CHAPTER 5

FOURIER TRANSFORM INFRA RED SPECTROSCOPIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF AND DOMPERIDONE IN PHARMACEUTICAL FORMULATIONS

Introduction:

Lansoprazole is 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl] methylsulfinyl]-1H-benzimidazole, is considered to be a safe and effective inhibitor of gastric acid hypersecretion [Metz DC et al., 1993]. It is being prescribed for ulcers of stomach and duodenum, infections caused by some bacteria along with other drugs, gastroesophageal reflux disease. Lansoprazole 30 mg once daily can relieve heartburn symptoms faster than omeprazole [Joel E Richter et al., 2001]. Domperidone is 6-chloro-3-[1-[3-(2-oxo-3H-benzimidazol-1-yl) propyl]piperidin-4-yl]-1H-benzimidazol-2-one, is an antidopaminergic drug, administered mainly to stop vomiting and nausea [Swann IL et al., 1979]. It is also used in the treatment of gastroparesis, to stimulate lactation, gastroesophageal reflux disease. Lansoprazole also known to enhance antidiabetic effect of sitagliptin and appears to have complementary mechanisms of action [ShaoJun Hao et al., 2014].

The combination of lansoprazole and domperidone is useful in gastroesophagus dysfunctions like functional dyspepsia. Both of these drugs are available individually in pharmaceutical preparations or in combination with other drugs and considered that there is a need for the development of new analytical technique to determine them simultaneously in their pharmaceutical samples provided under several brand names. As a consequence there are methods available in literature for the estimation of each of these drugs either in individual dosage forms or in combination with other drugs. Those
methods for the estimation of lansoprazole in 0.1 N sodium hydroxide include simple UV spectrophotometry and derivative spectroscopic techniques [Ozaltin N, 1999]. RP-HPLC method is available for estimation of in tablet dosage form with UV detection at 285 nm [S. Muthu Kumar et al, 2010]. PV Rao et al. explain the RP UPLC method for the analysis of lansoprazole and its degradation products at 285 nm for its capsule dosage forms [P. Venkata Rao et al., 2013]. The spectrophotometric estimation with colour producing reagents include formation of ion-pair complex with bromocresol purple and bromothymol blue [Okaram Zenita Devi et al., 2013], suprasen violet or tropaeolin [Parimi Uma Devi and Kannajosyula Murali Krishna, 2013]. Another spectrophotometric method involves the concept of oxidation of lansoprazole by bromine, followed by reaction of unreacted bromine with iron(II) to form iron(III) and subsequent colour complex formation either with thiocyanate or with orthophenanthroline [K.Basavaiah et al., 2007]. In another study, lansoprazole was estimated by reaction with metanil yellow or methyl orange, followed by extraction into chloroform [Iffath Rizwana et al, 2014]. Lansoprazole along with domperidone in methanolic sodium hydroxide was analysed simultaneously by spectrophotometry at 287 and 294 nm [Anil Kumar A et al, 2012]. Simultaneous equations were also used for the analysis of lansoprazole in presence of naproxen using UV spectroscopy [Nisha Choudhary et al., 2013]. Similarly domperidone alone and in combination with other drugs was analysed with many other methods such as FTIR [Ravi Prasad P et al., 2012], UV spectroscopy [Sohan S. Chitlange et al., 2010], voltammetry [El Shahawi MS et al., 2006] and HPLC [Maria Kobylinska and Kamila Kobylinska, 2000]. Domperidone with pantaprazole was estimated using RP HPLC [G. Srinivasa Rao et al., 2012]. Simultaneous analysis of domperidone along with
dexabeprazole using HPLC [Sohan S. Chitlange et al., 2010] and by solving simultaneous equations domperidone was determined along with pantaprazole [Swati U. Kalure et al., 2012] and domperidone along with esomeprazole [S. Lakshmana Prabu et al., 2008] using UV spectroscopy have been discussed in literature. A few methods are also available in literature for simultaneous analysis of lansoprazole and domperidone, through UV spectrophotometry [Anil Kumar SM et al., 2013, A.V. Kasture et al., 2007], HPTLC [M. Viyey Aanandhi et al., 2009] and HPLC [Shoyeb Ahmed and R. Vani, 2015, Bhavna Patel et al., 2009]. FTIR spectroscopy is considered to be a useful, sensitive, specific and robust tool for the analysis and quantification of drug molecules [Patel Rakesh et al., 2014]. FTIR analysis was applied for the estimation of lorazepam [Elaheh Konoz et al., 2012] and in estimation of ibuprofen [S.R. Matkovic et al., 2005] after extracting it into chloroform. Ciprofloxacin was extracted with methanol [S. Pandey et al., 2012] and erythromycin was estimated without any extraction into organic solvent [M. Ali et al., 2014]. FTIR technique was also used for simultaneous analysis of paracetamol and domperidone [Ravi Prasad P. et al., 2012], omeprazole and domperidone [Ravi Prasad P. et al., 2014] even in the presence of excipients by dispersion in potassium bromide. However, there appears to be no FTIR spectroscopic method for the simultaneous quantification of lansoprazole and domperidone, although it is used in their individual determinations as cited above. Lansaprazole was found to be degrading both in acidic and basic solutions forming many impurities [S. Battu and V.Pottabathini, 2015] which were interfering in its determination in aqueous medium. It is therefore in the present work powder dispersions of lansoprazole and domperidone in KBr were used for the determination of lansoprazole and domperidone were carried out individually as well
as simultaneously by FTIR method. Also, method is considered to be environmental friendly as no harmful solvent like chloroform is used either for extraction or sample preparation. The results obtained for the samples from this new method were compared with those of lansoprazole and domperidone determined separately in this work through UV spectrophotometric method adopted from the literature [Anil Kumar SM et al., 2012]. Considering the importance of lansoprazole and domperidone from this literature survey and noting certain limitations with methods available for these an attempt is through this work to develop environmental friendly procedures involved new FTIR spectroscopic method for their individual and simultaneous estimations.

