Structural and Qualitative Analysis of Lamotrigine

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Abstract

In the present study, the change in the quality of lamotrigine that falls under antiepileptic group at various storage conditions has been studied by FTIR and UV spectroscopic technique. The indications from the result emphasizes that it is essential to store the drugs under the prescribed condition to maintain their quality. The Vibrational spectral analysis also been carried out by employing FTIR, FT-Raman spectroscopy.

Keyword: Lamotrigine; FTIR; FT –Raman; UV spectroscopy

Introduction

A drug is a substance used in diagnosis, treatment or prevention of a disease or as a component of a medication used as a medicine which kills or inactivates germs that affects body function or origin. World health organization states epilepsy as the third most common neurological disease in the world after Alzheimer’s and Stroke. Taking this factor a detailed study on qualitative analysis using FTIR and UV spectroscopy and structural analysis using FTIR and FT Raman spectroscopy and has been carried on lamotrigine an antiepileptic drug chemically known as 6-(2, 3-dichlorophenyl)-1 2,4-triazine-3,5-diamine with a molecular formula C9H7Cl2N5. To investigate the structure and analysis of pharmaceutical active compounds spectroscopic techniques have been widely used in the recent past. Gunasekaran et al. [1-8] have done the qualitative analysis and structural confirmation on drugs using FTIR and UV spectroscopy.

Experimental

The spectroscopically pure grade sample of lamotrigine was purchased from a reputed Pharmaceutical company, Chennai, India and was used as such for the spectral measurements. FTIR spectrum of lamotrigine has been recorded in the range 4000 - 450 cm−1 in the solid state by adopting the KBr pellet technique and FT-Raman spectrum has been recorded in the range 4000 - 50 cm−1 using laser wave number 15,798 cm-1 as excitation sources on a computer interfaced BRUKER IFS 66V model Interferometer at IITM, Chennai. UV spectral measurements have been made using Cary SE –UV-VIS spectrophotometer in the wavelength region 200-400 nm at IIT, Chennai. All sharp bands observed in the spectra are expected to have an accuracy of ±1cm-1.

Result and Discussion

Vibrational assignment

Infrared and Raman spectra contain a number of bands at specific wave numbers. The aim of the vibrational analysis is to decide which of the vibrational modes give rise to each of these observed bands. The molecule lamotrigine has 23 atoms and possess Cs symmetry configuration. The molecular structure of lamotrigine is shown in Figure 1. The assignments for the fundamental modes of vibrations have been made on the basis of the position shape and intensity. The FTIR and FT- Raman spectra of lamotrigine were shown in Figures 2 and 3. The observed FTIR and FT-Raman frequencies for selected modes of vibrations for lamotrigine are presented in Table 1.

Figure 1: Molecular structure of lamotrigine.

Figure 2: FTIR Spectrum of lamotrigine.
Aromatic Deformation

CNC Stretching + NH

-1

C-Cl Stretching + C-N Stretching

-1

C-C Stretching
C-Cl Stretching + NH

C-H Asym. Stretching

1463

CC Stretching + C=N Stretching

NH

Aromatic Breathing + NH

-1

C-C Twisting

1434

C-H Asym. Stretching

3236

C-H Sym. Stretching

3589

NH\textsubscript{2} Symmetric Stretching

3672

NH\textsubscript{2} Symmetric Stretching

3704

NH\textsubscript{2} Asymmetric Stretching

3741

NH\textsubscript{2} Asymmetric Stretching


\textbf{Table 1:} Vibrational assignment for lamotrigine.

\textbf{NH\textsubscript{2} Group vibrations}

The \(\text{NH}\textsubscript{2}\) groups in the sample under investigation give rise to two symmetric and two asymmetric stretching vibrations. The frequency of asymmetric vibration is higher than that of symmetric one. It has frequency range of 3300 cm\(^{-1}\) to 3700 cm\(^{-1}\) [9]. In addition, \(\text{NH}\textsubscript{2}\) group has scissoring, rocking, wagging modes. The \(\text{NH}\textsubscript{2}\) scissoring mode has been suggested to lie in the region 1550 cm\(^{-1}\) to 1650 cm\(^{-1}\). In the present work \(\text{NH}\textsubscript{2}\) scissoring band occurs at 1531, 1584, 1621, 1642 cm\(^{-1}\) in the FTIR spectrum and at 1557, 1584, 1639 cm\(^{-1}\) in FT-Raman spectrum. Similarly \(\text{NH}\textsubscript{2}\) rocking vibration occurs at 1142 cm\(^{-1}\) in the FTIR and FT-Raman spectrum respectively. \(\text{NH}\textsubscript{2}\) twisting vibration occurs at 571 cm\(^{-1}\) and corresponding Raman band is observed at 571 cm\(^{-1}\).

