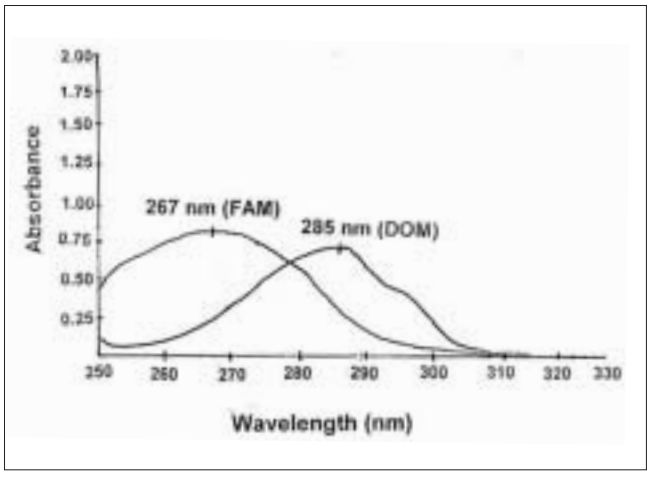


**Fig. 1: Overlain spectra of famotidine and domperidone**

$a_{y2}$ are absorptivities of DOM at $\lambda_{1 \text{ and}} \lambda_{2,}$ respectively, $C_x$ and $C_y$ are concentrations of FAM and DOM, respectively.

For estimation of a drug two such wavelengths were selected where the absorbances of other drug (interfering compound) is similar, so that the absorbance different at these wavelengths were directly proportional to the concentration of that drug. Wavelengths selected for the estimation of FAM were 275 nm, 291.1 nm, for DOM were 275 nm and 257.9 nm. A series of mixed standard solutions were prepared containing equal concentrations of each drug in the range 10-40 µg/ml (Table 1). The calibration curves for FAM and DOM were plotted between absorbance difference values at the selected wavelengths against concentrations.

Twenty tablets (Famodon, Ozone pharmaceutical Ltd., Indore Lable claim- FAM-20 mg and DOM-10 mg) were weighed and finally powdered. Powder equivalent to 20 mg of FAM and 10 mg of DOM were transferred to a 25 ml volumetric flask, to this 10 mg of DOM (standard drug) was added. Solvent was added up to the mark, sonicated for 15 min and filtered through whatman filter paper No 41. Filtrate was further diluted to get concentrations of 10-40 µg/ml of each drug. Absorbances were measured at the selected wavelengths for each method and concentrations of each drug in the formulation were found by using above methods. The results of analysis of tablet dosage form, statistical evaluation and recovery studies are shown in Table 2, 3 and 4, respectively.

The overlain spectra of FAM and DOM in the concentration ratio of 2:1 showed that FAM has interference at the peak of DOM. The criteria for obtaining maximum precision[15], (i.e., absorbance ratio ($a_{y2}$ / $a_{y1}$) ($A_1/A_2$) for FAM and ($A_2/A_1$) / ($A_{x2}$ /$a_{x1}$) for DOM should lie outside the range of 0.1-2.0 was satisfied for FAM but failed for DOM i.e., It was found to be 2.266 for FAM and 1.833 for DOM. Thus standard edition of DOM was done before analysis. This edition not only increases the intensity of the absorbance but also satisfies the minimum criteria for simultaneous equation method and improves the result of the methods.

Simultaneous equation method based on the principle that, the total absorbance of the components in a mixture is the sum of individual absorbances. Two wavelengths selected to frame the simultaneous equation method were 267 nm and 285 nm, since at these two wavelengths; ratio of absorptivities of two components were maximum. This method requires only absorptivities of the two drugs at 267 nm and 285 nm (Table 1). SD obtained from replicate analysis was found to be <0.906 for FAM and <0.600 for DOM, Which indicates the precision of the method and recovery studies lies between 99.5-101.4%, indicating the proposed method is accurate.

**TABLE 1: REGRESSION ANALYSIS OF THE CALIBRATION CURVES**

| Concentration (µg/ml) | Method-1 | | | | Method-2 | |
|---|---|---|---|---|---|---|
| | Famotidine Absorbances at | | Domperidone Absorbances at | | Famotidine $A_{275\text{-}291.1}$* | Domperidone $A_{275\text{-}257.9}$* |
| | 267 nm | 285 nm | 267 nm | 285 nm | | |
| 10 | 0.299 | 0.134 | 0.095 | 0.290 | 0.216 | 0.176 |
| 20 | 0.579 | 0.250 | 0.181 | 0.552 | 0.407 | 0.346 |
| 30 | 0.849 | 0.380 | 0.272 | 0.810 | 0.618 | 0.510 |
| 40 | 1.115 | 0.497 | 0.362 | 1.069 | 0.821 | 0.684 |
| 50 | 1.390 | 0.625 | 0.452 | 1.301 | - | - |
| 60 | 1.654 | 0.741 | 0.541 | 1.577 | - | - |
| Intercept | 0.0180 | 0.0054 | 0.0021 | 0.0209 | 0.0036 | 0.0028 |
| Slope | 0.0274 | 0.0123 | 0.0090 | 0.0260 | 0.0204 | 0.0170 |
| $r^2$ | 0.9997 | 0.9997 | 0.9999 | 0.9994 | 0.9997 | 0.9999 |