**Experimental:**

**Materials and Methods:**

Nicolet iZ 10 FTIR spectrometer (Thermo Scientific, USA) with DTGS detector and Omni Smart Transmission accessory was used to record the FTIR spectra. Using Omnic software, spectra of the samples were acquired and processed. Double Beam UV-Vis Spectrophotometer, model Spectrascan UV 2600 (Chemito, Chennai, India) was used to record UV spectra of the samples. Pure drug samples of lansoprazole and domperidone were obtained as gift samples from Microlabs, Bangalore. Potassium bromide was of spectroscopic grade which was further dried before using it for the sample dispersion and other reagents used were of analytical grade. Pharmaceutical samples of Lansoft DM (15 mg Lans + 5 mg Dom), Lanspro-D (30 mg Lans+30 mg Dom), Lansol (15 mg Lans), Lansol (30 mg Lans), Domstal (20 mg Dom) and Vomistop (10 mg Dom) were purchased from local market.
Preparation of standards and samples for FTIR for calibration:

0.1 g of pure samples of lansoprazole or domperidone and 4.9 g KBr were weighed separately and transferred them into an agate mortar provided with pestle. The mixture was homogenized by grinding the samples together so as to get 20000 mg/Kg, 20000 ppm (w/w) dispersions of each. 0.1 g of this mixture was further dispersed in 4.9 g KBr which is corresponding to 400 ppm (w/w) of each drug sample. It was considered as a standard solid solution of the drug samples. 1 g of this was diluted with 8 g with KBr for obtaining their 50 ppm solid dispersions. A known weight corresponding to 400 ppm and 50 ppm drug standard solid dispersions were further diluted in appropriately weighed amounts of KBr or used them as such for obtaining the drug concentrations in the range 5 to 400 ppm.

Preparation of binary mixture for their simultaneous analysis:

A series of 3:1 ratio synthetic mixture containing lansoprazole and domperidone were ground with KBr to get dispersions, 30:10, 60:20, 90:30, 120:40 and 150:50 ppm respectively corresponding to the lansaprazole linearity range and 120:40, 150:50, 180:60, 210:70 and 240:80 ppm respectively corresponding to the domperidone linear range that were prepared from standard stock dispersions in obtaining calibration graphs. Similarly, series of dispersions from 1:1 ratio binary synthetic mixture containing lansoprazole and domperidone, 10:10, 20:20, 30:30, 40:40 and 50:50 ppm corresponding to linearity range of lansoprazole and 40:40, 50:50, 60:60, 70:70 and 80:80 ppm corresponding to the established linear range for domperidone were prepared. Measurements were made after homogenizing the sample, followed by pellet preparation
and corresponding peak area measurement. Calibration graphs were plotted and from their regression equations the drug contents were determined.