\textbf{C-Cl Vibrations}

The C-Cl stretching vibrations give generally strong bands in the region 710-505 cm\(^{-1}\) [10]. Compounds with more than one chlorine atom exhibit very strong bands due to the asymmetric and symmetric stretching modes. Hence in the present investigation the bands at 578,624,717,738 cm\(^{-1}\) in FTIR spectrum and 571 cm\(^{-1}\) in the FT-Raman spectrum are assigned to the C-Cl stretching Vibrational mode. The band at 210 cm\(^{-1}\) in the FT-Raman spectrum corresponds to the C-Cl scissoring mode.

\textbf{C=N vibrations}

The ring C=N stretching vibrations [11] occur in the region 1645-1575 cm\(^{-1}\).S. Gunasekaran and Leela Abraham [12] have observed the C=N stretching band at 1612 cm\(^{-1}\) in benzocaine. Referring to the above assignments the bands at 1531, 1584 and 1642 cm\(^{-1}\) in FTIR and 1557, 1584 cm\(^{-1}\) in FT Raman spectrum in lamotrigine are assigned to C=N symmetric and asymmetric stretching vibrations respectively.

\textbf{Aromatic vibrations}

The aromatic C-H stretching vibrations generally appear in the region 3000-3250 cm\(^{-1}\) in substituted benzenes [13]. Many researchers reported the C-H stretching frequency for the benzene derivatives are in this region. Considering this, in the present case, the bands at 3204, 3212 cm\(^{-1}\) in FTIR and 3230 cm\(^{-1}\) in FT Raman are assigned to C-H asymmetric stretching vibrations in lamotrigine. The bands observed at3236 cm\(^{-1}\) in FTIR and 3251 cm\(^{-1}\) in FT Raman are assigned to C-H symmetric stretching for the same molecule. The Vibrational bands at 1142 cm\(^{-1}\) corresponds to aromatic breathing and1052 cm\(^{-1}\) and 1054 cm\(^{-1}\) are assigned to aromatic C-H in plane bending in FTIR and FT Raman spectrum respectively. The band at 1221 cm\(^{-1}\) in the FTIR spectrum corresponds to aromatic deformation.

\textbf{Qualitative analysis}

Drug quality is a source of great concern worldwide as pharmaceutical products plays an important role in improving the health and promoting the well being of every individual. Use of poor quality drugs has serious health implications and wasted resources. Temperature is one of the important environmental parameter that plays a key role in maintaining the drug quality. Drug must be stored, handled and transported according to predetermined conditions as supported by stability data. Drugs which are not stored under the recommended temperature conditions might degrade even prior to the expiration date. Among the various methods for the analysis, spectroscopic techniques are a predominant tool used to analyze the quality of drugs under different storage conditions. In the present work FTIR and UV spectroscopic methods have been applied to check the nature and the quality of the drug sample lamotrigine when it is exposed to sunlight, ice point etc.

The FTIR overlay spectra and the corresponding absorbance of the drug have been recorded when stored under prescribed condition as per the guidelines of Indian Pharmacopeia, exposed to sunlight (50°
C) and maintained at ice point (0°C) and are presented in Figure 4 and Table 2 which clearly indicates change in the absorbance values with change in storage condition.

The internal standard ratio is calculated among the various absorption modes of vibration of the drug and the results are tabulated in Table 3. The internal standard ratios evaluated clearly shows the deterioration in the quality of the sample due to alteration in the storage conditions.