Method 1: Simultaneous equation method, Method 2: Dual wavelength method, $r^2$: Correlation coefficients, *Absorbance difference

**TABLE 2: ANALYSIS OF TABLET FORMULATION**

| Method | Batch | Lable claim (mg/ tablet)* | | Amount found (mg/tablet)* | | % of label claim* | |
|---|---|---|---|---|---|---|---|
| | | Famotidine | Domperidone | Famotidine | Domperidone | Famotidine | Domperidone |
| | I | 20 | 20 | 19.947 | 19.802 | 99.735 | 99.010 |
| 1 | II | 20 | 20 | 20.046 | 19.963 | 100.23 | 99.815 |
| | III | 20 | 20 | 19.971 | 20.022 | 99.855 | 100.11 |
| | I | 20 | 20 | 19.952 | 19.884 | 99.762 | 99.420 |
| 2 | II | 20 | 20 | 19.893 | 19.921 | 99.465 | 99.605 |
| | III | 20 | 20 | 20.197 | 20.123 | 100.60 | 100.61 |

*Mean of six readings

**TABLE 3: STATISTICAL EVALUATION**

| Method | Batch | Standard deviation | | Coefficient of variation | | Standard error | |
|---|---|---|---|---|---|---|---|
| | | Famotidine | Domperidone | Famotidine | Domperidone | Famotidine | Domperidone |
| | I | 1.204 | 0.404 | 1.207 | 0.408 | 0.602 | 0.202 |
| 1 | II | 0.652 | 0.871 | 0.651 | 0.871 | 0.326 | 0.435 |
| | III | 0.861 | 0.526 | 0.862 | 0.525 | 0.431 | 0.263 |
| | I | 0.940 | 1.266 | 0.942 | 1.273 | 0.470 | 0.663 |
| 2 | II | 1.135 | 0.976 | 1.141 | 0.980 | 0.567 | 0.488 |
| | III | 1.043 | 1.320 | 1.104 | 1.312 | 0.521 | 0.660 |

**TABLE 4: RECOVERY STUDY DATA**

| Method | Conc. of drug in tablet (µg/ml) | | Conc. added to the tablets sample (µg/ml) | | Amount recovered | | % recovery | |
|---|---|---|---|---|---|---|---|---|
| | FAM | DOM | FAM | DOM | FAM | DOM | FAM | DOM |
| I | 20 | 20 | 5 | 5 | 5.016 | 5.069 | 100.32 | 101.38 |
| | 20 | 20 | 10 | 10 | 10.128 | 9.954 | 101.28 | 99.541 |
| | 20 | 20 | 15 | 15 | 15.069 | 15.061 | 100.24 | 100.41 |
| II | 20 | 20 | 5 | 5 | 4.866 | 4.964 | 98.32 | 99.29 |
| | 20 | 20 | 10 | 10 | 9.856 | 9.837 | 98.56 | 98.37 |
| | 20 | 20 | 15 | 15 | 14.779 | 14.887 | 98.53 | 99.25 |

The principle lying behind dual wavelength method is that, the difference in absorbances is directly proportional to the concentration of the drug. Two wavelengths selected for FAM is 275 nm and 291.1 nm and for DOM 257.9 nm and 275 nm. Two working calibration curved were plotted, that are ($A_{275}$ – $A_{291.1}$) Vs. concentration for FAM and ($A_{275}$ - $A_{257.9}$) Vs. concentration for DOM. By utilizing the values of slope and intercept from the obtained equations, the concentration of FAM and DOM can be estimate in the tablet dosage form. However, this method requires absorbances of three wavelengths. SD obtained from replicate analysis was found to be <1.039 for FAM and <1.187 for DOM, Which indicate the precision of the method and recovery study lies between 98.4-99.3, indicating the accuracy of the proposed method. Both methods are applicable to estimate the amounts of FAM and DOM in the tablet dosage form containing both the drugs. A comparative study of tablet analysis was done (Table 5) and it was concluded that simultaneous equation method is superior. Both the methods were found to be simple, accurate, precise, rapid and economical, hence can be employed for the routine analysis of tablets in pharmaceutical industries.

**TABLE 5: COMPARATIVE STUDY OF RESULTS OF TABLET ANALYSIS**

| Parameters | Famotidine | | Domperidone | |
|---|---|---|---|---|
| | Method 1 | Method 2 | Method 1 | Method 2 |
| S. D.* | 0.906 | 1.039 | 0.600 | 1.187 |
| C.O.V.* | 0.908 | 1.049 | 0.601 | 1.194 |
| S. E.* | 0.453 | 0.520 | 0.300 | 0.593 |
| % recovery | 100.64 | 98.803 | 100.44 | 98.971 |

SD - Standard deviation, COV - Coefficient of variation, SE - Standard error, *Mean of three batches.

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