**Preparation of pharmaceutical samples for formulation analysis:**

10 tablets from each pharmaceutical preparation were weighed, ground to a fine powder and a quantity equivalent to concentration in calibration range was dispersed in spectral grade dried KBr.

**Procedure for pellet preparation for FTIR measurements:**

Quantification measurements using compression discs suffer from errors arising due to transferring of discs to the sample compartment and variation in disc thickness [G.H. Jeffery et al., 1989]. To overcome this, each time, 25 mg of dispersed pure samples or formulation samples were weighed accurately into nuts, fixed with anvils, compressed using wrenches [James W. Robinson et al., 2014], left aside for 15 minutes and then nut was kept in sample holder inside the FTIR transmission accessory directly, without removing from the die. Using OMNIC software, spectrum was recorded in the range 400-4000 cm⁻¹. Before running dispersed samples and standards, background was collected with KBr pellet each time. After acquiring spectrum of each sample it was subjected to autosmooth to remove noise, and multiplied it with factor 1000.

**Preparation of standards and samples for UV spectroscopic analysis:**

Dispersions containing 1000 ppm each of lansoprazole and domperidone were prepared separately in methanol and 0.1 N sodium hydroxide mixture in the ratio 70:30. Suitable concentrations of 2–18 ppm dispersions of lansoprazole and 4–36 ppm of domperidone were further prepared and analyzed with UV spectrophotometer by scanning them between 200–400 nm. Pharmaceutical samples containing lansoprazole
and domperidone were powdered and sonicated and dissolved in methanolic sodium hydroxide, filtered and made upto appropriate concentrations with the same solvent. The results of the new method were compared with the UV spectroscopic method [Anil Kumar SM et al., 2012] by measuring absorbances of binary mixture for lansoprazole at 294 nm and for domperidone at 287 nm respectively and were calculated by solving simultaneous equations.

**Results and discussion:**

**Measurements done using UV spectrophotometric analysis:**

Apart from chromatographic techniques, UV and FTIR spectroscopic methods are common for organic compound analysis. In UV spectroscopic simultaneous estimation of binary mixtures, simultaneous equations were solved to obtain the concentration of each component as in the following mixtures, domperidone at 286.5 nm and dexabeprazole at 258.5 nm [Sohan S. Chitlange et al, 2010], domperidone at 284 nm and esomeprozole at 301 nm [S. Lakshmana Prabu et al., 2008], paracetamol at 250 nm and domperidone at 285 nm [Kalra Kapil et al., 2009], lansoprazole at 284 nm and naproxen at 271 nm [Nisha Choudhary et al., 2013], where the peaks were well separated. But, for simultaneous estimation of lansoprazole and domperidone using UV spectroscopy [Anil Kumar SM et al, 2012, A.V. Kasture et al., 2007], the spectra were at very close wavelengths as shown in Fig. 1.
Further, the aqueous solution of lansoprazole either in acid or in basic medium undergoes hydrolytic degradation [S. Battu and V. Pottabathini, 2015] at elevated temperature. This was observed even in this study as the methonolic solution of lansoprazole turns to brown colour even if it was stored in the refrigerator at 50° C. However, as a reference method for simultaneous assay, UV spectrophotometric method was used [Anil Kumar SM et al., 2012] by solving simultaneous equations as no other spectroscopic method was available for simultaneous analysis of both. Pure standards of lansoprazole (2-10 ppm), domperidone (4-20 ppm), 1:1 and 3:1 binary mixtures containing both, were prepared and absorbances were measured at 294 nm and 287 nm. Overlaid spectra of binary mixture solutions of lansoprazole and domperidone in the ratio 1:1 with different concentrations used for the assay and are shown in Fig. 2.

Fig. 1: UV spectra of [A]: 50 ppm solution of lansoprazole with λmax=294 nm, [B]: 80 ppm domperidone with λmax=287 nm and [C]: 50 ppm solution of lansoprazole and domperidone mixed in 1:1 ratio with λmax=287 nm
Fig. 2: Overlaid spectra of binary solutions of lansoprazole and domperidone in the ratio 1:1, corresponding to concentration of (a) 4:4 ppm (b) 8:8 ppm (c) 12:12 ppm (d) 16:16 ppm and (e) 20:20 ppm and sample spectra are not marked.