The result obtained by FTIR study has been confirmed by UV spectral studies. The UV spectrum of the sample in pure form and at different storage conditions has been recorded to identify the variation in the wavelength maximum (\(\lambda_{\text{max}}\)) and is tabulated in Table 4. The UV spectrum of lamotrigine at different storage conditions is presented in Figure 5. It is inferred from the result obtained, that the quality will definitely alter when it is kept under the unprescribed environmental conditions.
### Table 3: Internal standard evaluation for lamotrigine.

| Condition of Exposure | Internal Standard of specific modes of vibration at 3451cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/3451 A3317/3451 A3212/3451 A2136/3451 A1584/3451 A1556/3451 A1431/3451 A1109/3451 A624/3451 |
| At ice point | 1.0000 0.9695 0.9732 0.4251 0.8745 1.0136 1.0095 0.9439 0.4778 |
| Exposed to sunlight | 1.0000 0.9811 0.9811 0.3832 0.8397 1.0076 0.993 0.9289 0.4651 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 3317cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/3317 A3317/3317 A3212/3317 A2136/3317 A1584/3317 A1556/3317 A1431/3317 A1109/3317 A624/3317 |
| At ice point | 1.0314 1.0000 1.0038 0.4385 0.902 1.0454 1.0413 0.9736 0.4929 |
| Exposed to sunlight | 0.9905 1.0000 1.0275 0.4431 0.9385 0.9679 1.0561 0.9986 0.5448 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 3212cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/3212 A3317/3212 A3212/3212 A2136/3212 A1584/3212 A1556/3212 A1431/3212 A1109/3212 A624/3212 |
| At ice point | 1.0275 0.9961 1.0000 0.4368 0.8986 1.0415 1.0373 0.9699 0.491 |
| Exposed to sunlight | 0.9731 0.9824 1.0000 0.4353 0.92 1.0375 1.0357 0.981 0.5352 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 2136cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/2136 A3317/2136 A3212/2136 A2136/2136 A1584/2136 A1556/2136 A1431/2136 A1109/2136 A624/2136 |
| At ice point | 2.3518 2.2801 2.2888 1.0000 2.0568 2.3838 2.3743 2.2199 1.1239 |
| Exposed to sunlight | 2.2354 2.2567 2.297 1.0000 2.1179 2.1845 2.3384 2.2536 1.2295 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 1584cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/1584 A3317/1584 A3212/1584 A2136/1584 A1584/1584 A1556/1584 A1431/1584 A1109/1584 A624/1584 |
| At ice point | 1.1434 1.1085 1.1127 0.4861 1.0000 1.1589 1.1543 1.0793 0.5464 |
| Exposed to sunlight | 1.1908 1.1684 1.1694 0.4564 1.0000 1.2 1.1282 1.1062 0.5539 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 1556cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/1556 A3317/1556 A3212/1556 A2136/1556 A1584/1556 A1556/1556 A1431/1556 A1109/1556 A624/1556 |
| At ice point | 0.9665 0.9564 0.9601 0.4194 0.8628 1.0000 0.996 0.9312 0.4714 |
| Exposed to sunlight | 0.9923 0.9736 0.9745 0.3803 0.8333 1.0000 0.9854 0.9218 0.4615 |

| Condition of Exposure | Internal Standard of specific modes of vibration at 624cm⁻¹ |
|------------------------|----------------------------------------------------------|
| Prescribed storage condition | A3451/624 A3317/624 A3212/624 A2136/624 A1584/624 A1556/624 A1431/624 A1109/624 A624/624 |
| At ice point | 2.0925 2.0287 2.0364 0.8997 2.1209 2.104 2.1125 1.9751 1.0000 |
| Exposed to sunlight | 2.1499 2.1094 2.1112 0.8239 2.1803 2.1684 1.135 1.9972 1.0000 |

### Table 4: lamotrigine stored at different conditions.

| Storage condition | Absorbance at λ=304 nm |
|-------------------|-------------------------|
| Light Resistance Container (LRC) | 0.5996 |
| Ice point | 0.5538 |
| Sunlight | 0.3537 |

### Conclusion

A satisfactory Vibrational assignment of the drug with the FTIR and FT- Raman spectra recorded confirms the basic functional groups present in the lamotrigine. FTIR and UV spectroscopic technique have been employed for the qualitative analysis of lamotrigine. The FTIR and UV spectrum recorded clearly denotes the change in the absorbance values with storage condition emphasizing the fact that the drug should always be kept under the guidelines provided for storage to maintain their quality.

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