The molar extinction coefficients were calculated by plotting graphs involving absorbance values and concentrations in millimolar units at 294 nm for lansoprazole and at 287 nm for domperidone and corresponding to respective absorbance values that were measured in the specified range are indicated in Fig. 3 and 4.

Fig. 3: Calibration plot of lansoprazole used for calculation of molar extinction coefficient at 294 nm (■) and at 287 nm (x) for the solutions in the concentration range 0.0054 mM – 0.027 mM corresponding to 2 – 10 ppm solution.
**Fig. 4**: Calibration plot of domperidone used for calculation of molar extinction coefficient at 294 nm (■) and at 287 nm (x) for the solutions in the concentration range 0.0094 mM – 0.047 mM corresponding to 4 – 20 ppm solution.

The molar extinction coefficient values of lansoprazole and domperidone obtained from the graphs which were used in the simultaneous calculation of binary mixtures were; $E_{\text{Lans294}}=2.807\times10^4$, $E_{\text{Lans287}}=2.042\times10^4$, $E_{\text{Dom294}}=1.403\times10^4$ and $E_{\text{Dom287}}=1.134\times10^4$ respectively.

Concentrations of unknown samples in pharmaceutical preparations were calculated simultaneously ($C_{\text{Dom}}$ and $C_{\text{Lans}}$) from the following equations by measuring absorbance values of both lansoprazole and domperidone at two wavelengths 294 and 287 nm respectively ($A_{\text{mix294}}$ and $A_{\text{mix287}}$)

$$C_{\text{Dom}} = \frac{A_{\text{mix294}} \times E_{\text{Lans287}} - A_{\text{mix287}} \times E_{\text{Lans294}}}{E_{\text{Dom287}} \times E_{\text{Lans287}} - E_{\text{Lans294}} \times E_{\text{Dom287}}}$$

$$C_{\text{Lans}} = \frac{A_{\text{mix294}} \times E_{\text{Dom287}} - A_{\text{mix287}} \times E_{\text{Dom294}}}{E_{\text{Dom287}} \times E_{\text{Lans294}} - E_{\text{Lans287}} \times E_{\text{Dom294}}}$$

The values obtained by these measurements were compared with those of FTIR analyses and are shown in Table 5.
Measurements done using FTIR spectrometric analysis:

FTIR spectroscopy helps in understanding different functional groups present in a compound with the help of peaks and using these peaks, even some of the properties of material can be accessed [Rai Muhammad Amir et al., 2013]. Knowing the importance of FTIR spectroscopy for making analysis in the fields of food and agriculture, environmental, pharmaceutical, petroleum, polymer [Patel Rakesh et al., 2014] have inspired us to develop an approach for simultaneous drug analysis. Further, multicomponent analysis using FTIR method produces eco friendly and straightforward results in many drug analysis [Ravi Prasad P et al., 2012, Ravi Prasad P. et al., 2014, Muhammad Ali Mallah et al., 2012], which was extended to our study also and as such in the new FTIR method does not involve solving simultaneous equations.

Selection of the peaks for the purpose of quantification using FTIR spectrometer:

FTIR spectroscopic technique is very useful as it gives distinct and unique peaks if the molecules are different [Peter R. Griffiths and James A. De Haseth, 2007]. Like other spectroscopic techniques, if no interference from other substances happen, then quantitative analysis can be made by measuring intensity at specific wavelength and Beer Lambert relationship holds good [G.H. Jeffery et al., 1989]. The extended idea of these works was used for simultaneous quantification of lansoprazole and domperidone due to unique functional groups present in lansoprazole and domperidone. Both are benzimidazole derivatives but with different functional groups as in Fig. 5 and the spectra of the samples were having significant, distinct and non overlapping peaks, Fig. 6.
Fig. 5: Structure of lansoprazole [A] and domperidone [B] showing different functional groups attached to produce distinguishable and non overlapping IR peaks.

Lansoprazole has a strong peaks at 1173 cm\(^{-1}\) corresponding to ether group (C–O–C), peak arising due to C–F bond stretching at 1117 cm\(^{-1}\), sulphoxide group stretching (S=O) at 1039 cm\(^{-1}\), C–S bond stretching at 750 cm\(^{-1}\) [Barbara H. Stuart, 2004]. Similarly, domperidone has a unique and strong absorption peak at 1687 cm\(^{-1}\) due to carbonyl amide stretch (C=O) which is not found in lansoprazole. Other than carbonyl stretching frequency, some more peaks are prominent at 860 cm\(^{-1}\) due stretching vibration of C–Cl, at 1485 cm\(^{-1}\) due to C–H bending vibrations, at 1267 cm\(^{-1}\) due to C–N stretching and at 747 cm\(^{-1}\) due to CH\(_2\) rocking in methylene chain vibrations [Brian C. Smith, 2002]. However, for the quantification of lansoprazole and domperidone simultaneously, peak at 1173 cm\(^{-1}\) corresponding to ether group for lansoprazole and peak at 1687 cm\(^{-1}\) corresponding to carbonyl group for domperidone were selected, Fig. 3. Even in the mixture of lansoprazole and domperidone, the said two peaks appear very sharp, strong and can be easily distinguished. Aromatic stretching and out of plane bending vibrations occurring at 690-900 cm\(^{-1}\) and 3050-1150 cm\(^{-1}\) are not strong and well defined. Since both these drugs have aromatic C–H bonds, secondary N–H groups in common, the peaks arising by these vibrations are common to both and are not taken for analysis. Aromatic out of plane deformations of aromatic group also produce peaks in the range 680 - 785 cm\(^{-1}\), which is seen in domperidone also at 747 cm\(^{-1}\). But peak
located at 750 cm$^{-1}$ was assigned for C-S bond stretching because in the binary mixture, even though, both contain aromatic group but peak due to C-S was more prominent.

![FTIR spectrum](image.png)

**Fig. 6**: FTIR spectrum for A: 200 ppm of lansoprazole in KBr, B: 300 ppm domperidone in KBr and C: 1:1 mixture of 200 ppm each of lansoprazole and domperidone in KBr scanned between 400 to 4000 cm$^{-1}$

In the spectrum of binary mixture, peaks of lansoprazole were well defined and no shift in wave numbers was observed. But in the spectrum of binary mixture, peaks due to domperidone were shifted by about 4-5 cm$^{-1}$ when compared to spectrum of pure
compounds. The choice of peaks selected in the new method was confirmed by measuring the areas of selected peaks at different wave numbers which give highest value of regression coefficient when measured with different ratios of lansoprazole and domperidone as indicated by the results in Table 1.

**Table 1:** Regression values measured by plotting calibration graphs for different peaks with different ratios of lansoprazole and domperidone

<table>
<thead>
<tr>
<th>Peak (cm⁻¹)</th>
<th>Peak assigned to the group</th>
<th>Regression values of mixture of lansoprazole and domperidone in the ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1173</td>
<td>C–O–C stretch in Lans</td>
<td>0.9990 0.9986 0.9957 0.9966 0.9984 0.9977</td>
</tr>
<tr>
<td>1039</td>
<td>S=O stretch in Lans</td>
<td>0.9984 0.9863 0.9880 0.9904 0.9982 0.9923</td>
</tr>
<tr>
<td>1267</td>
<td>C=N stretch in Lans</td>
<td>0.9942 0.9865 0.9781 0.9947 0.9714 0.9850</td>
</tr>
<tr>
<td>1579</td>
<td>Pyridine ring stretch in Lans</td>
<td>0.9885 0.9740 0.9908 0.9990 0.9861 0.9877</td>
</tr>
<tr>
<td>1117</td>
<td>C–F stretch in Lans</td>
<td>0.9994 0.9845 0.9928 0.9878 0.9951 0.9919</td>
</tr>
<tr>
<td>750</td>
<td>C–S stretch in Lans</td>
<td>0.9588 0.9902 0.9841 0.9922 0.9835 0.9818</td>
</tr>
<tr>
<td>1687</td>
<td>C=O stretch of amide group in Dom</td>
<td>0.9984 0.9881 0.9843 0.9972 0.9981 0.9932</td>
</tr>
<tr>
<td>860</td>
<td>C–Cl stretch in Dom</td>
<td>0.9975 0.9893 0.9922 0.9844 0.9990 0.9925</td>
</tr>
<tr>
<td>1485</td>
<td>Benzene ring stretch in Dom</td>
<td>0.9899 0.9875 0.9901 0.9752 0.9844 0.9854</td>
</tr>
<tr>
<td>1622</td>
<td>N–H in amides in Dom</td>
<td>0.9758 0.9841 0.9848 0.9842 0.9887 0.9835</td>
</tr>
<tr>
<td>792</td>
<td>Aromatic out-of-plane deformations in Dom</td>
<td>0.9845 0.9788 0.9866 0.9978 0.9989 0.9893</td>
</tr>
</tbody>
</table>

**Optimization of FTIR spectral conditions:**

**Scan speed & Resolution:** Resolution is the ability to resolve the peaks into distinguishable components and in FTIR instrument this was achieved using the aperture size. Resolution was varied between the intervals of 0.06-3.85 cm⁻¹. After resolving the peaks, aperture size was set to 4 corresponding to a resolution of 0.482 cm⁻¹ for all the measurements which gave net and sharp peaks.

**Number of scans:** Weak signals can be intensified with increasing the number of scans, the values can be set by choosing 1, 8, 16, 32 and 64. More number of scans gave better...
defined peaks, however an optimum of 16 scans was set for all the measurements to get well defined peaks and speedy results.

**Selection of area or height:** Using Omnic software, it was possible to calculate both peak height and peak area of each peak in the acquired spectrum. Peak height measurement gives absorbance at peak top only whereas peak area measurements give absorbances of many different data points in the same peak [Brian C. Smith, 2002]. Since there is a shift of 1-5 cm\(^{-1}\) wave numbers corresponding to sample and standards in the binary mixture, peak height measurements gave higher values of RSDs and less recovery values compared to peak area values. Therefore, area under peak (AUP) was measured for linearity, accuracy, precision and all other calculations.

**Analytical parameters:**

**Linearity:** Linearity of lansoprazole was assessed by taking average of three replicates for the peak at 1173 cm\(^{-1}\) for the spectra obtained in the concentration range 10-200 ppm. Similarly, domperidone was linear in the range 40-300 ppm and this was assessed by taking the average of peak area at 1687 cm\(^{-1}\). The overlaid spectra for peak area calculation to determine the linearity of lansoprazole is shown in Fig. 7 and corresponding regression line in Fig. 9 and the analytical parameters are given in Table 1. Similarly the overlaid spectra for peak area calculations and to determine the linearity of domperidone are shown in Fig. 8 and the corresponding regression line in Fig. 10.

**Limit of Detection and Quantification:** The LOD is deduced by measuring the area (M) of the analyte signal at minimum concentration of the analyte (C) beyond which the analyte signal disappears [Muhammad Ali Mallah et al., 2012]. This was performed in six replicates and the standard deviation (SD) was calculated.
LOD = 3 x SD x C/M

Similarly LOQ was deduced using the equation,

LOQ = 10 x SD x C/M

**Fig. 7:** Overlaid spectra of lansoprazole standards in absorbance mode of 10-200 ppm concentrations and used for the calculation of linearity, showing Area Selection tool and the top spectrum marked as A is corresponding to tablet dispersion in KBr.

**Fig. 9:** Overlaid spectra of domperidone standards in absorbance mode of 40-300 ppm concentrations and used for the calculation of linearity, showing Area Selection tool and the top spectrum marked as A is corresponding to sample.
**Fig. 8:** Calibration curve for lansoprazole in the range 10-200 ppm (w/w) in KBr showing regression equation and regression coefficient

**Fig. 10:** Calibration curve for domperidone in the range 25-300 ppm (w/w) in KBr showing regression equation and regression coefficient

**Table 2:** Analytical parameters for individual estimation of lansoprazole and domperidone after KBr dispersion

<table>
<thead>
<tr>
<th>Analytical parameter</th>
<th>Lansoprazole</th>
<th>Domperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection wavenumber</td>
<td>1173 cm(^{-1})</td>
<td>1687 cm(^{-1})</td>
</tr>
<tr>
<td>Linear range</td>
<td>10-200 ppm, w/w</td>
<td>25-300 ppm, w/w</td>
</tr>
<tr>
<td>Regression equation</td>
<td>(y = 2.353x + 13.25)</td>
<td>(y = 2.137x + 40.17)</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>(R^2 = 0.999)</td>
<td>(R^2 = 0.998)</td>
</tr>
<tr>
<td>LOD</td>
<td>2.240 ppm</td>
<td>5.910 ppm</td>
</tr>
<tr>
<td>LOQ</td>
<td>7.410 ppm</td>
<td>19.510 ppm</td>
</tr>
</tbody>
</table>
**Precision:** Repeatability of the proposed method was evaluated at three levels by preparing each sample six times and recording the spectra. In the absorbance mode, area under the curve at 1173 cm\(^{-1}\) for lansoprazole and at 1687 cm\(^{-1}\) for domperidone were recorded using regression equation, concentration was calculated and % RSD was deduced. Reproducibility of the method was evaluated similarly, preparing samples having three different concentrations in the linearity range using the regression equations for five successive days. Area under peak was measured and concentration was determined. The values are tabulated in Table 2. The intraday precision value of 0.361 for lansoprazole and 0.581 for domperidone are showing that the analysis is highly reproducible. By using the same procedure, the experiment was repeated with samples stored under dry conditions after three months and still the %RSD was found to be 1.652 for lansoprazole and 1.952 for domperidone, indicating the high reproducibility of the method.

**Table 3:** Repeatability and reproducibility data of Lansoprazole and Domperidone.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Actual concentration (ppm)</th>
<th>Intra-day precision</th>
<th>Inter-day precision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Measured concentration (ppm) (^a)</td>
<td>% RSD</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>10</td>
<td>9.94</td>
<td>0.367</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>59.36</td>
<td>0.099</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>119.58</td>
<td>0.619</td>
</tr>
<tr>
<td>Domperidone</td>
<td>25</td>
<td>25.14</td>
<td>0.655</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100.26</td>
<td>0.280</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>199.85</td>
<td>0.810</td>
</tr>
</tbody>
</table>

\(^a\) – average of five determinations on the same day at different times  
\(^b\) – average of five determination on five successive days

**Accuracy:** The interference of excipients was assessed using the recovery studies by adding the drug to the preanalysed samples of 50 ppm each of lansoprazole and domperidone at 80, 100 and 120% levels. The results obtained are tabulated in Table 4.
There was no interference by the common excipients present in tablet formulations for the determination of lansoprazole at 1173 cm$^{-1}$ and domperidone at 1687 cm$^{-1}$.

**Table 4**: Recovery studies of lansoprazole and domperidone at three concentration levels.

<table>
<thead>
<tr>
<th>Drug</th>
<th>% level of excess drug added to 50 ppm</th>
<th>Amount added (mg)</th>
<th>Total amount (ppm)</th>
<th>Amount recovered (ppm)$^a$</th>
<th>% recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lansoprazole</td>
<td>80</td>
<td>40</td>
<td>90</td>
<td>89.62</td>
<td>99.57</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>50</td>
<td>100</td>
<td>98.85</td>
<td>98.85</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>60</td>
<td>110</td>
<td>110.42</td>
<td>100.38</td>
</tr>
<tr>
<td>Domperidone</td>
<td>80</td>
<td>40</td>
<td>90</td>
<td>90.87</td>
<td>100.96</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>50</td>
<td>100</td>
<td>98.25</td>
<td>98.25</td>
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<tr>
<td></td>
<td>120</td>
<td>60</td>
<td>110</td>
<td>111.23</td>
<td>101.11</td>
</tr>
</tbody>
</table>

$^a$ – average of three determinations

Quantification of lansoprazole and domperidone in tablet formulations using standard and synthetic mixtures:

For the analysis of single drug containing commercial formulations of lansoprazole and domperidone, Lansol 15 mg, Lansol 30 mg, Domstal 20 mg and Vomistop 10 mg, the regression equation obtained during linearity analysis was used. For the analysis of Lansoft DM (label claim of 15 mg Lans and 5 mg Dom), the prepared synthetic mixture in the ration 3:1 of lansoprazole and domperidone, was dispersed in KBr to get five standards corresponding to concentration range 10-50 ppm of lansoprazole and 60-100 ppm of domperidone. The spectrum was acquired three times for each one of five concentrations of lansoprazole and five concentrations of domperidone. Area under the curves were used for constructing two calibration curves for lansoprazole and domperidone and were used to evaluate the drug content.

Similarly, for the analysis of Lanspro-D (label claim of 30 mg Lans and 30 mg Dom), a 1:1 synthetic mixture was prepared corresponding to concentration range of lansoprazole (10-50 ppm) and concentration range of domperidone (60-100 ppm) were
prepared and using regression equation, drug content was calculated [Ravi Prasad P et al., 2012, Ravi Prasad P et al., 2014]. The results were summarized in Table 5. The results obtained by FTIR and UV spectroscopic methods were comparable; however, the precision values were high in case of FTIR analysis.

Table 5: Individual and simultaneous quantification of lansoprazole and domperidone in pharmaceutical preparations.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Label claim (mg)</th>
<th>Using FTIR spectroscopic method</th>
<th>Using UV spectroscopic method [13]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Amount found (mg)</td>
<td>% Assay</td>
</tr>
<tr>
<td>Tablet 1</td>
<td>15 Lans</td>
<td>14.86</td>
<td>99.06</td>
</tr>
<tr>
<td>Tablet 2</td>
<td>30 Lans</td>
<td>29.76</td>
<td>99.20</td>
</tr>
<tr>
<td>Tablet 3</td>
<td>20 Dom</td>
<td>19.24</td>
<td>98.20</td>
</tr>
<tr>
<td>Tablet 4</td>
<td>10 Dom</td>
<td>9.74</td>
<td>97.44</td>
</tr>
<tr>
<td>Tablet 5</td>
<td>15 Lans</td>
<td>14.95</td>
<td>99.66</td>
</tr>
<tr>
<td>Tablet 5</td>
<td>5 Dom</td>
<td>4.84</td>
<td>96.80</td>
</tr>
<tr>
<td>Tablet 6</td>
<td>30 Lans</td>
<td>29.53</td>
<td>98.43</td>
</tr>
<tr>
<td>Tablet 6</td>
<td>30 Dom</td>
<td>29.64</td>
<td>98.80</td>
</tr>
</tbody>
</table>

a and b – average of three determinations with FTIR and UV spec methods

Conclusion:

The proposed method indicates that the applicability of FTIR spectroscopy is not limited only for qualitative analysis and single drug formulations [Ravi Prasad P. et al., 2012, Elaheh Konoz et al., 2012, S.R. Matkovic et al., 2005, S. Pandey et al., 2012, M. Ali et al., 2014], but can be extended to simultaneous quantitative analysis of two or more drugs whenever two compounds with different functional groups produce distinguishable and non-overlapping IR peaks. The selection of the peaks for quantification for lansoprazole at 1173 cm\(^{-1}\) and 1687 cm\(^{-1}\) for domperidone were statistically proven by evaluation of regression coefficient values by choosing different peaks in the binary mixture. Results of assay of the pharmaceutical samples by new method, when compared to the determined using the literature UV spectroscopic method [Anil Kumar SM et
al., 2012], the FTIR method is found to be highly precise with average %RSD not more than 0.83 and also there was no positive error in the determination. The new FTIR method for estimation of lansoprazole and domperidone is very simple in view of sample preparation, eco friendly as no organic solvents were used [Elaheh Knoz et al., 2012, S.R. Matkovic et al., 2005, M. Ali et al., 2014] and has added advantage of preserving of the prepared standards and samples without any changes over six months under dry conditions. The method is highly reproducible, precise and accurate and it can be used for simultaneous as well as separate quantification of lansoprazole and domperidone in pharmaceutical industries.
Summary:

A simple, rapid and specific method is developed for the first time using transmission FTIR spectroscopy to estimate lansoprazole and Domperidone in their pure and combined dosage forms. Quantifications were carried out using weighed quantities of dispersed drug samples in potassium bromide pellets. Areas of the peaks at 1173 cm$^{-1}$ (C–O–C stretch) for lansoprazole and at 1687 cm$^{-1}$ (C=O stretch in amide) for domperidone in their FTIR spectra were found to be linearly proportional to their respective concentrations and quantifications were performed at those peaks. Analytical parameters namely linearity, precision, accuracy and recovery were established and the method was found to be highly precise with %RSD=0.361 for lansoprazole and %RSD=0.581 for domperidone respectively.
References:


