

Figure 1. Representative XRPD patterns of rifaximin Form  $\mu$ .

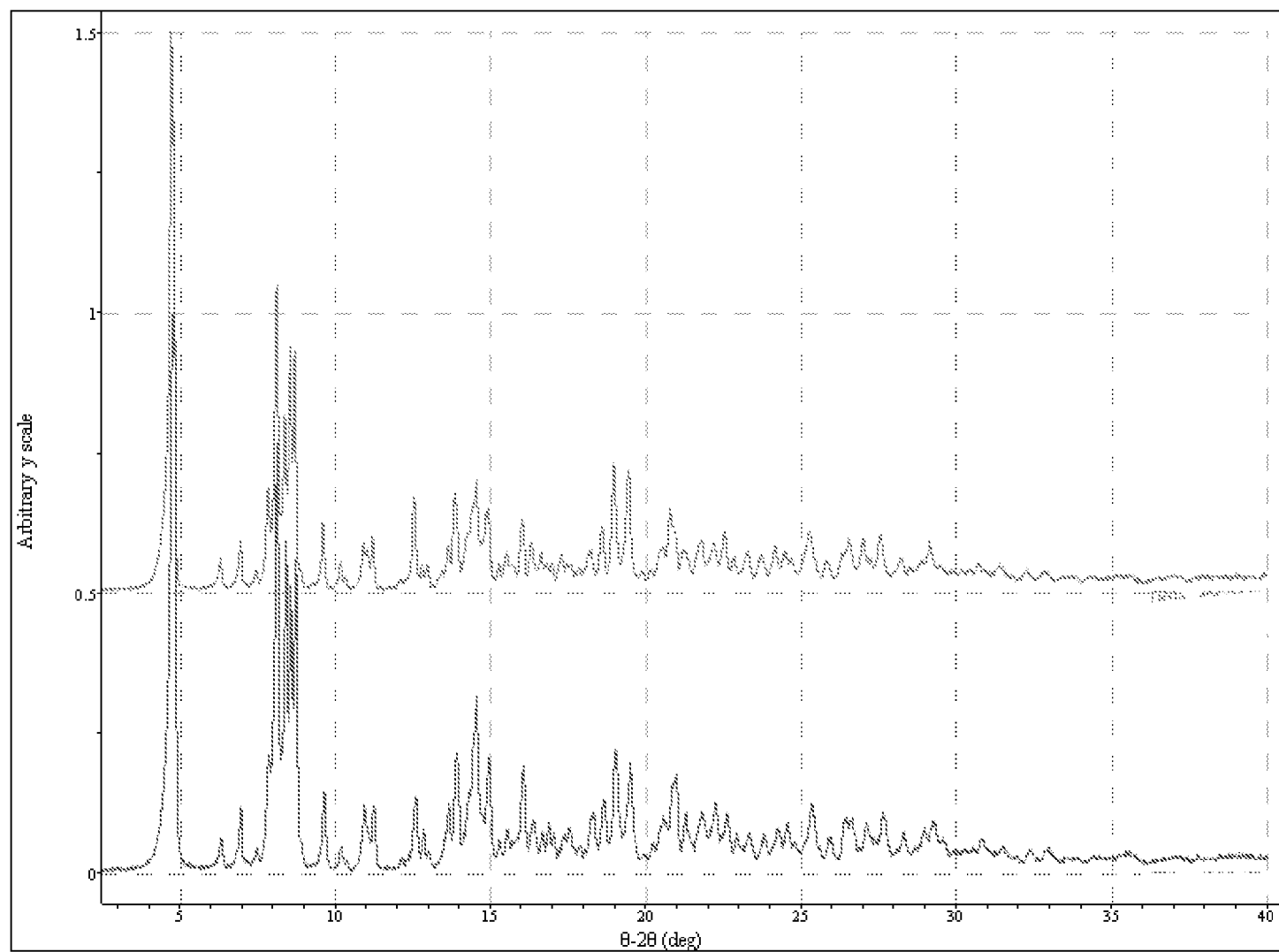


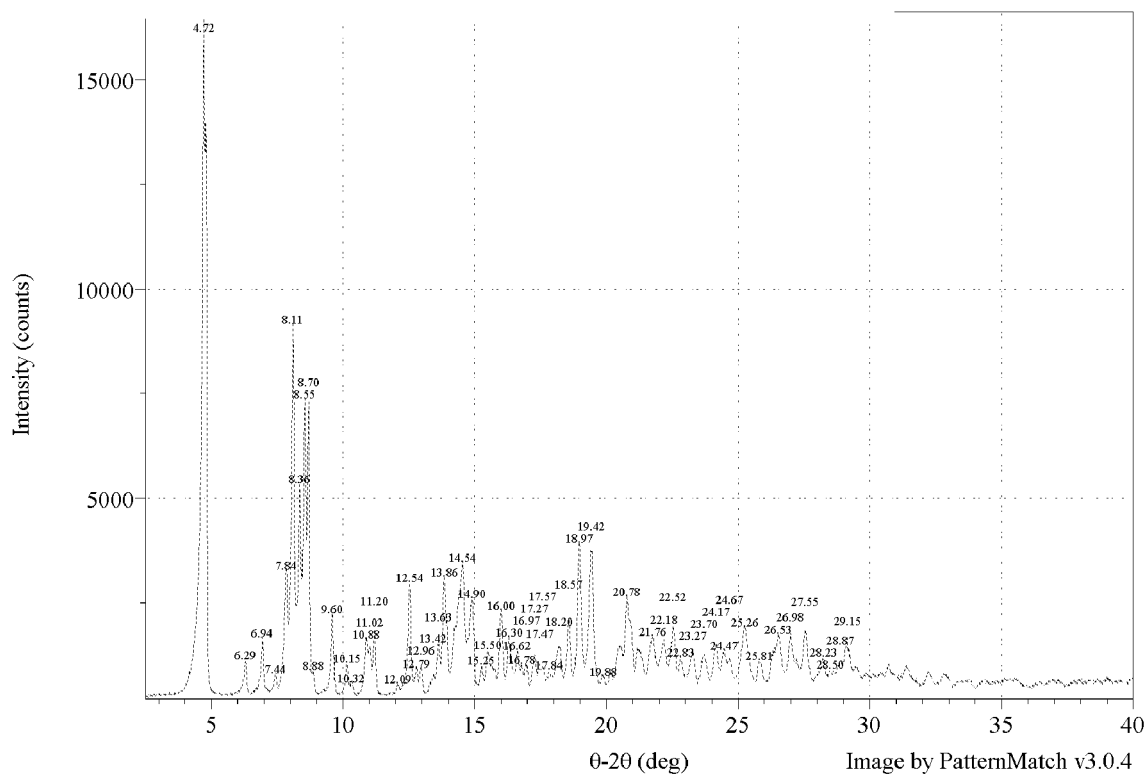
Figure 2. List of observed peaks for rifaximin Form  $\mu$ .

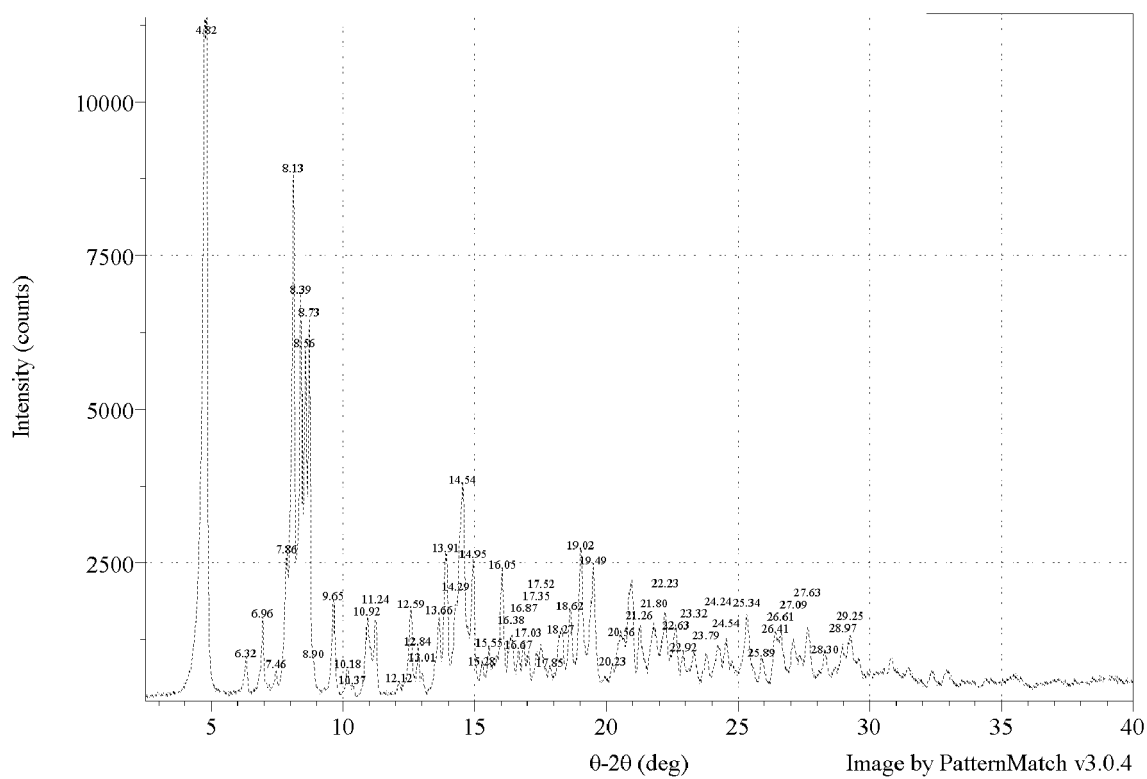
Figure 3. List of observed peaks for rifaximin Form  $\mu$ .

Figure 4. Tentative indexing solution for rifaximin Form  $\mu$ . bars indicate allowed reflections based on the unit cell dimensions and the assigned space group.

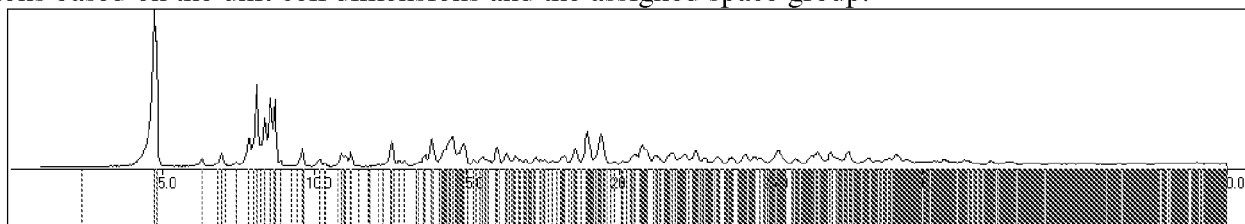


Figure 5. Tentative indexing solution for rifaximin Form  $\mu$ . bars indicate allowed reflections based on the unit cell dimensions and the assigned space group ( $P2_1$ , #4).

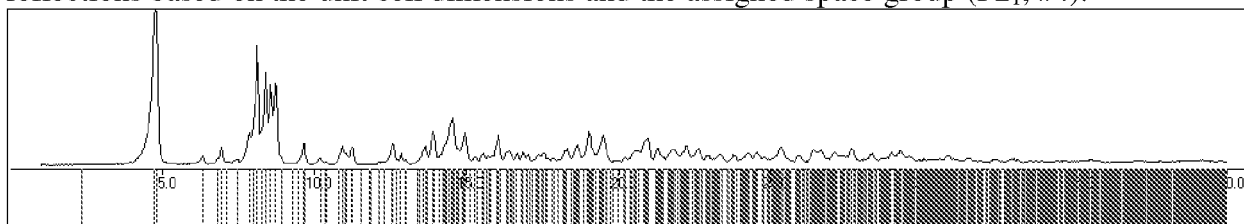


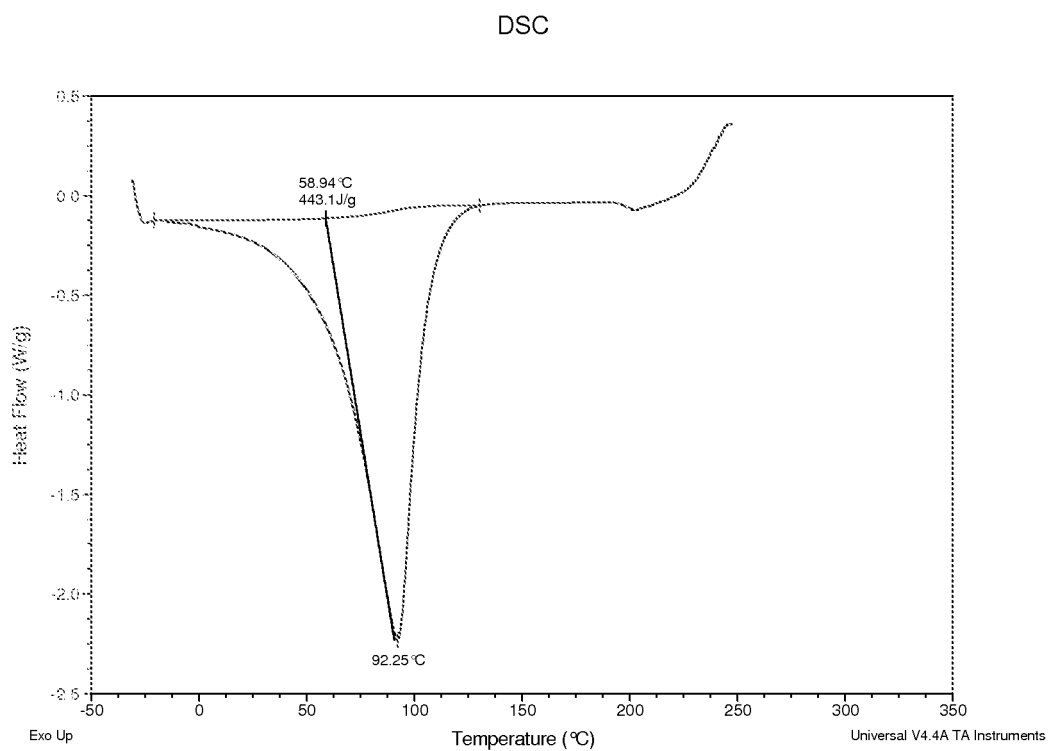
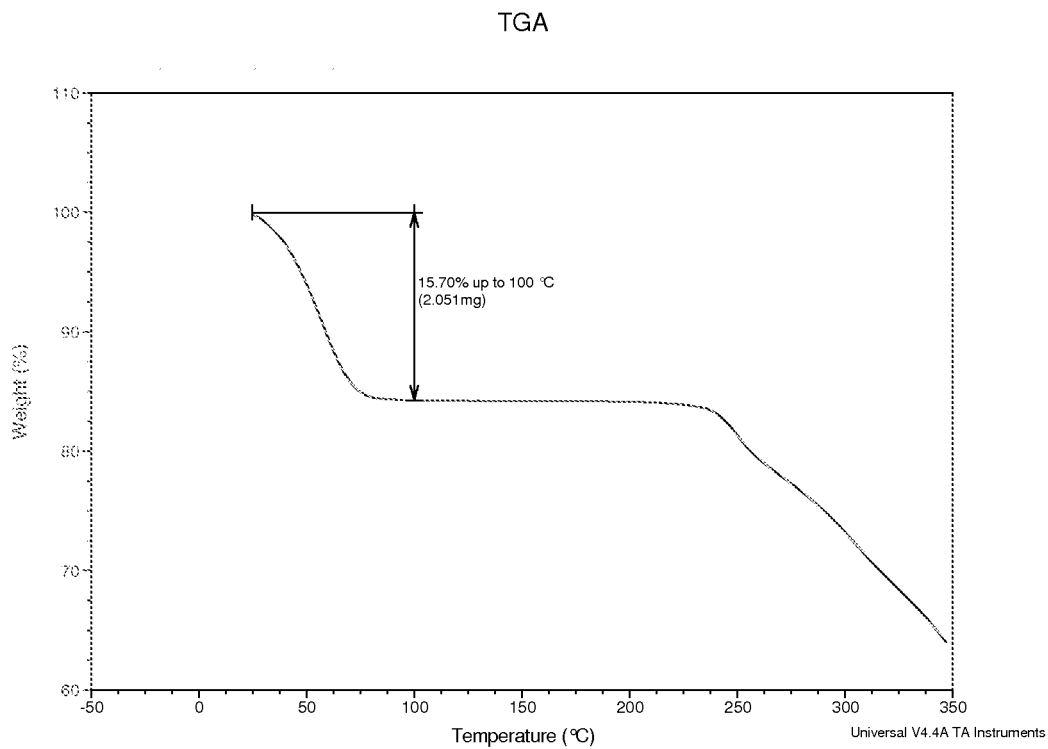
Figure 6. DSC and TGA thermograms of rifaximin Form  $\mu$ .

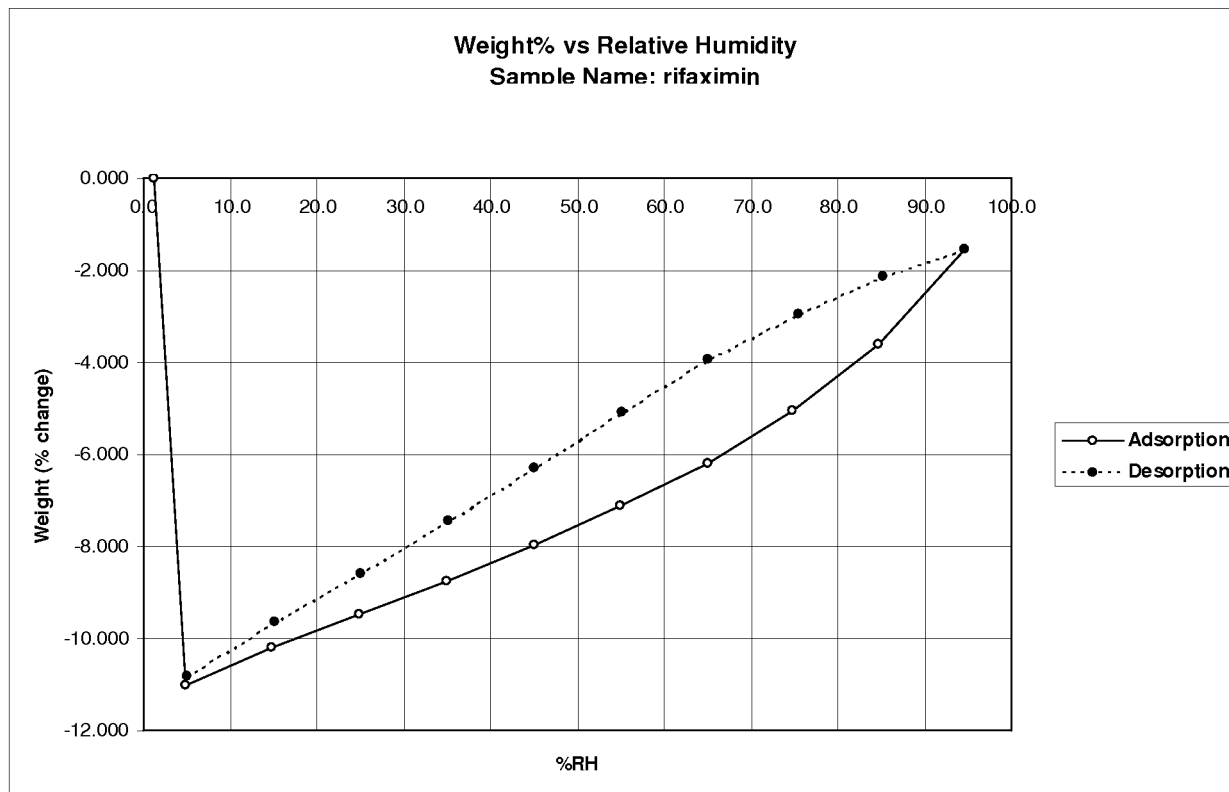
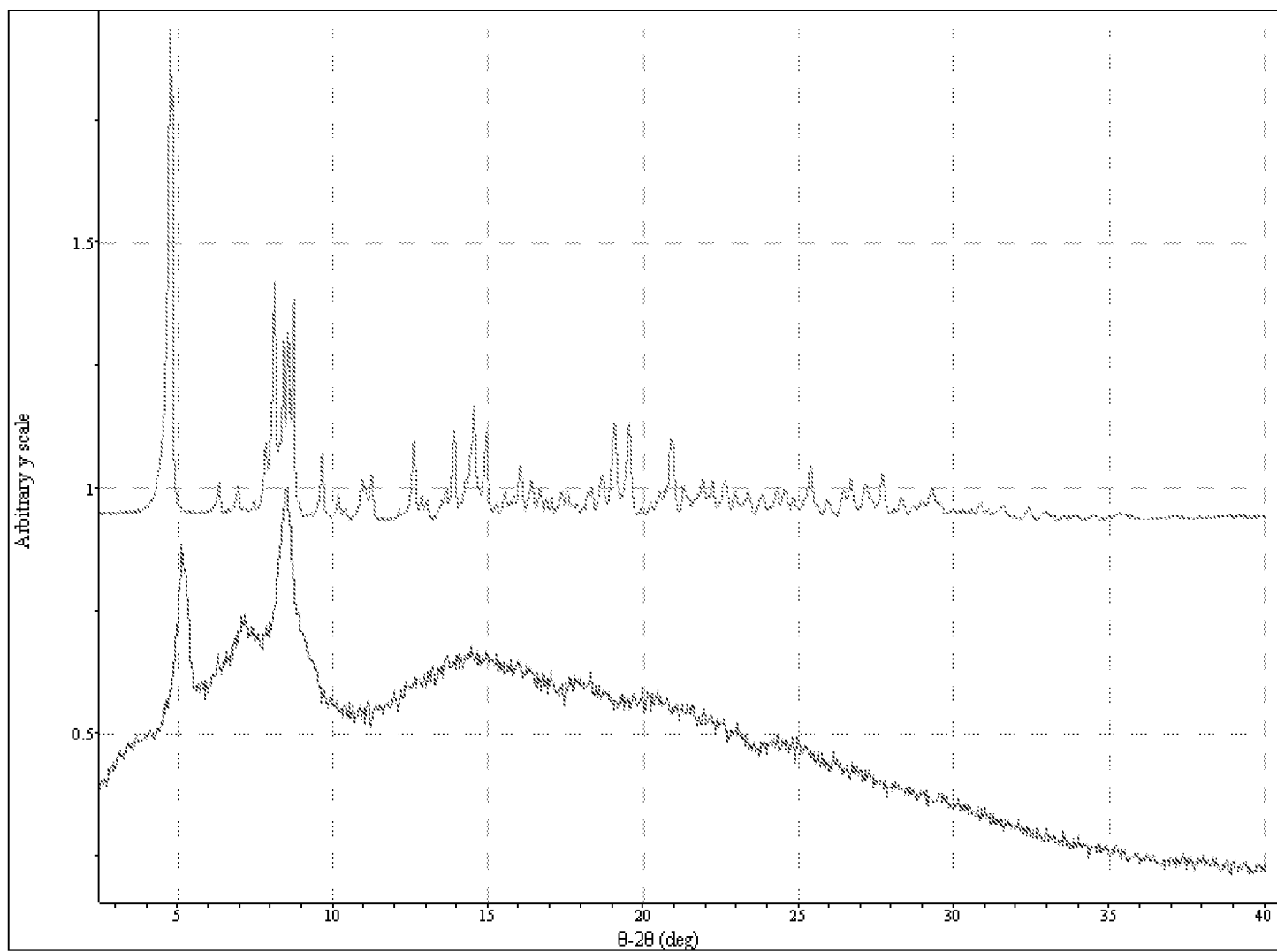
Figure 7. Moisture sorption of rifaximin Form  $\mu$ .

Figure 8. Post-Moisture sorption XRPD of rifaximin Form  $\mu$ .

Top: before moisture sorption;

Bottom: after moisture sorption (Form  $\gamma$ ).



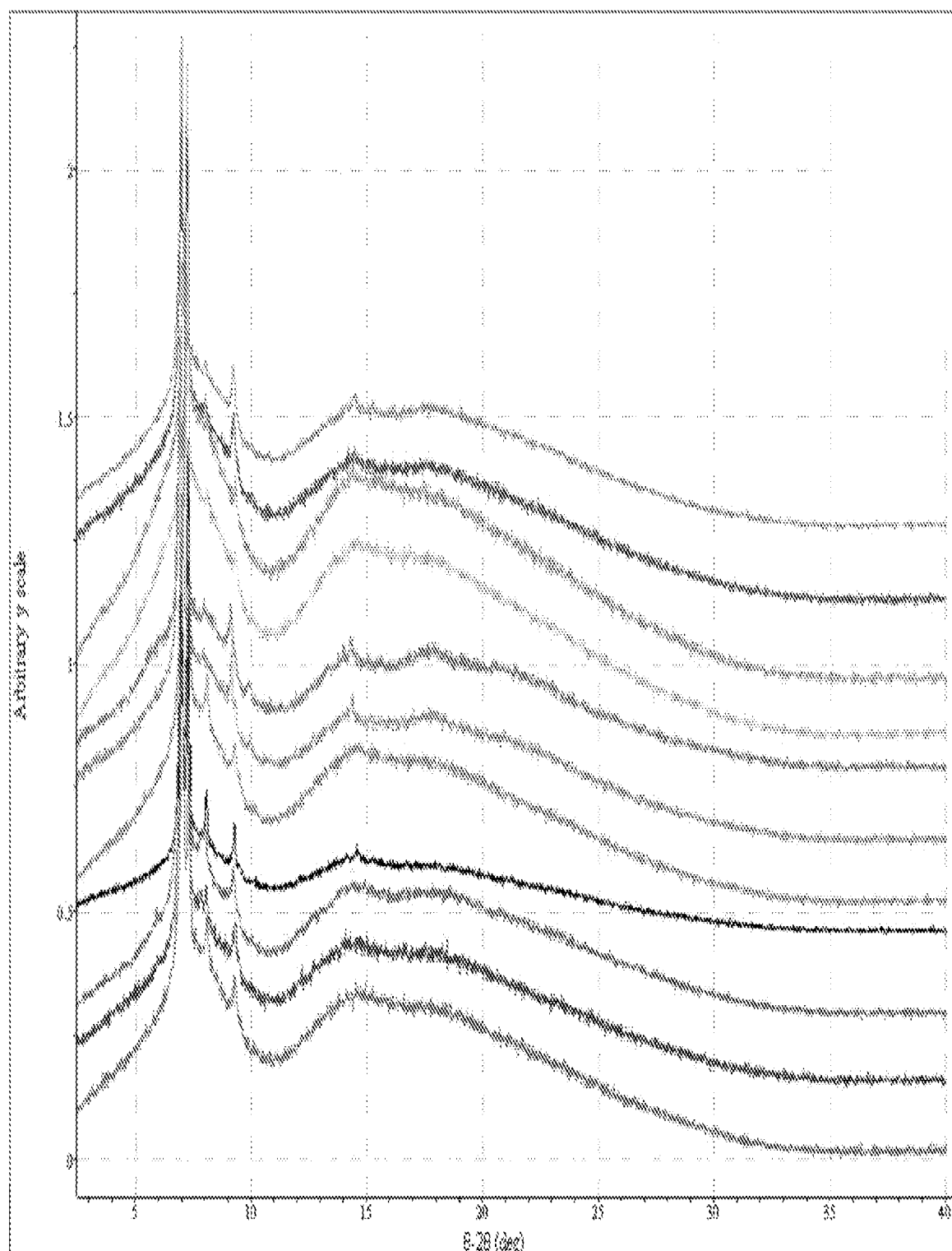


Figure 9

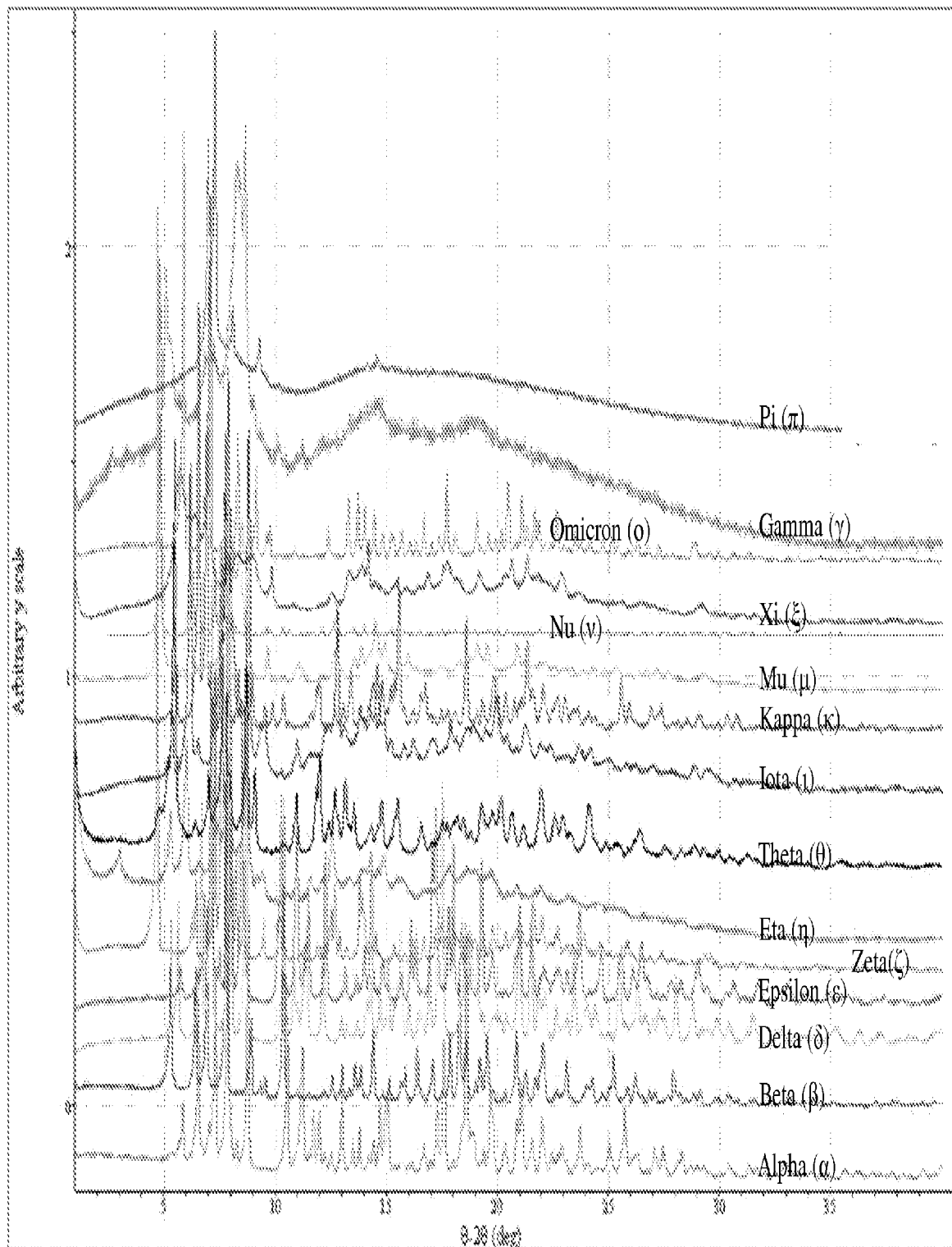


Figure 10

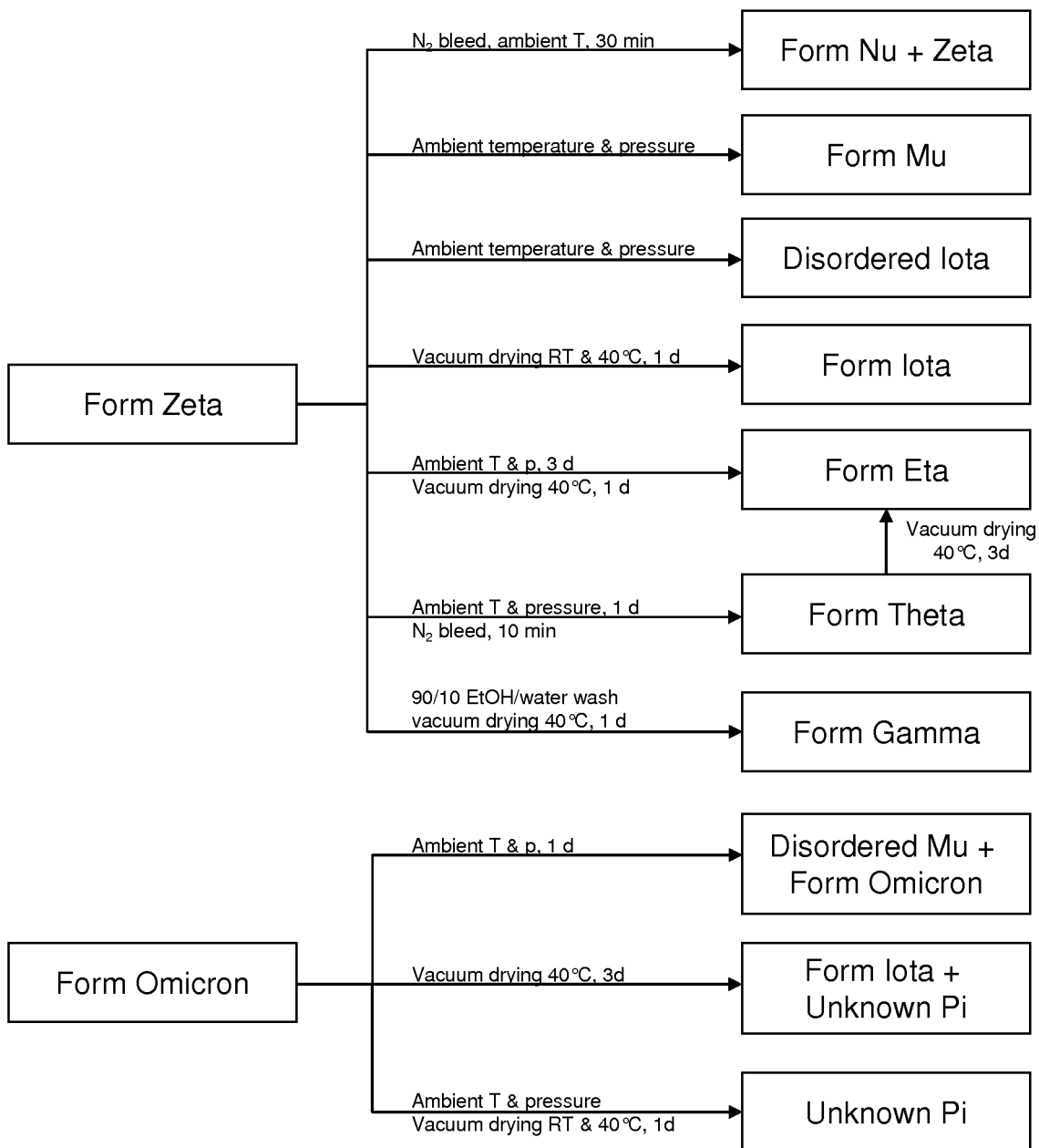
**Figure 11 Summary of Results of Drying Experiments.**

**Figure 12: XRPD patterns of samples of Rifaximin Unknown Pi.**

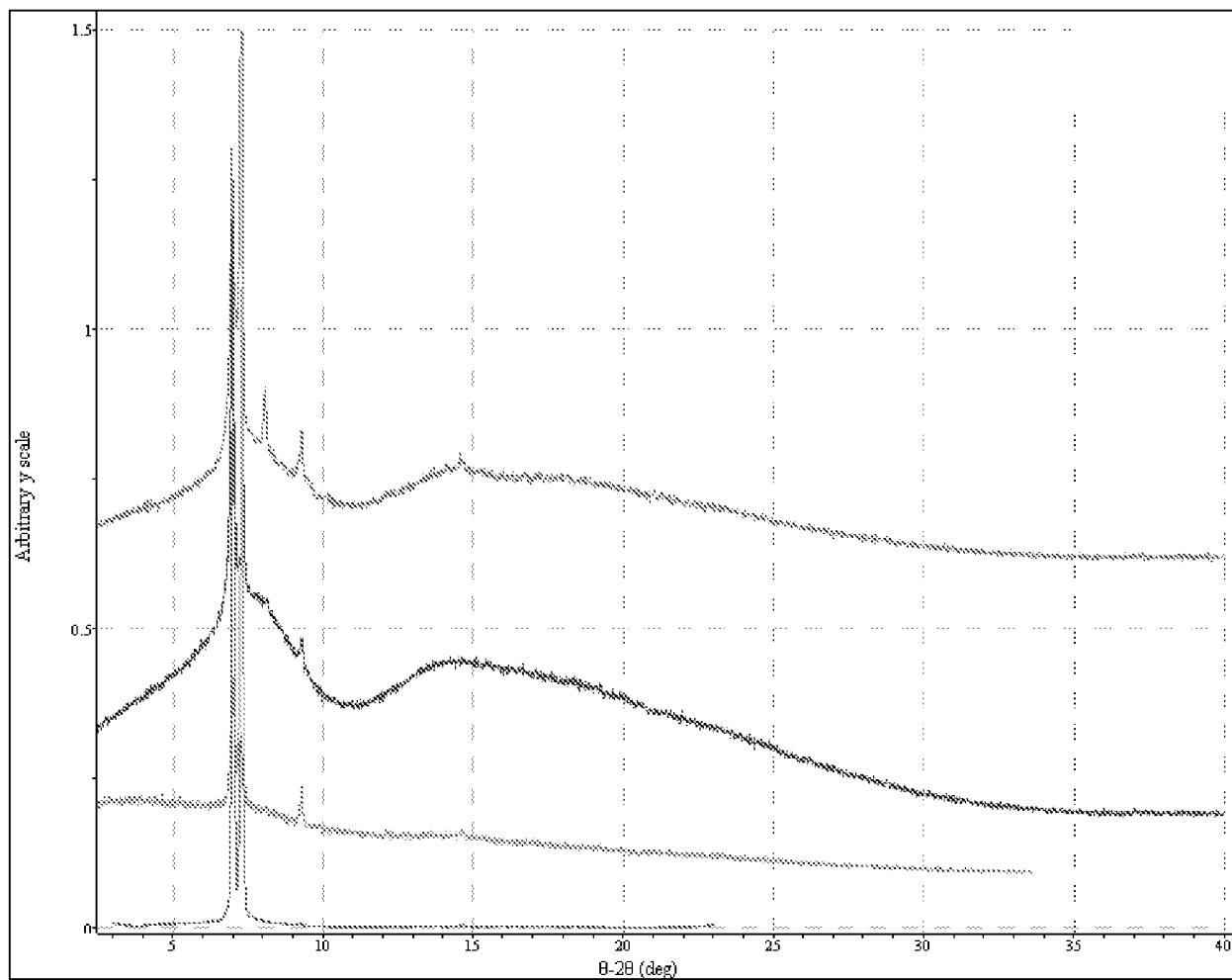


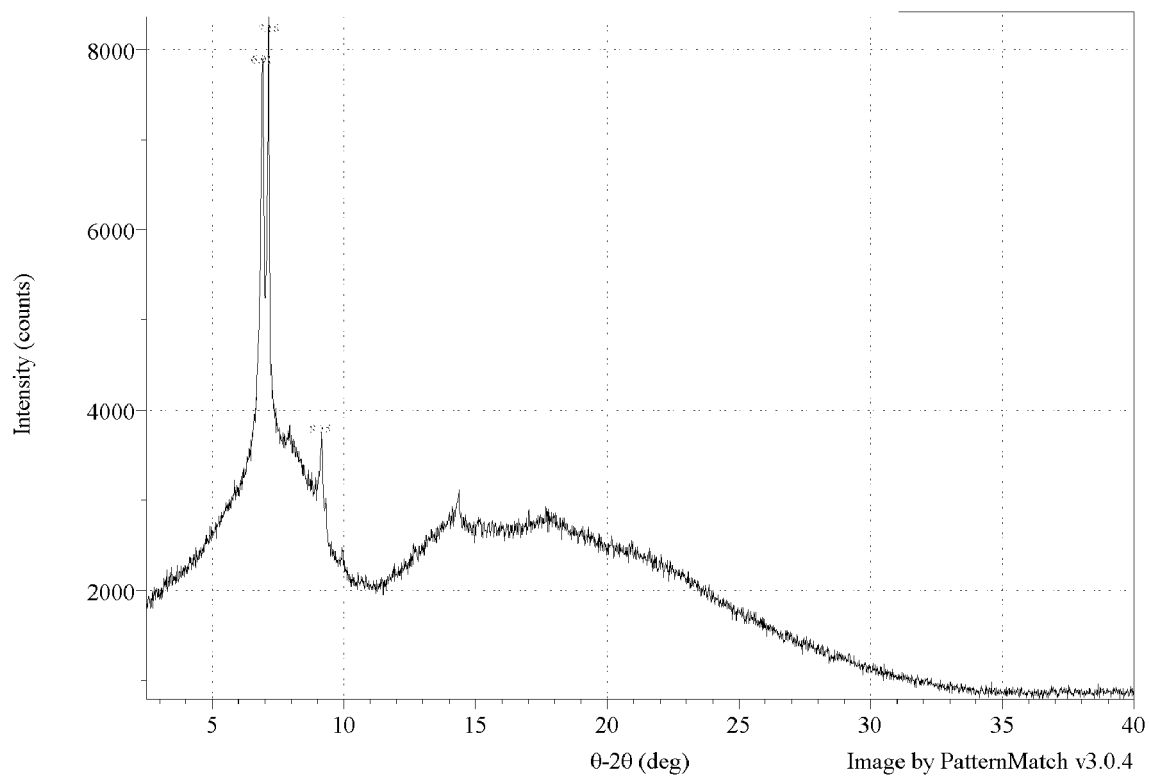
**Figure 13. List of observed peaks for Rifaximin Pi,**

**Figure 14. List of observed peaks for Rifaximin Pi,**

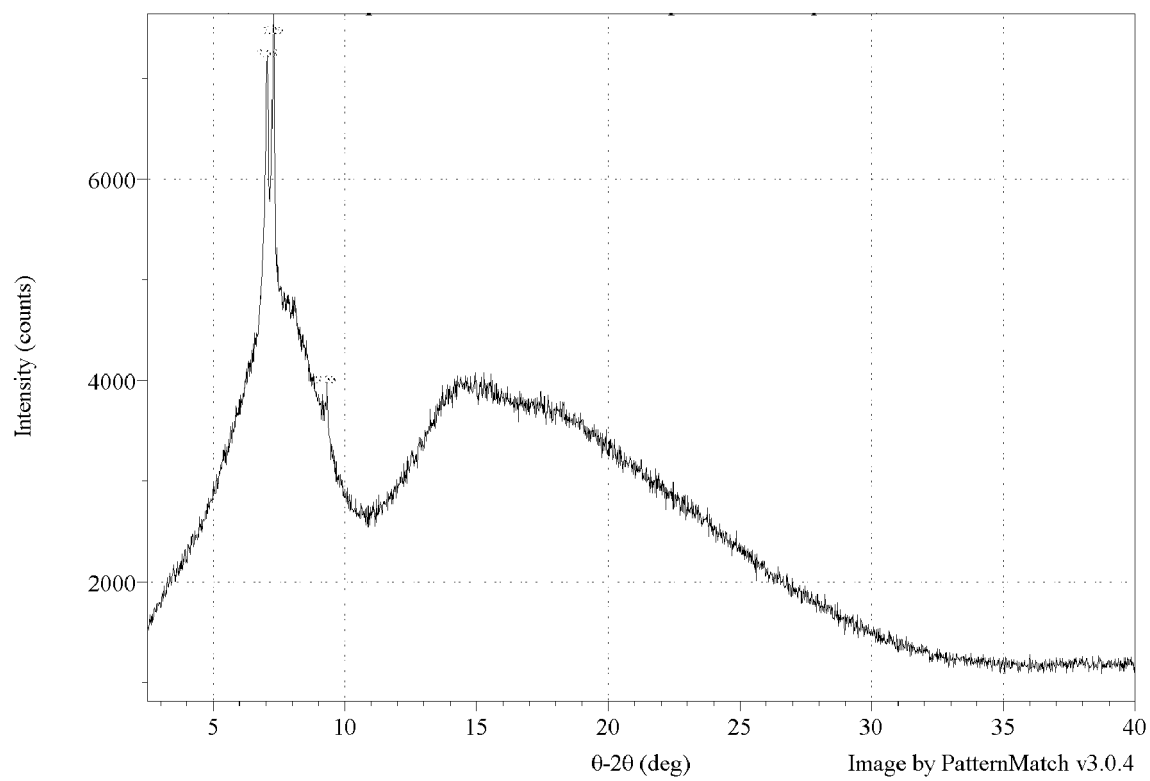


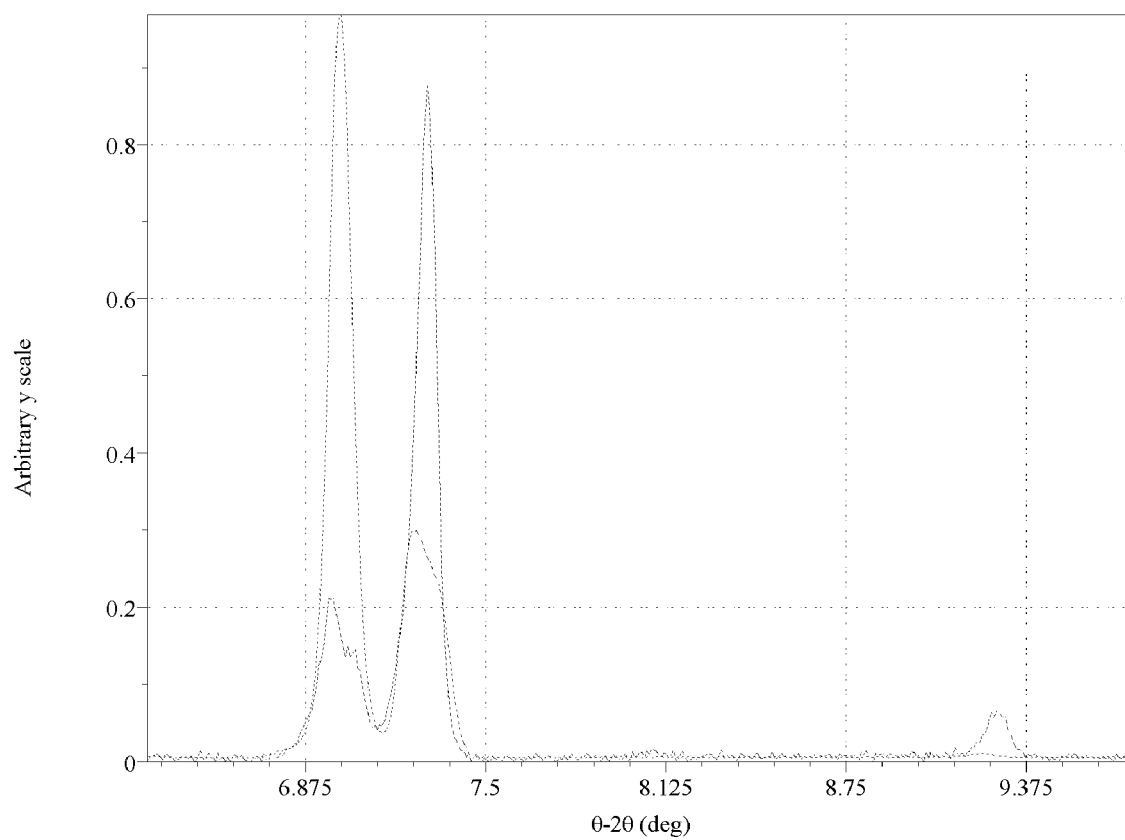
**Figure 15. Comparison of XRPD patterns of Rifaximin**

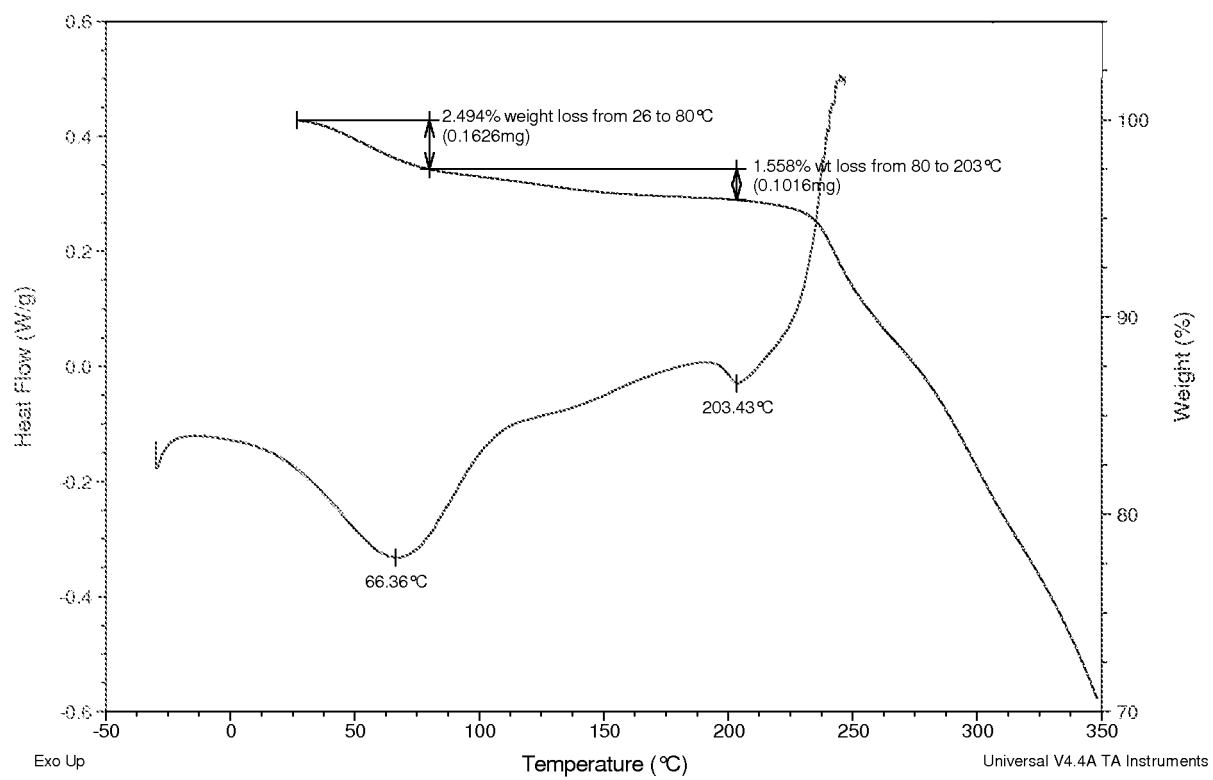
**Figure 16. Thermal analysis of Rifaximin Pi**

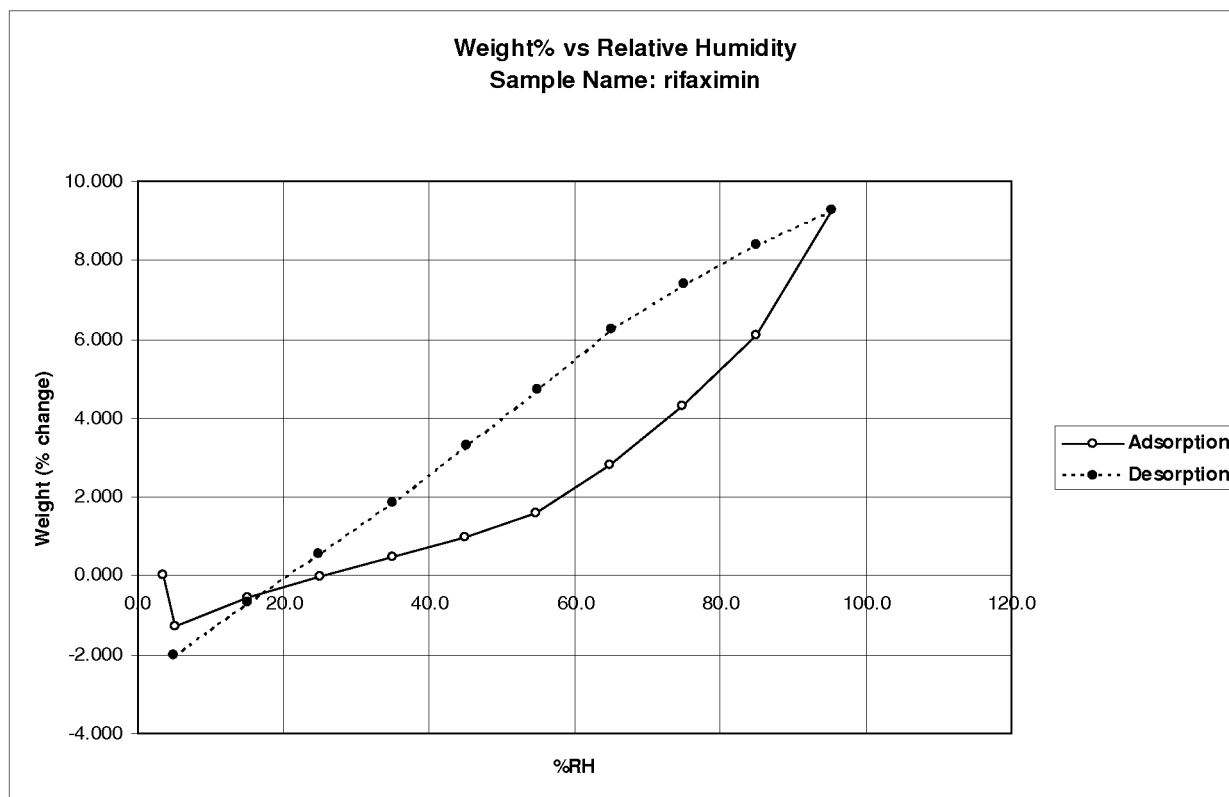
**Figure 17. Dynamic vapor sorption isotherm of a sample of Rifaximin Pi**

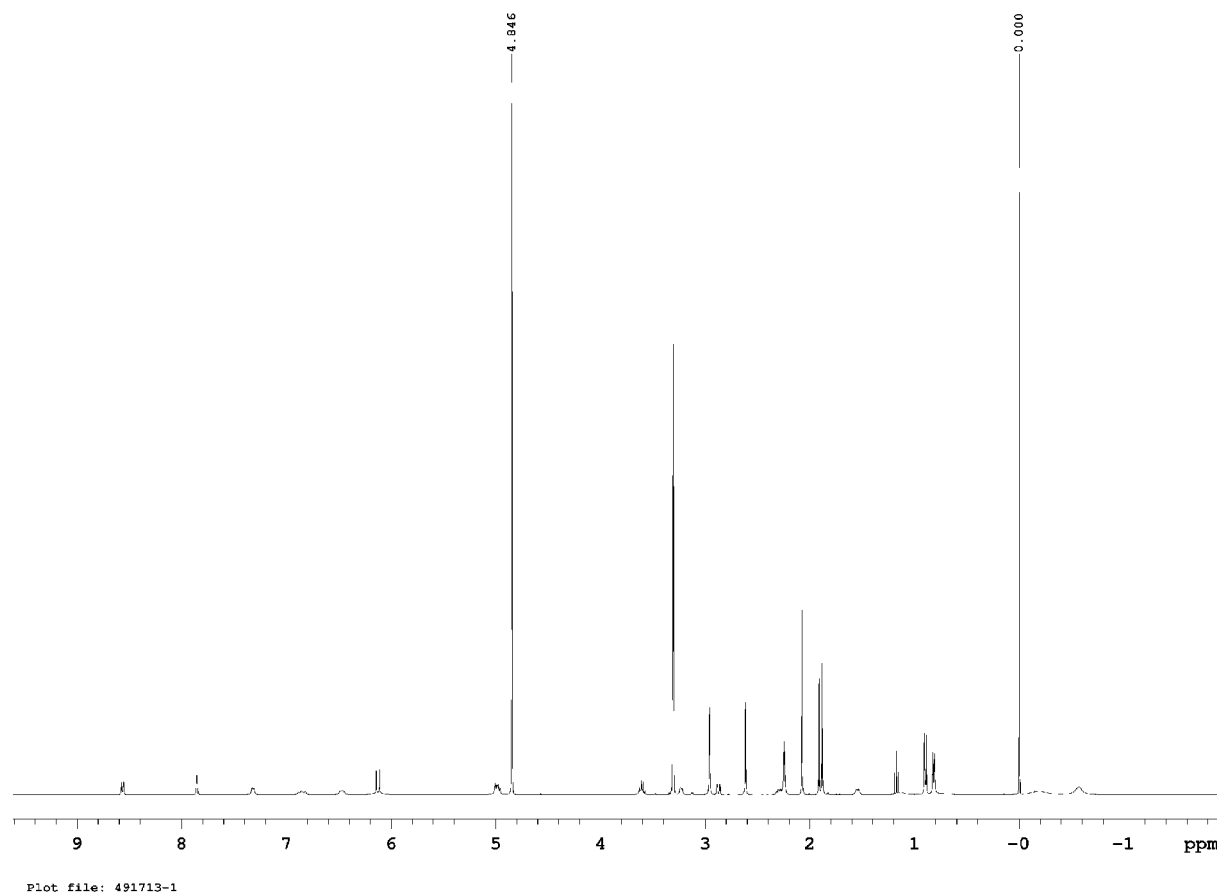
**Figure 18. Proton NMR spectrum of Rifaximin Pi**

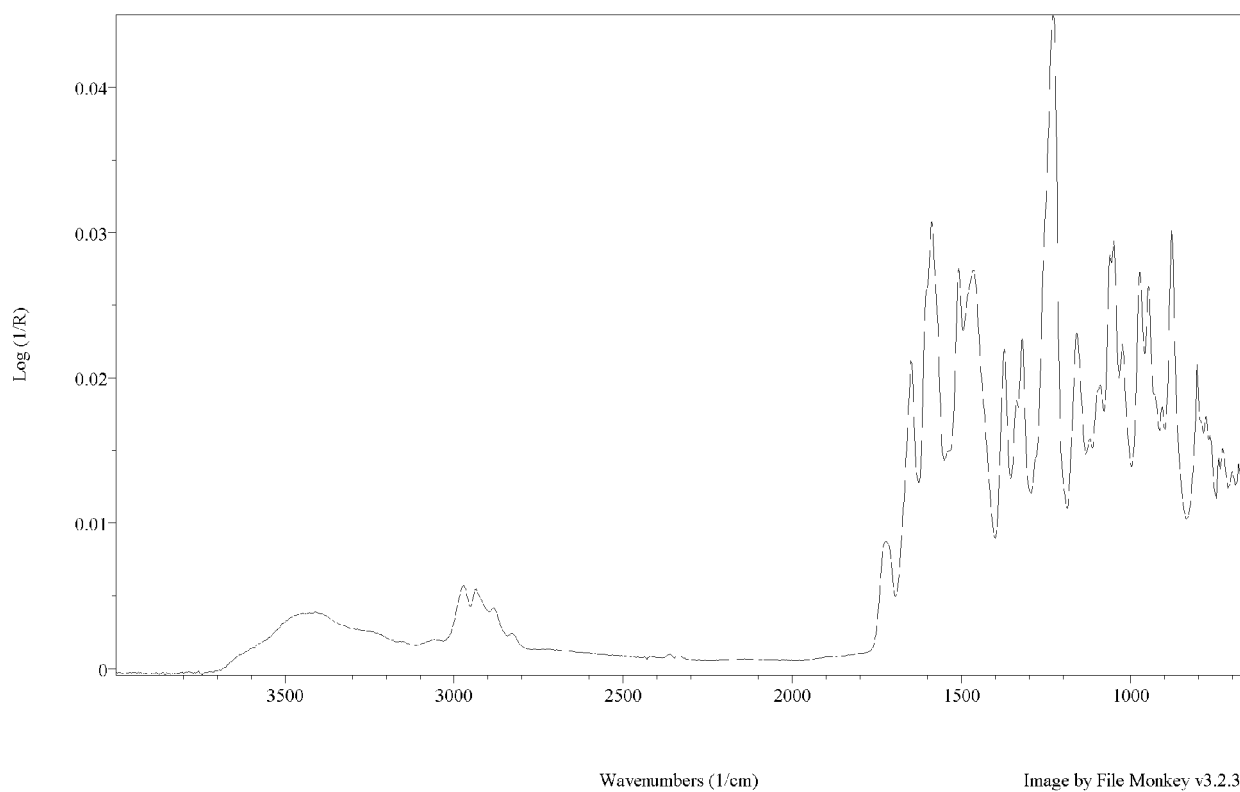
**Figure 19. ATR-IR spectrum of Rifaximin Pi**

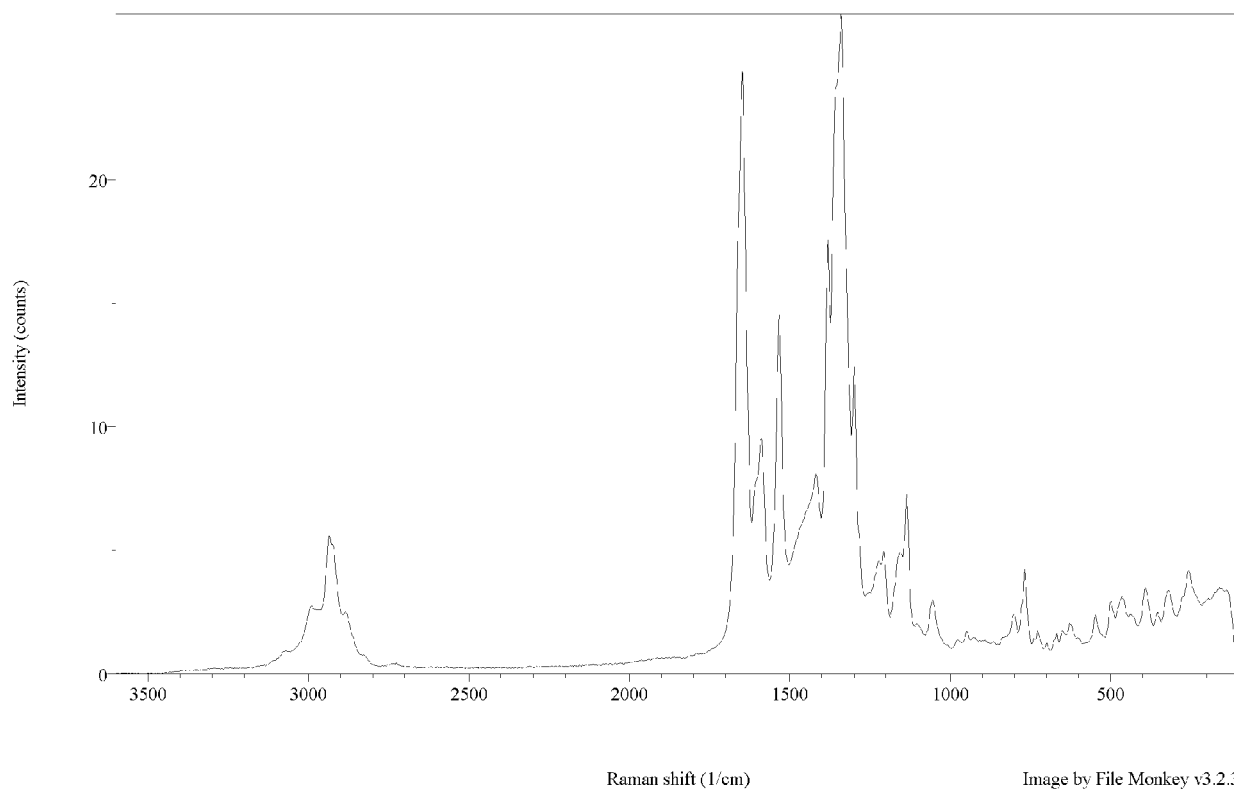
**Figure 20. Raman spectrum of Rifaximin Pi**

**Figure 21. Solid state carbon NMR spectrum of Rifaximin  $\text{HCl}$**

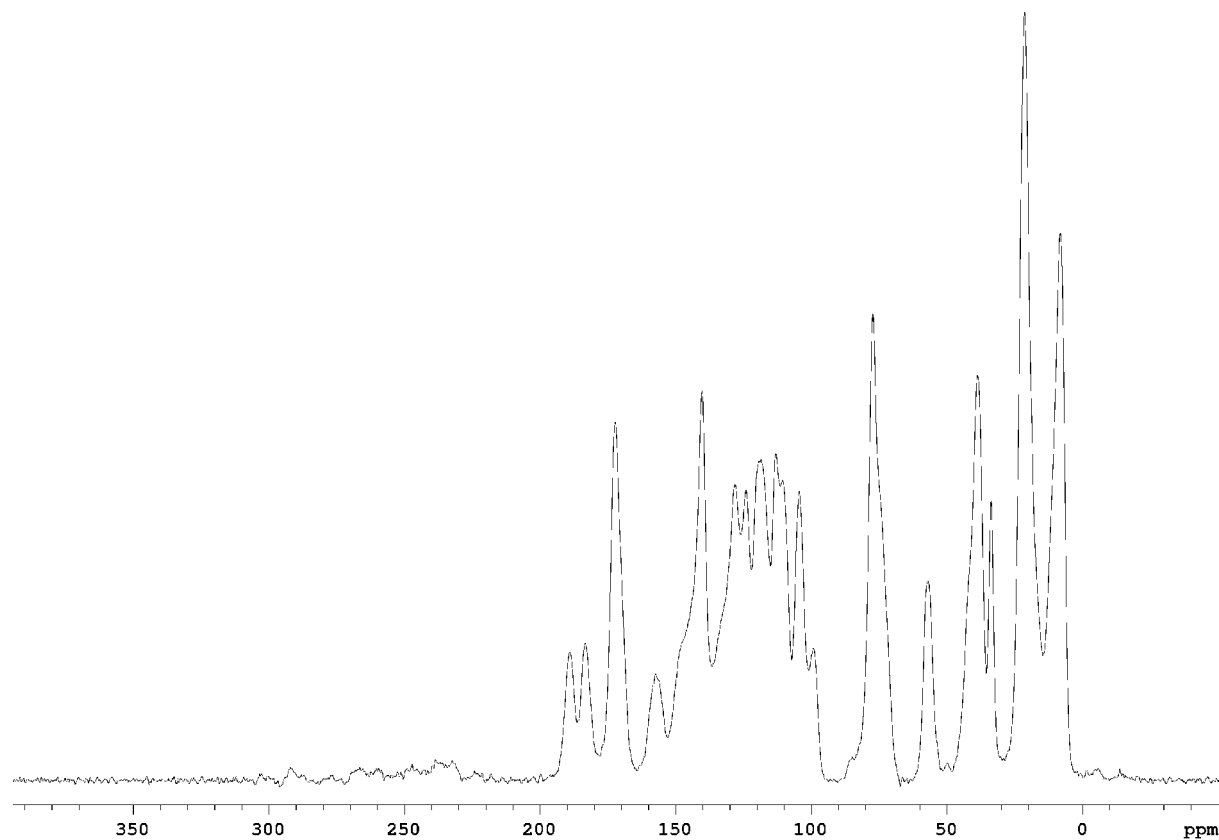


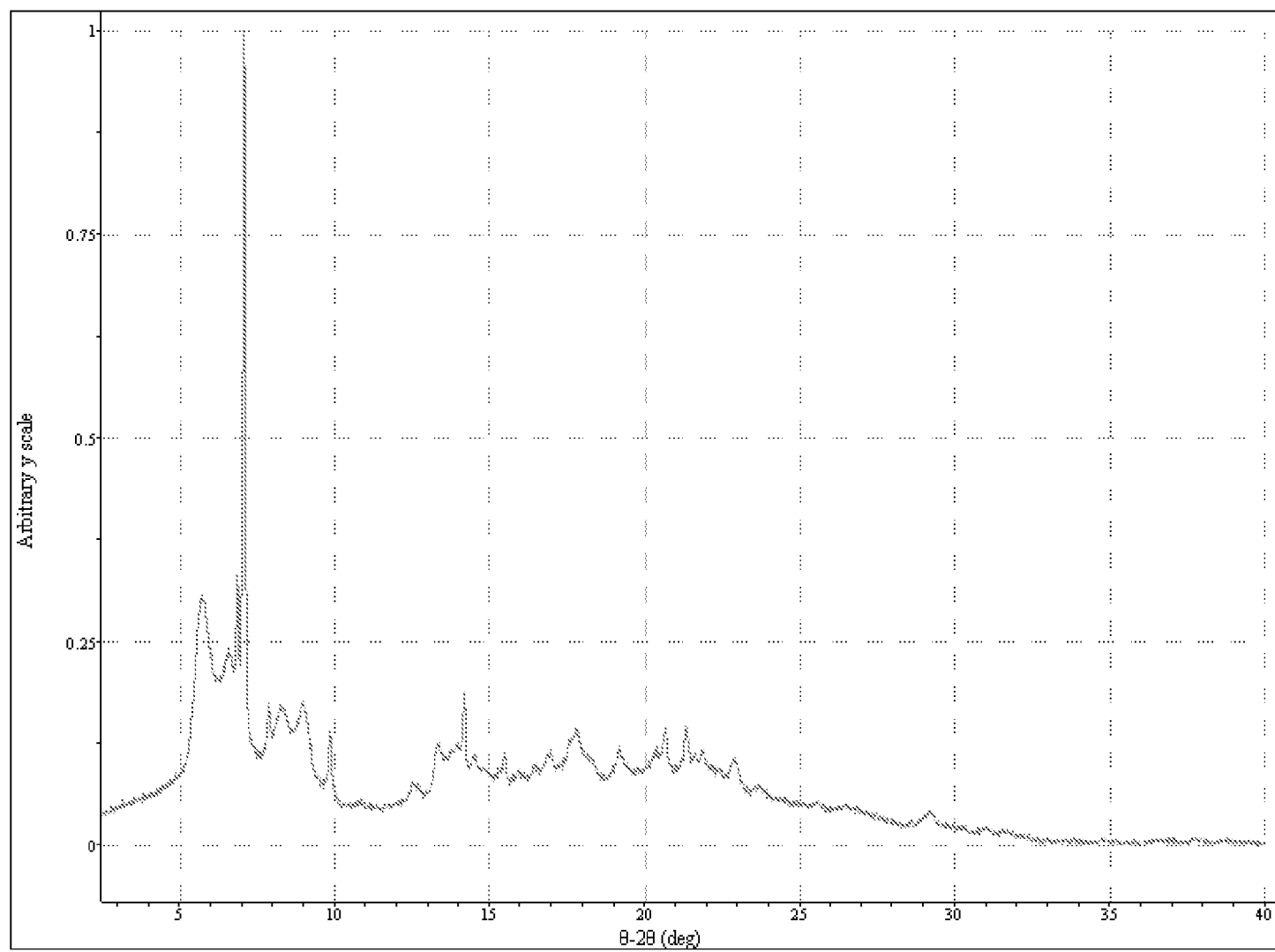
**Figure 22** XRPD Pattern of Rifaximin Form Xi ( $\xi$ ).

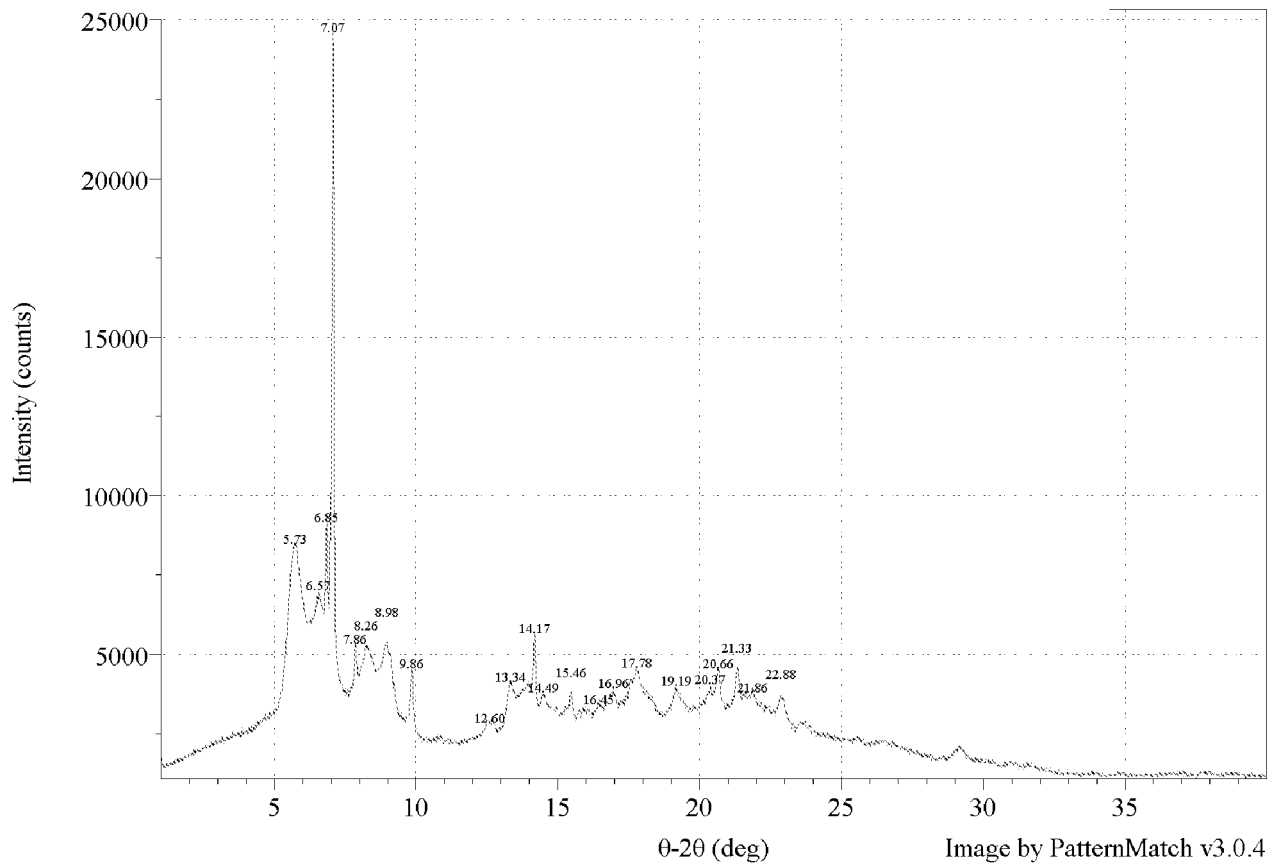
**Figure 23 List of Observed Peaks for Rifaximin Form Xi ( $\xi$ )**

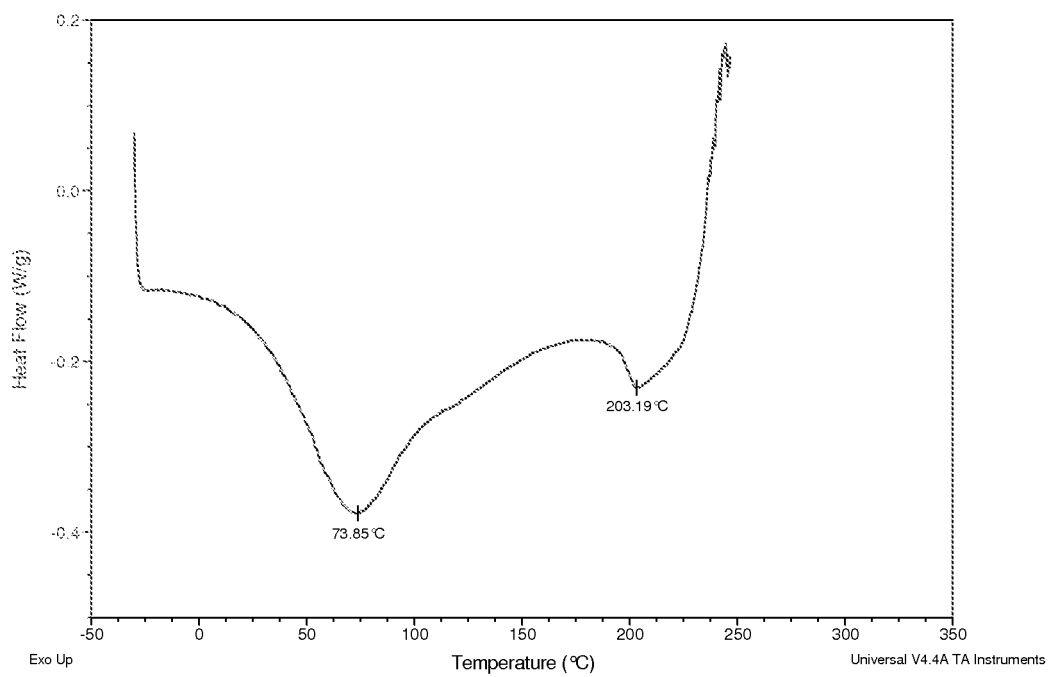
**Figure 24** DSC Thermogram of Rifaximin Form Xi ( $\xi$ ).

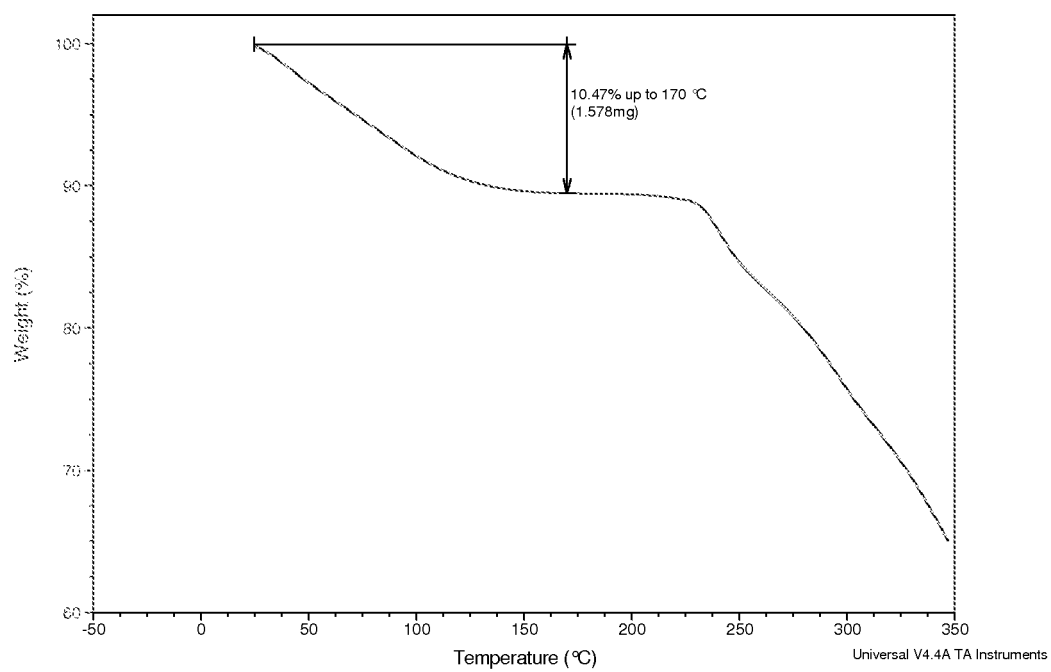
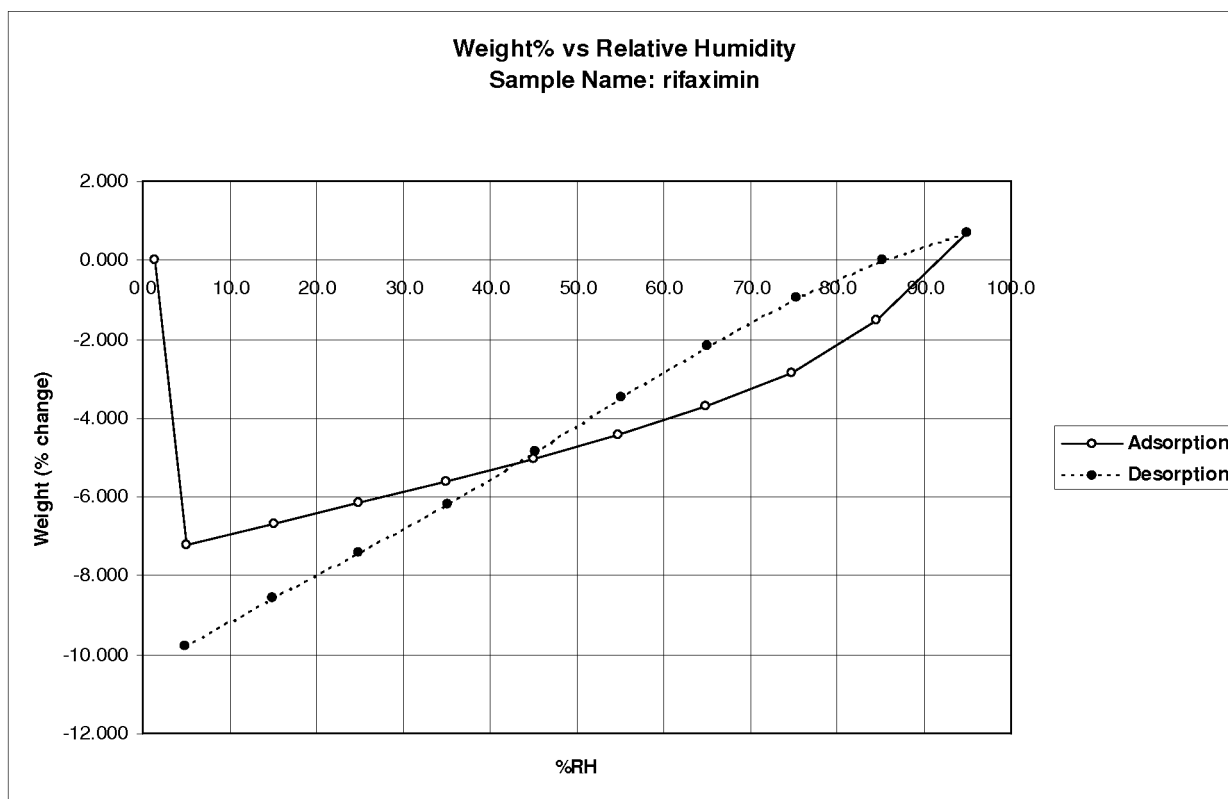
**Figure 25 TGA Thermogram of Rifaximin Form Xi ( $\xi$ ).**

Figure 26 Moisture Sorption Isotherm of Rifaximin Form Xi ( $\xi$ ).



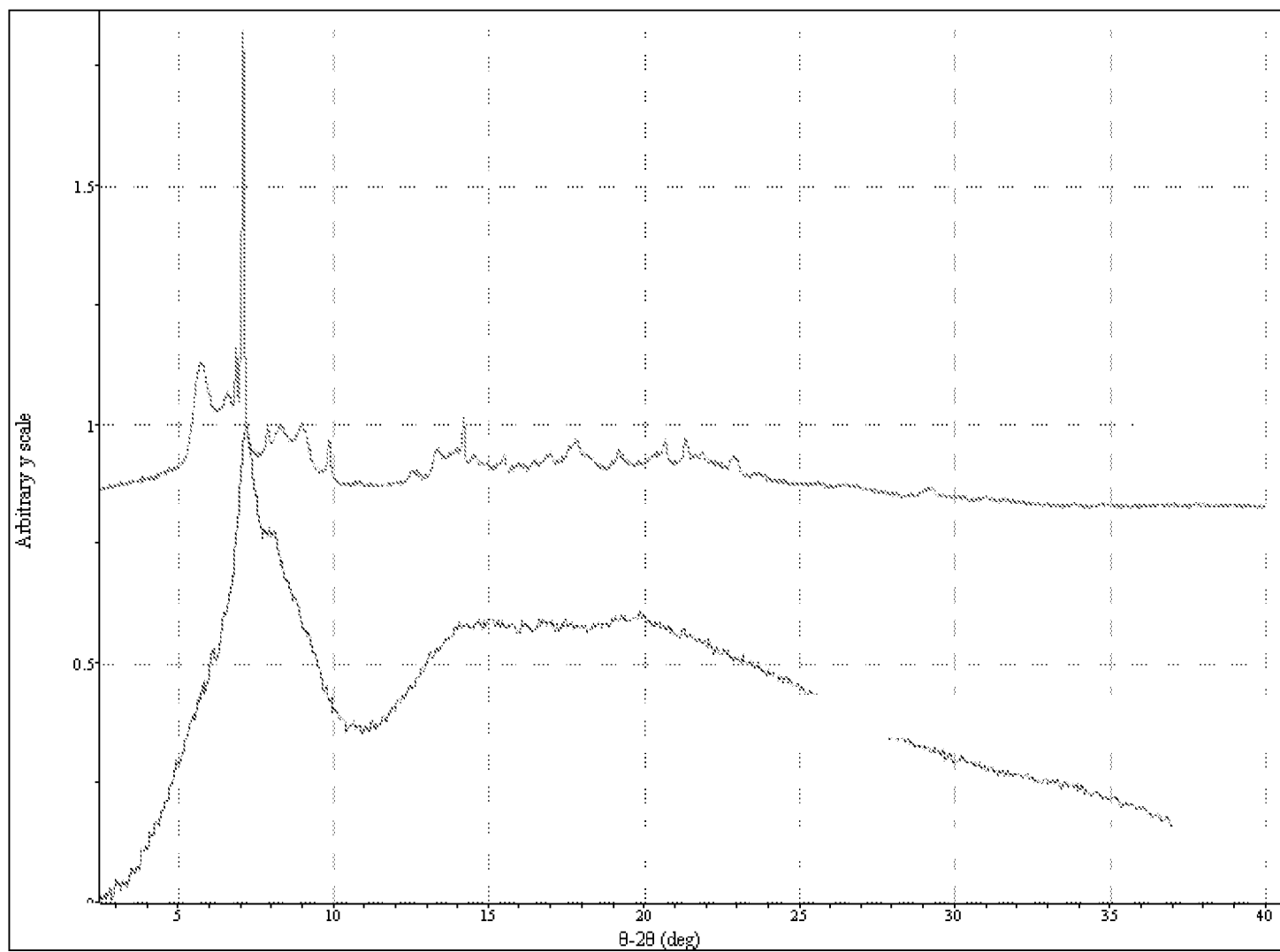


Figure 27 XRPD pattern of Rifaximin Form Xi ( $\xi$ ) Before and After the Moisture Sorption Experiment

Figure 28

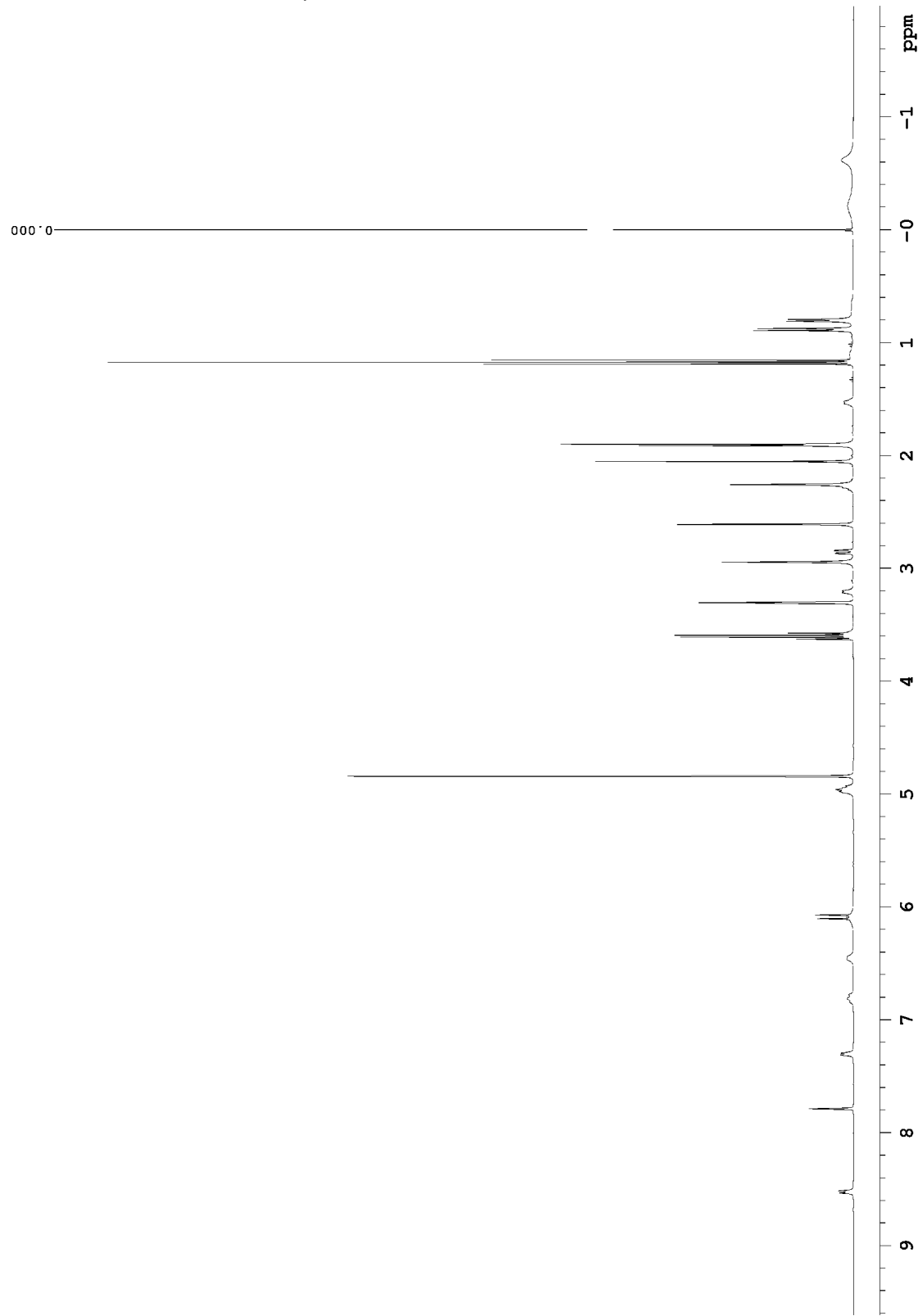


Figure 29 Solid State NMR Spectrum of Rifaximin Form Xi( $\xi$ ).

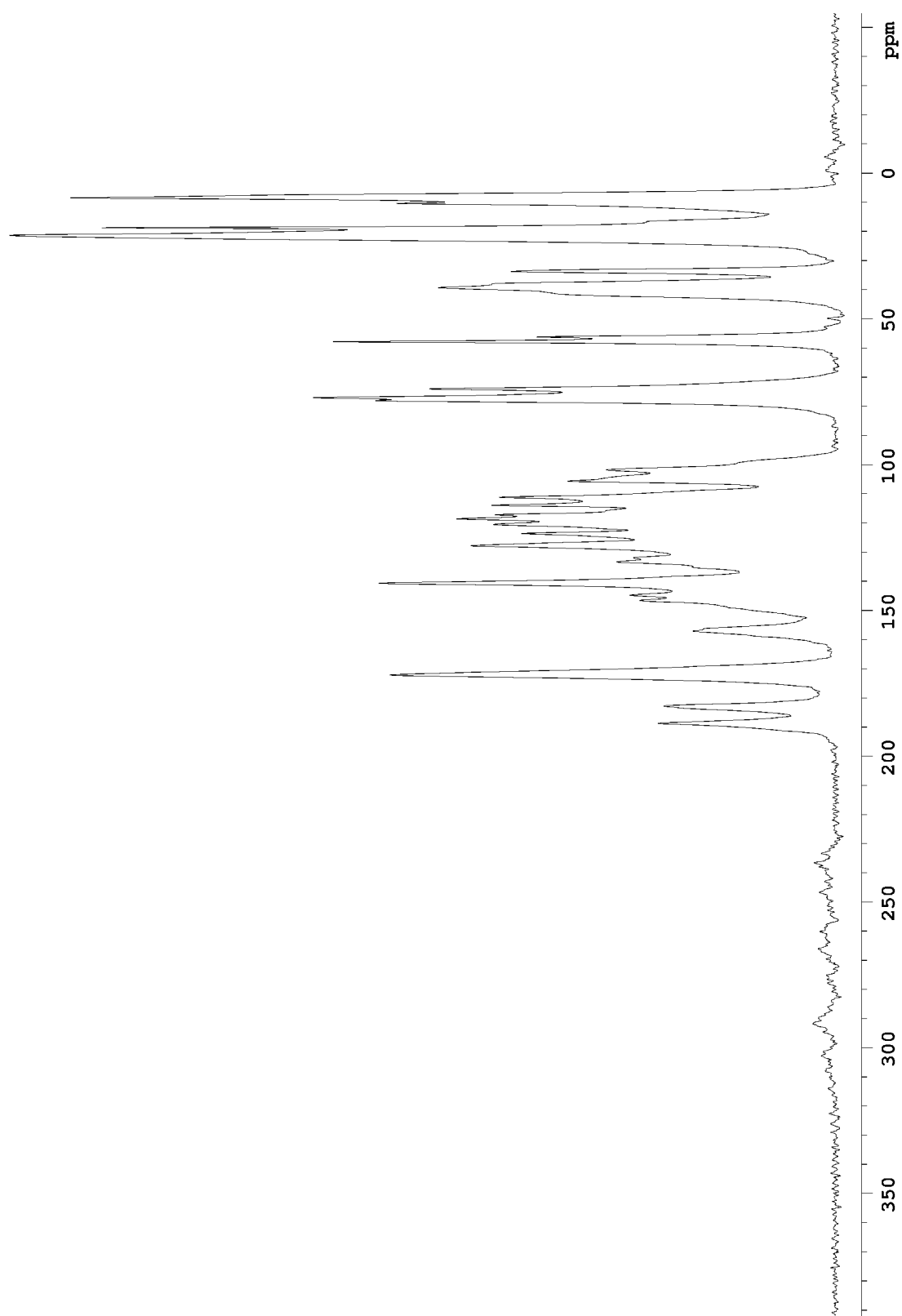


**Figure 30 Infrared (IR) Spectrum of Rifaximin Form Xi( $\xi$ ).**

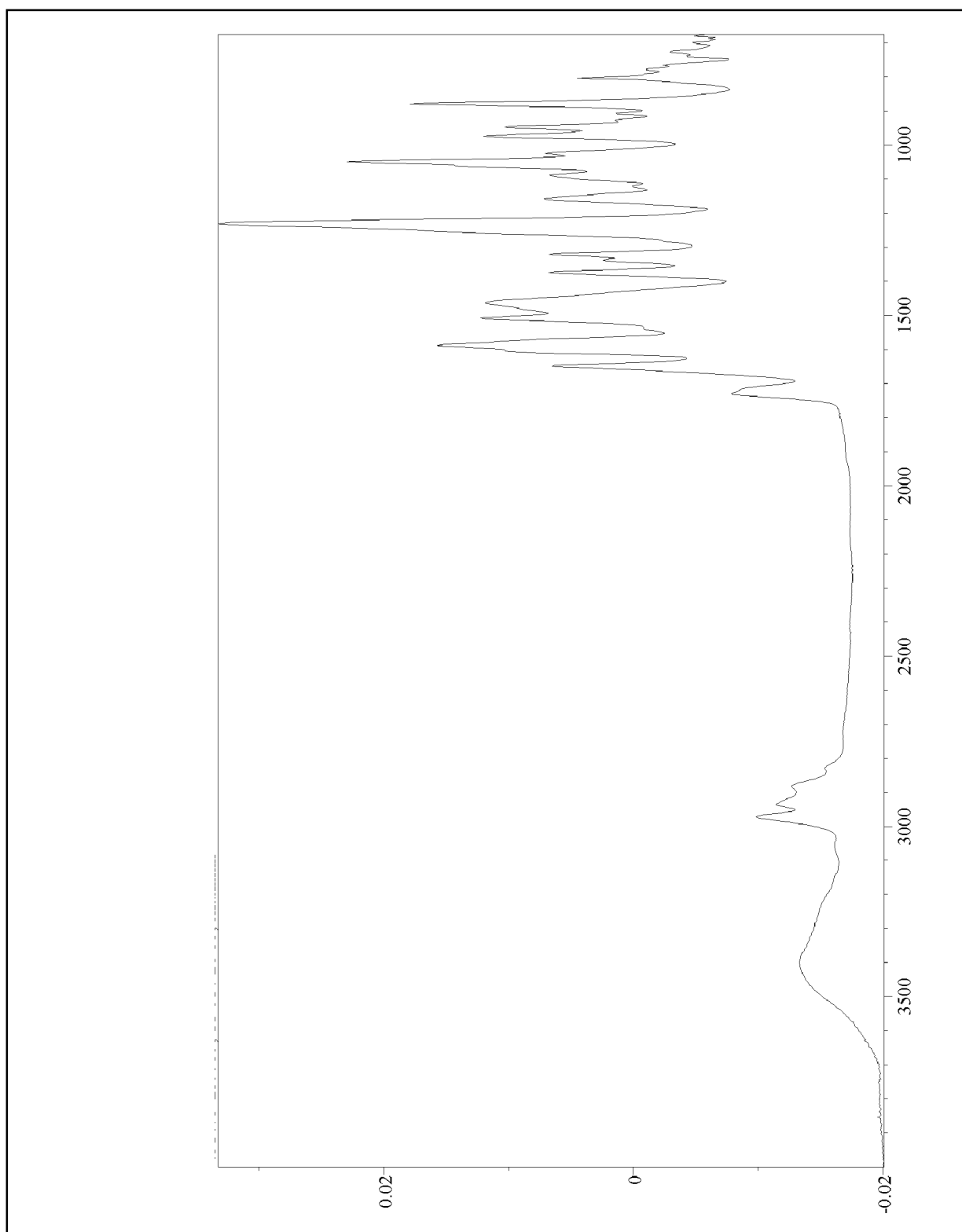


Figure 31 Raman Spectrum of Rifaximin Form Xi( $\xi$ ).

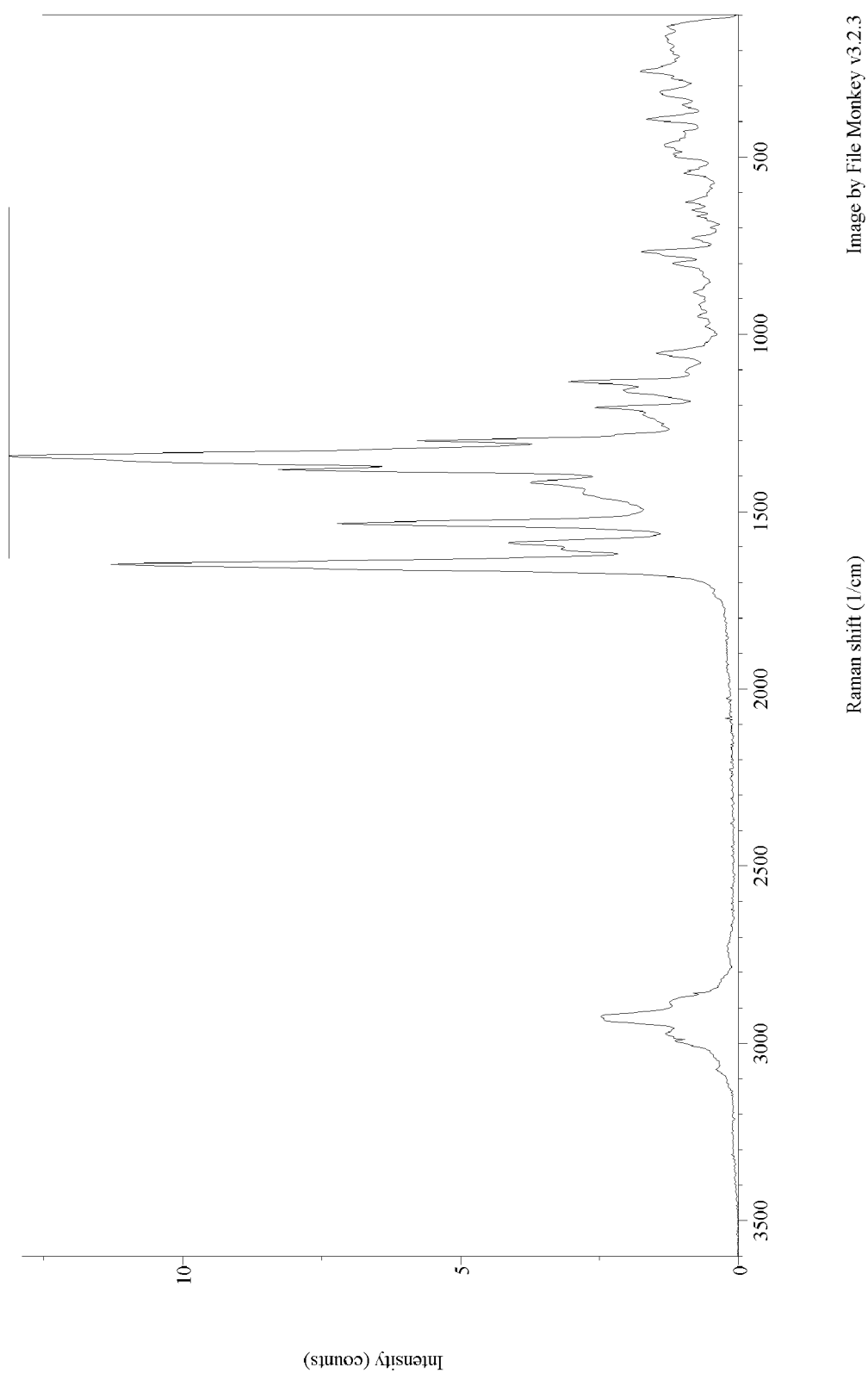


Figure 32

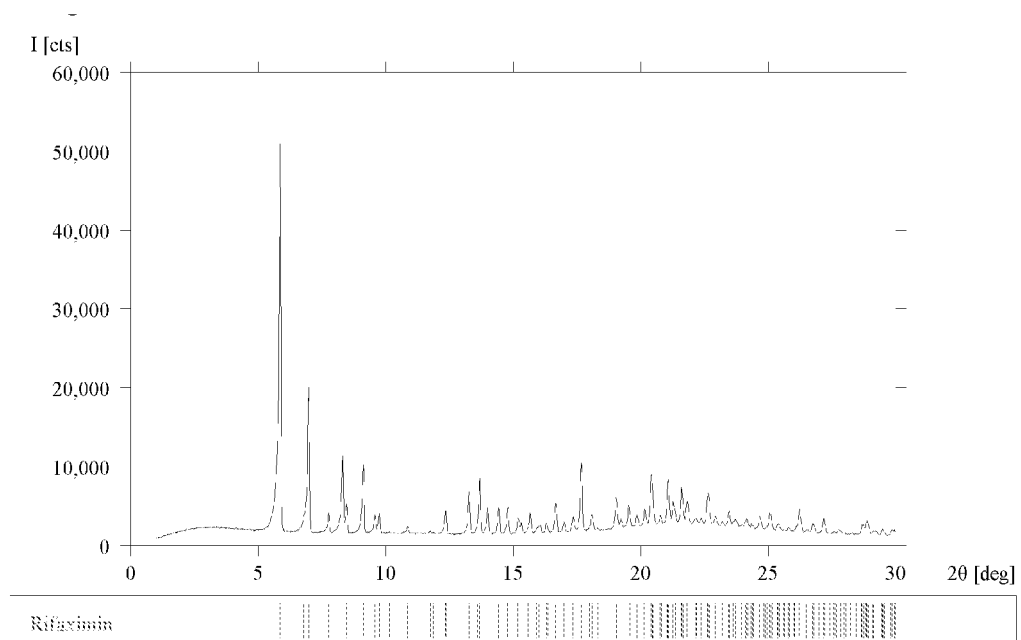


**Figure 33. Indexed unit cell parameters of Rifaximin**

|                               | Rifaximin                            |
|-------------------------------|--------------------------------------|
| Bravais Type                  | Primitive<br>Orthorhombic            |
| a [Å]                         | 12.636                               |
| b [Å]                         | 18.461                               |
| c [Å]                         | 26.003                               |
| $\alpha$ [deg]                | 90                                   |
| $\beta$ [deg]                 | 90                                   |
| $\gamma$ [deg]                | 90                                   |
| Volume [Å <sup>3</sup> /cell] | 6,065.7                              |
| Chiral Contents?              | Chiral                               |
| Extinction Symbol             | P - 21 21                            |
| Space Group(s)                | P2 <sub>2</sub> 2 <sub>1</sub> (18)* |
| Source                        | Triads Algorithm                     |

\* = Unconventional space group setting.

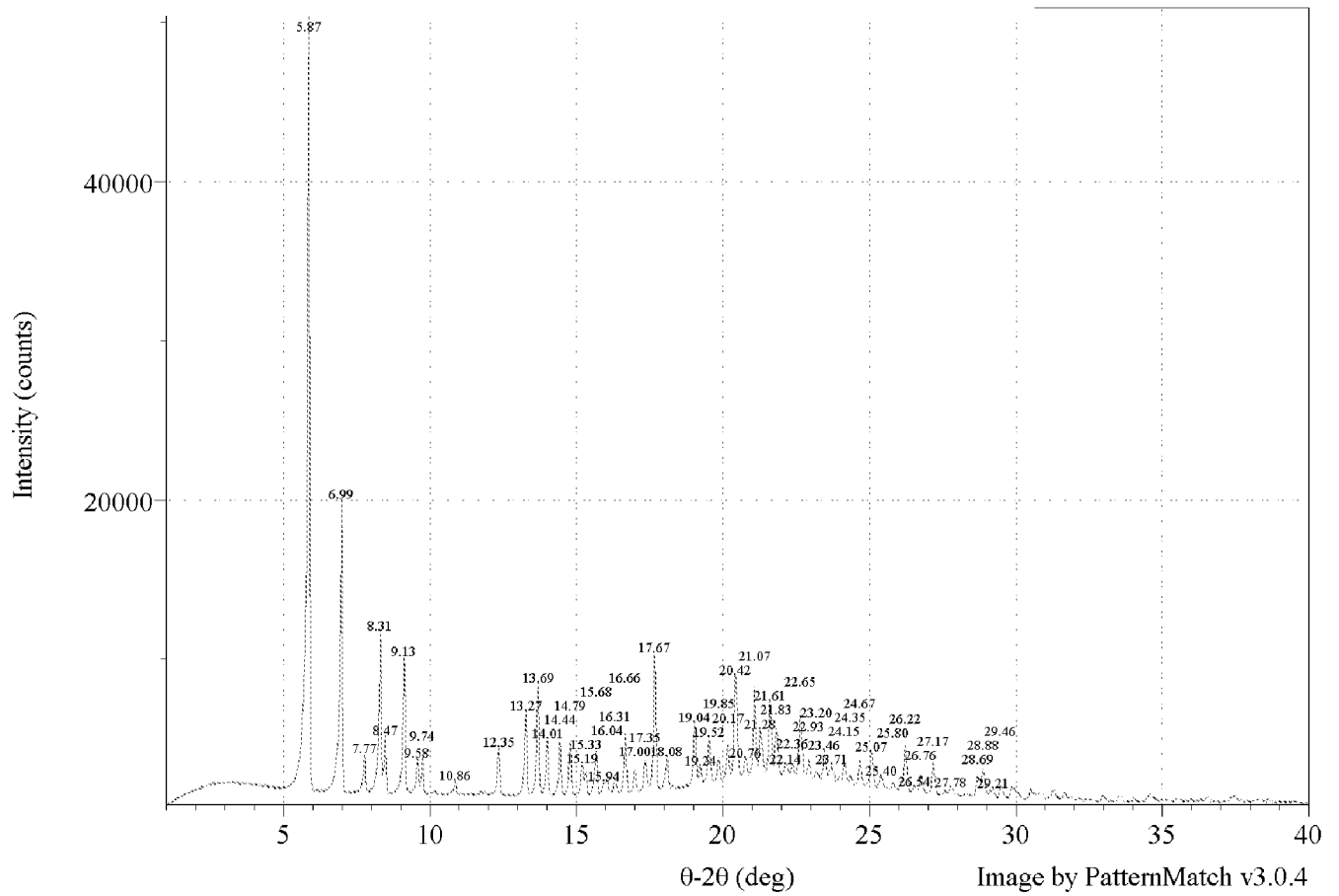
**Figure 34. List of observed peaks for Rifaximin, Form Omicron**

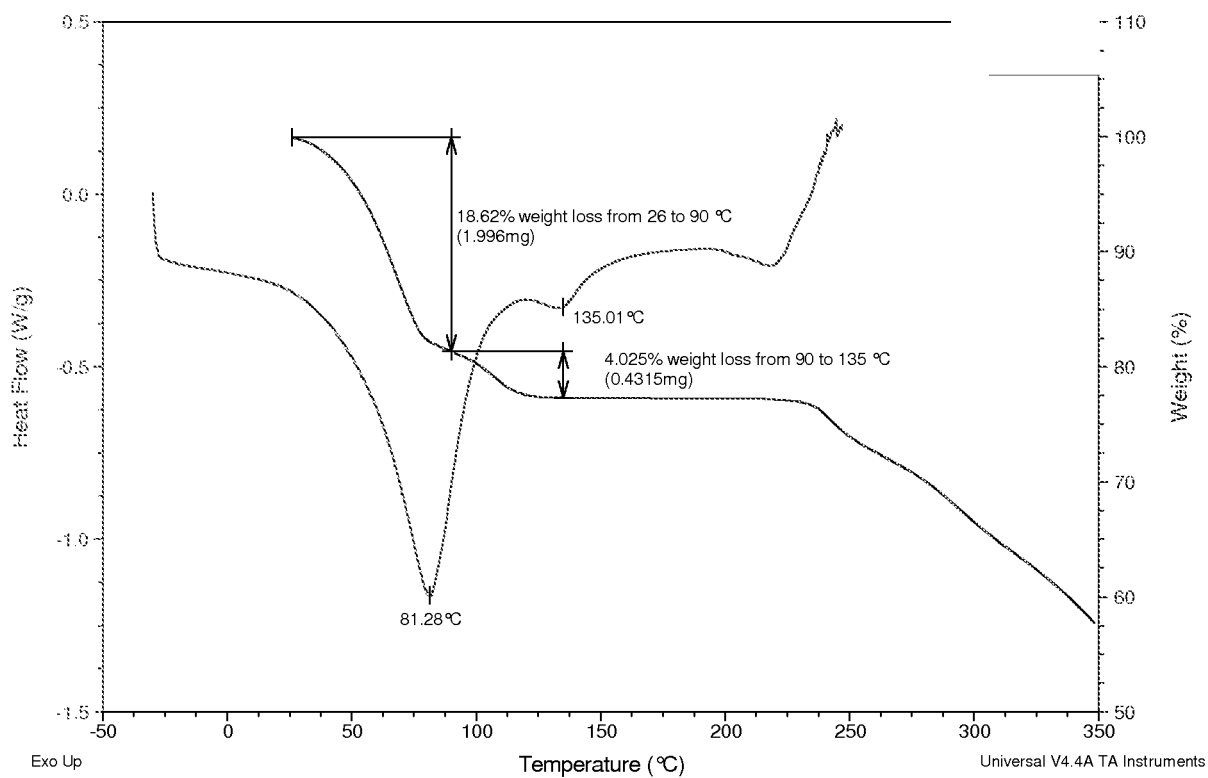
**Figure 35. Thermal analysis of Rifaximin Form Omicron,**

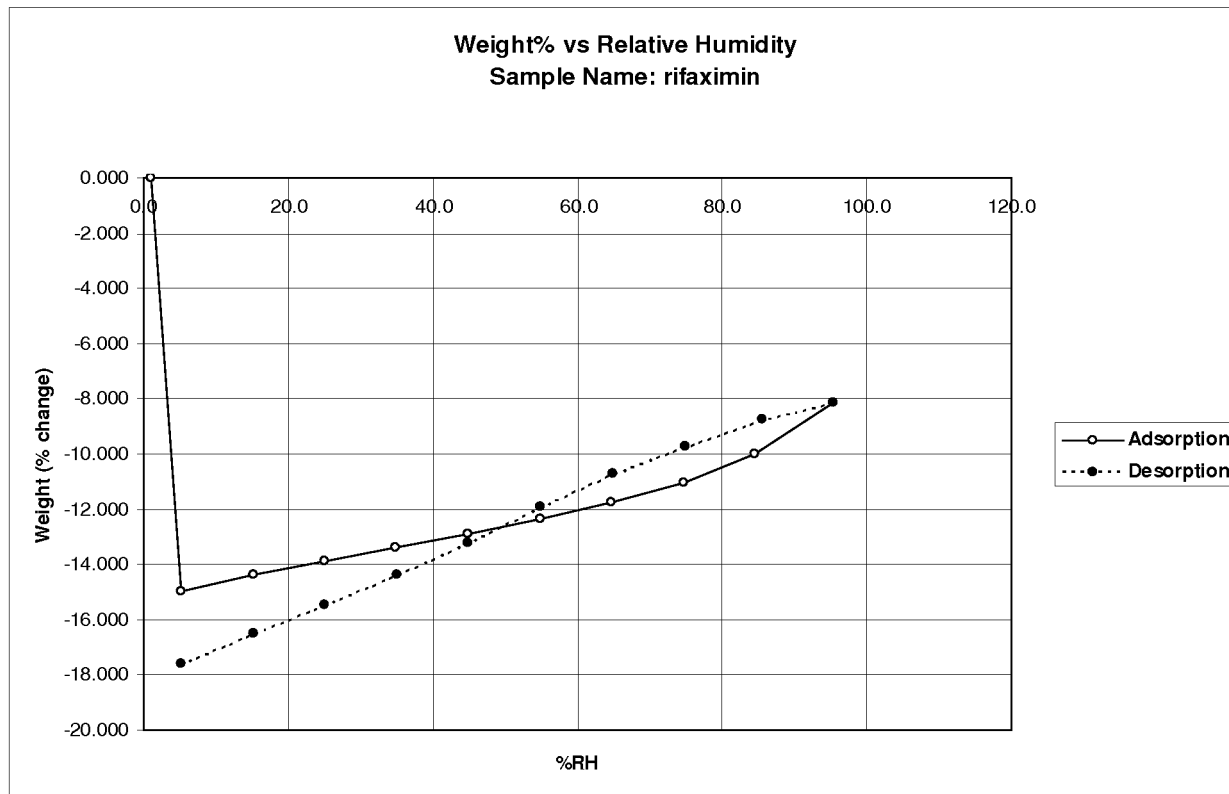
**Figure 36. Dynamic vapor sorption isotherm of a sample of Rifaximin Form Omicron**

**Figure 37. Comparison of XRPD patterns of Rifaximin Form Omicron and the post-DVS sample, Form Iota.**

Top: Form Iota

Bottom: Form Omicron

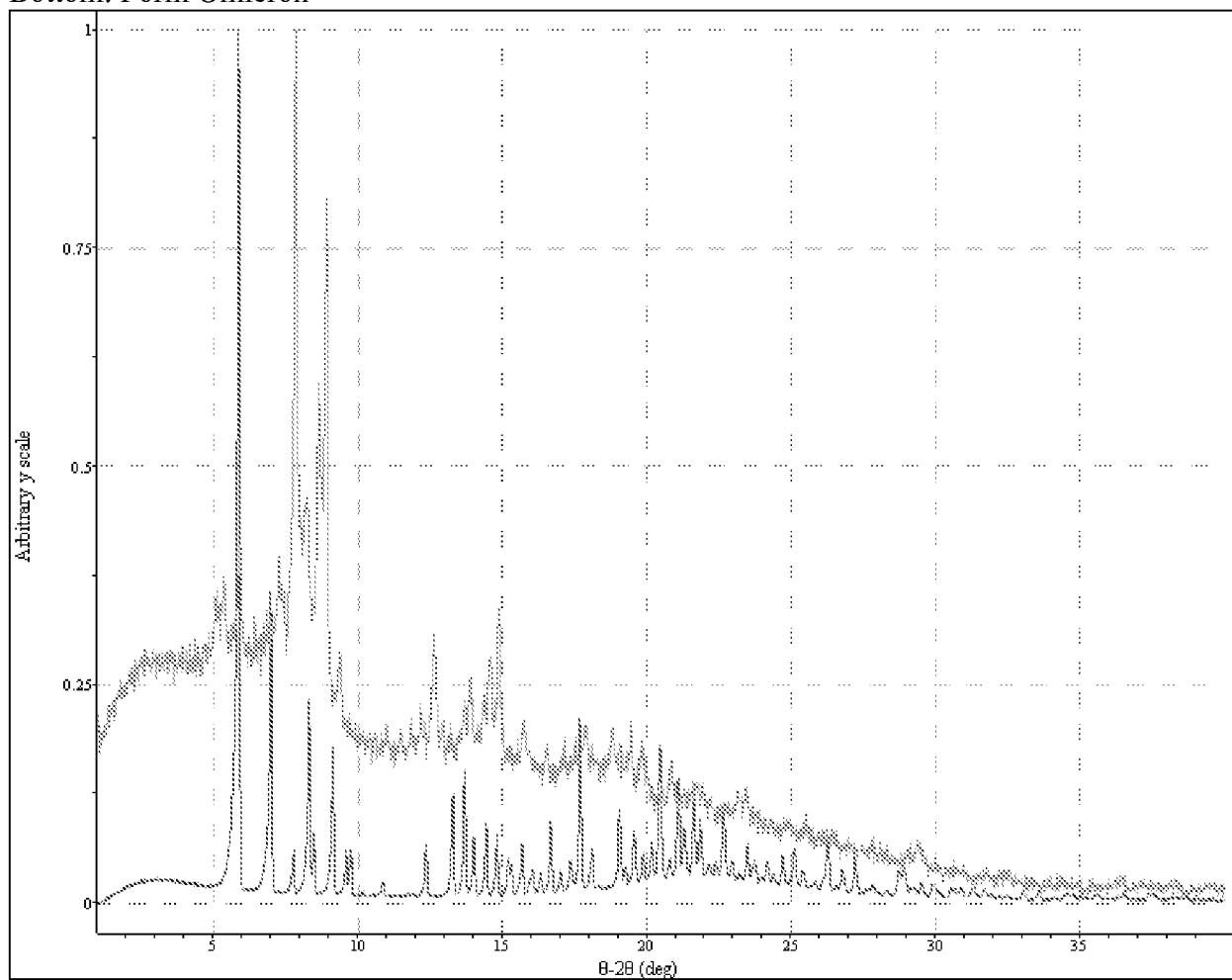


**Figure 38. ATR-IR spectrum of Rifaximin Form Omicron,**

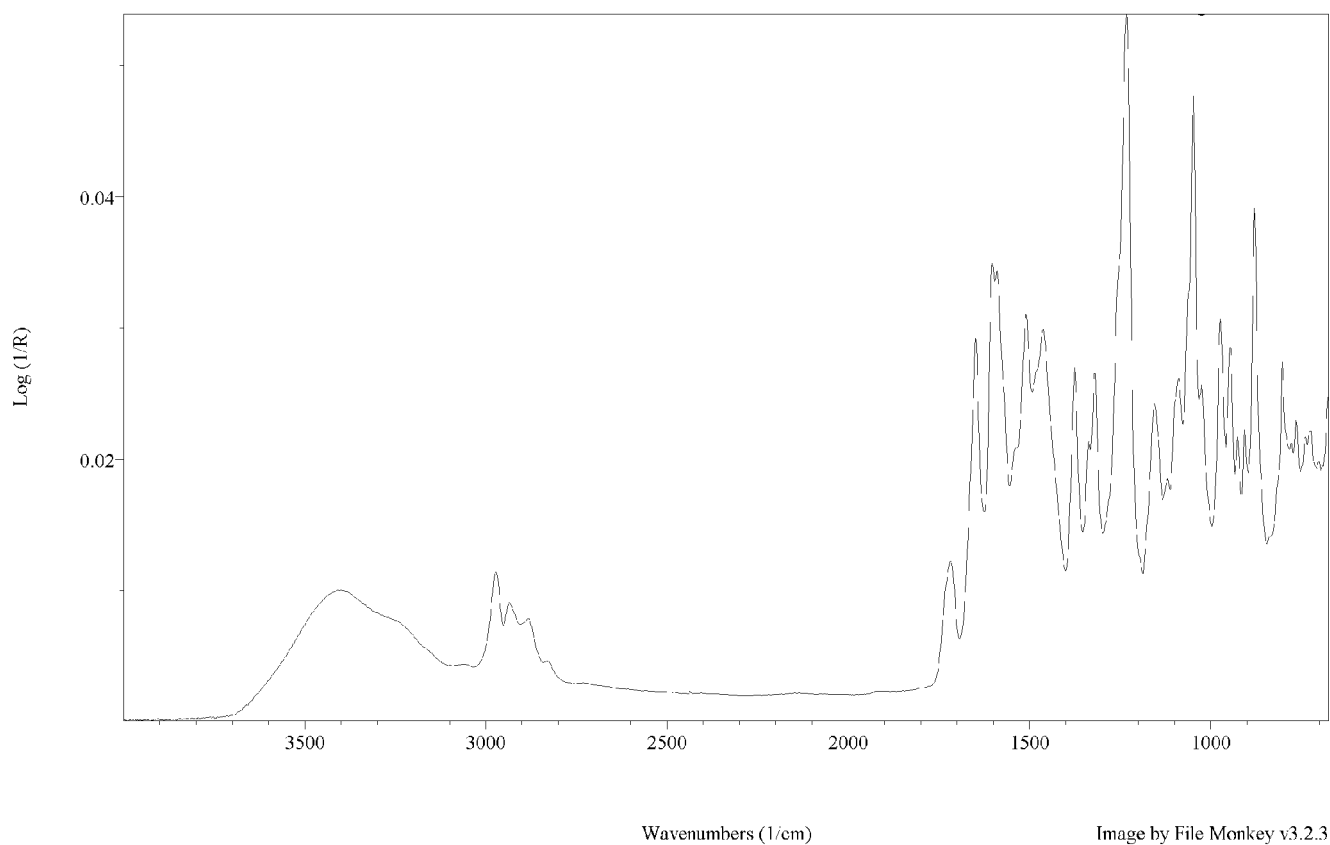


**Figure 39. Raman spectrum of Rifaximin Form Omicron,**

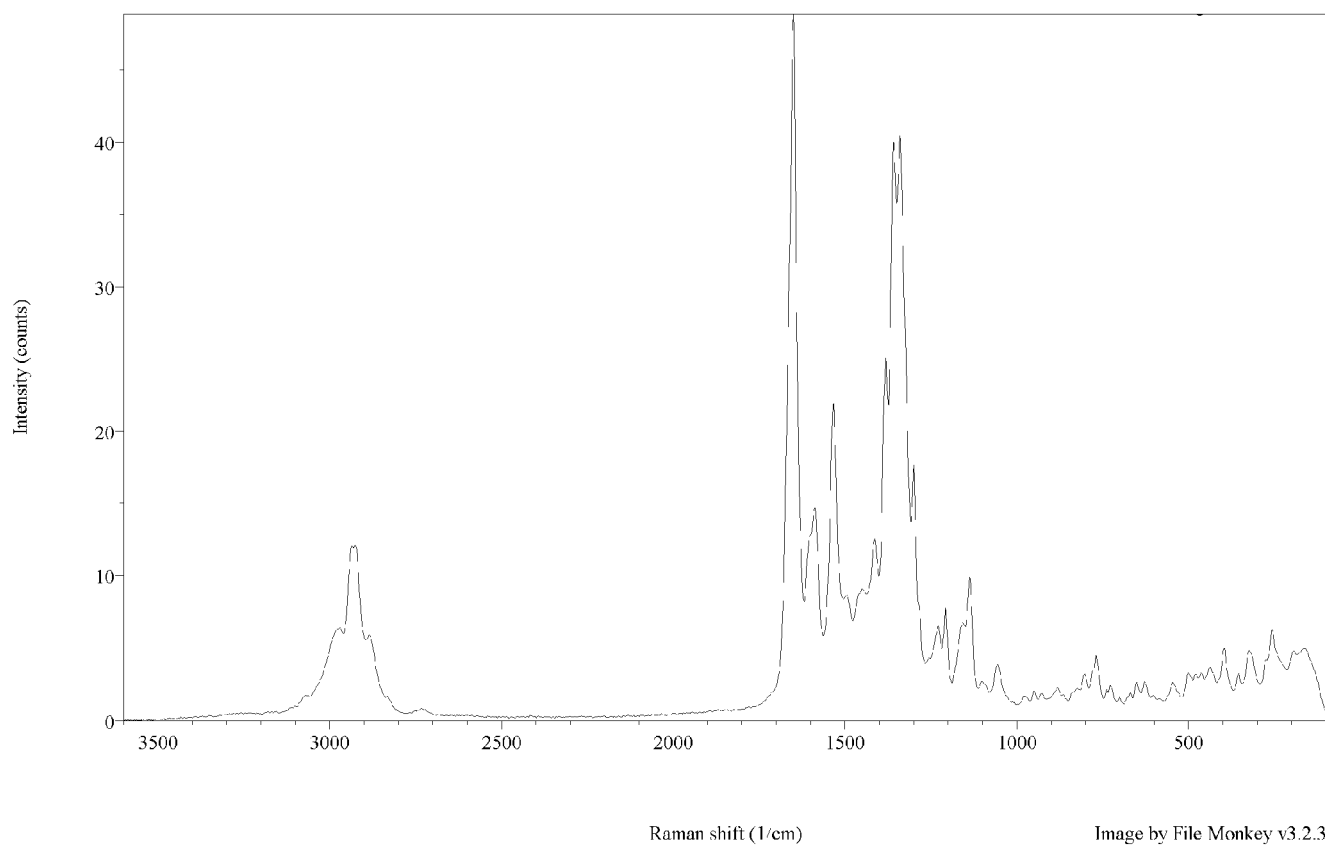


Figure 40. Solution  $^1\text{H}$  NMR spectrum of Rifaximin Form Omicron

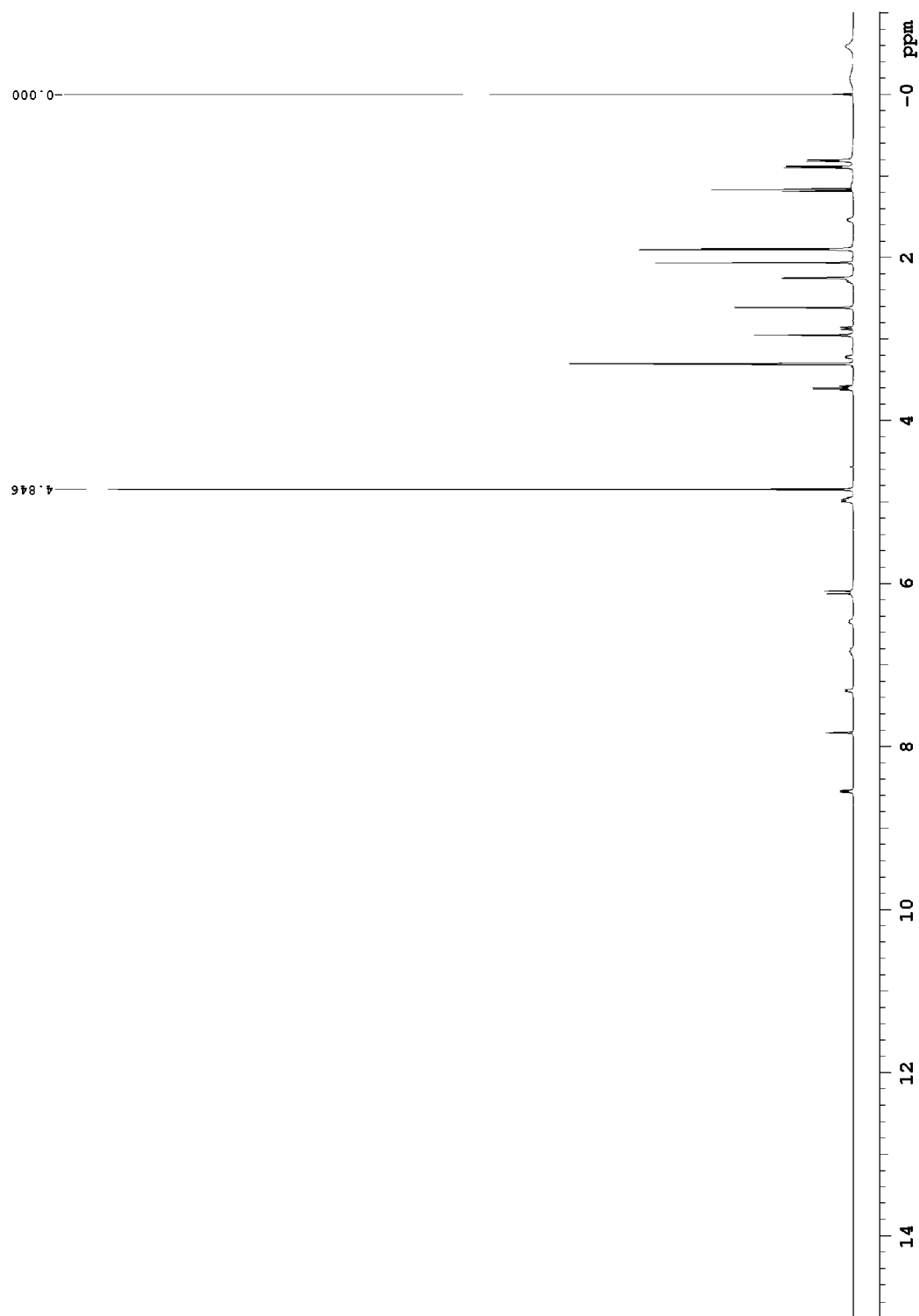


Figure 41. Solid state  $^{13}\text{C}$  NMR spectrum of Rifaximin Form Omicron

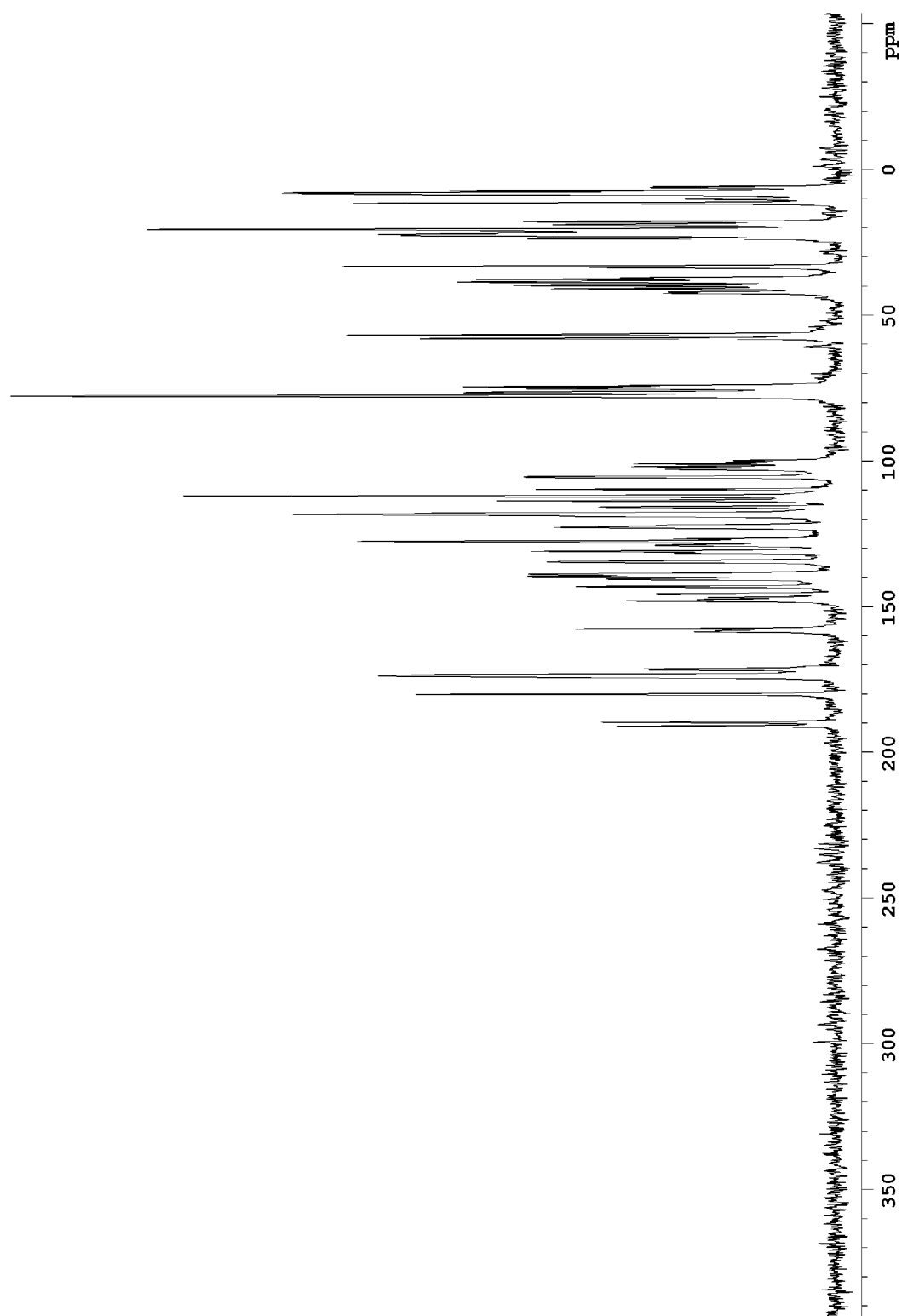


Figure 42

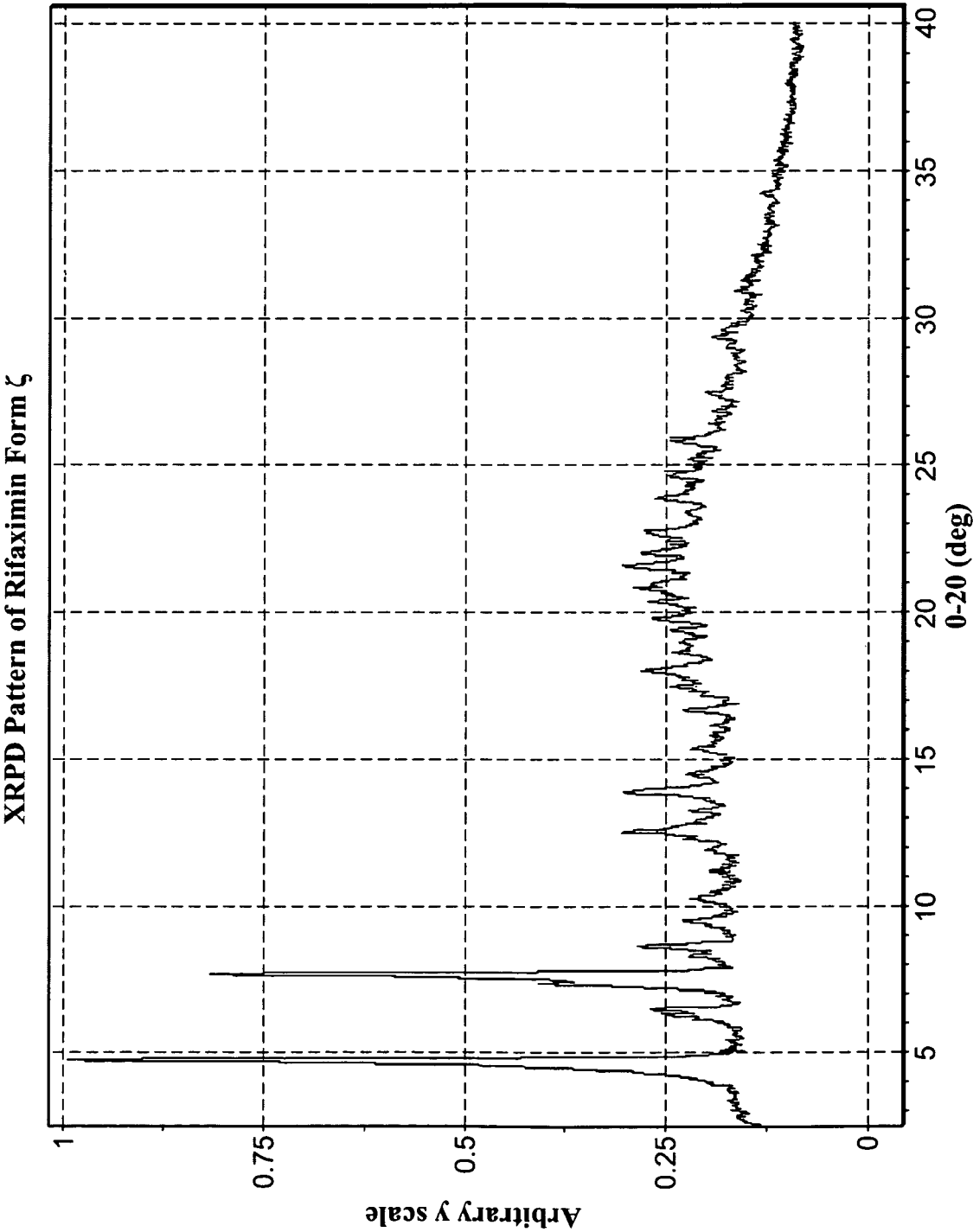


Figure 43

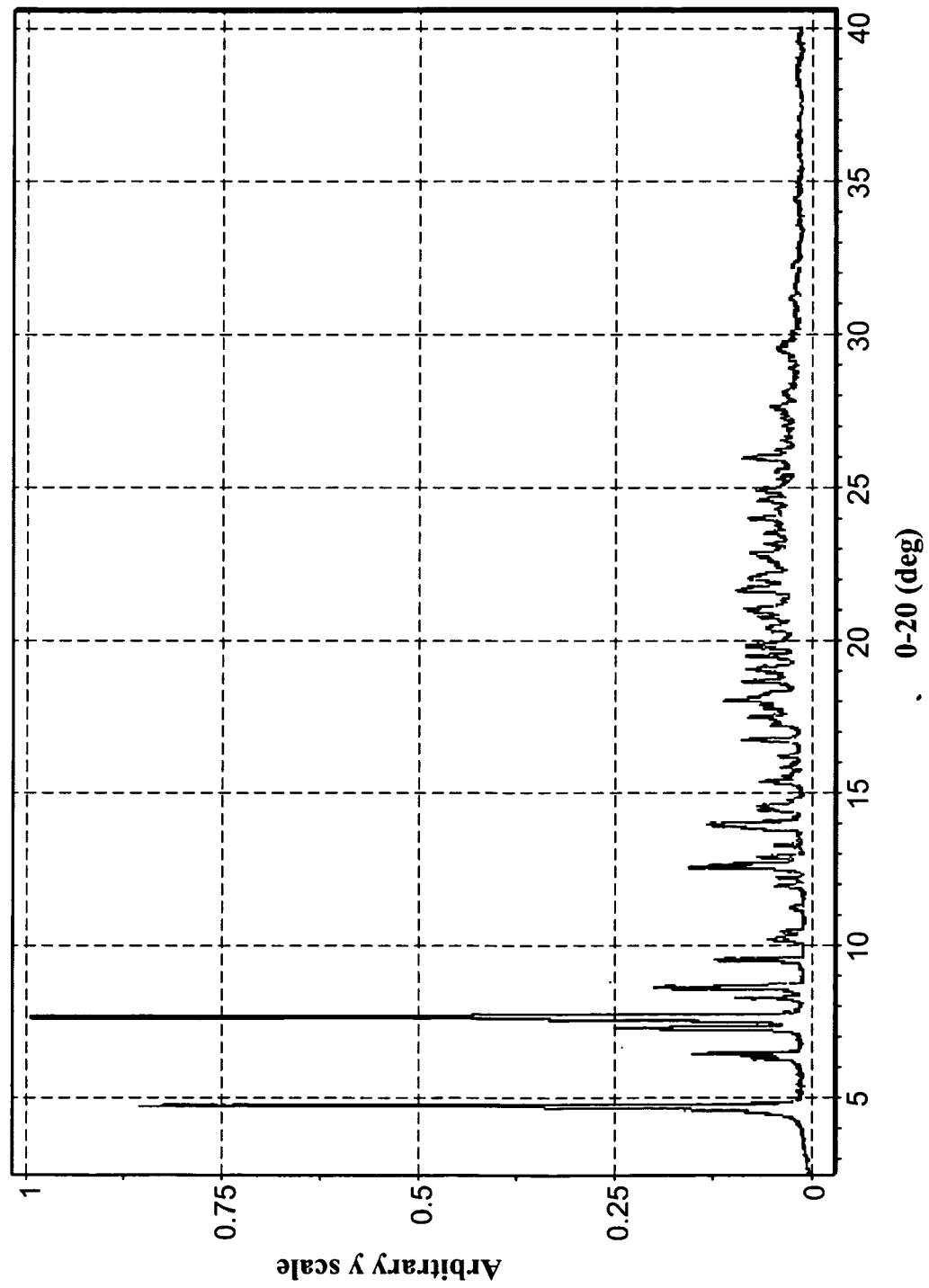


Figure 44

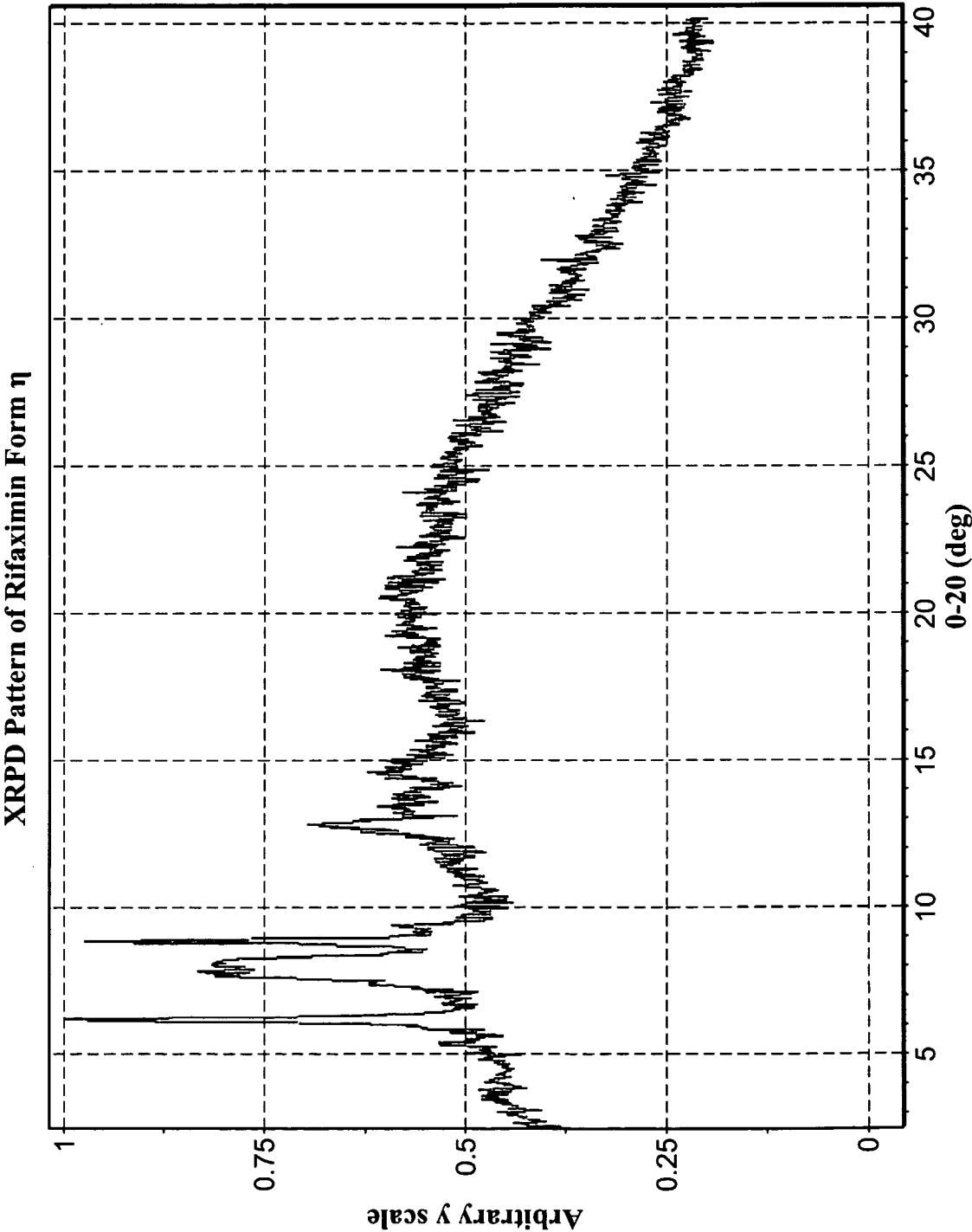


Figure 45

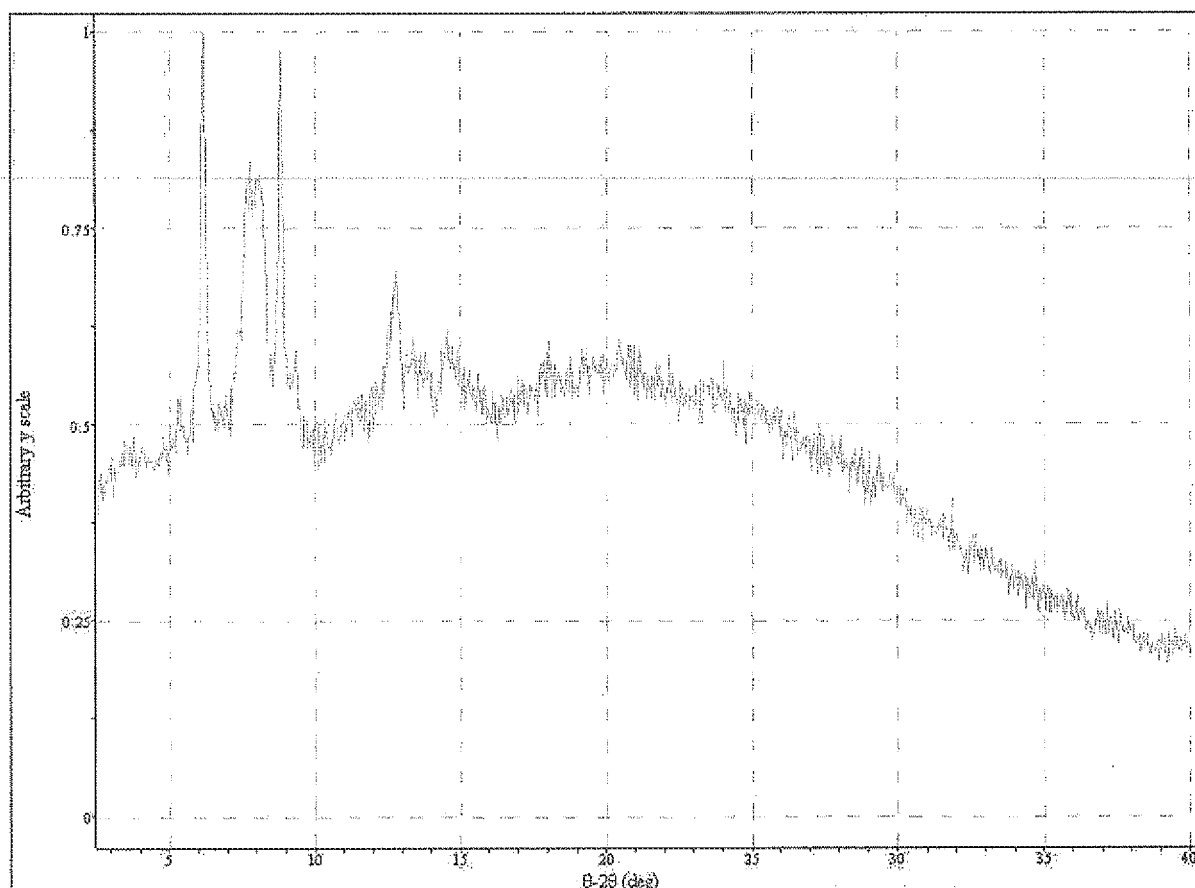
XRPD Pattern of Rifaximin Form  $\eta$ 

Figure 46

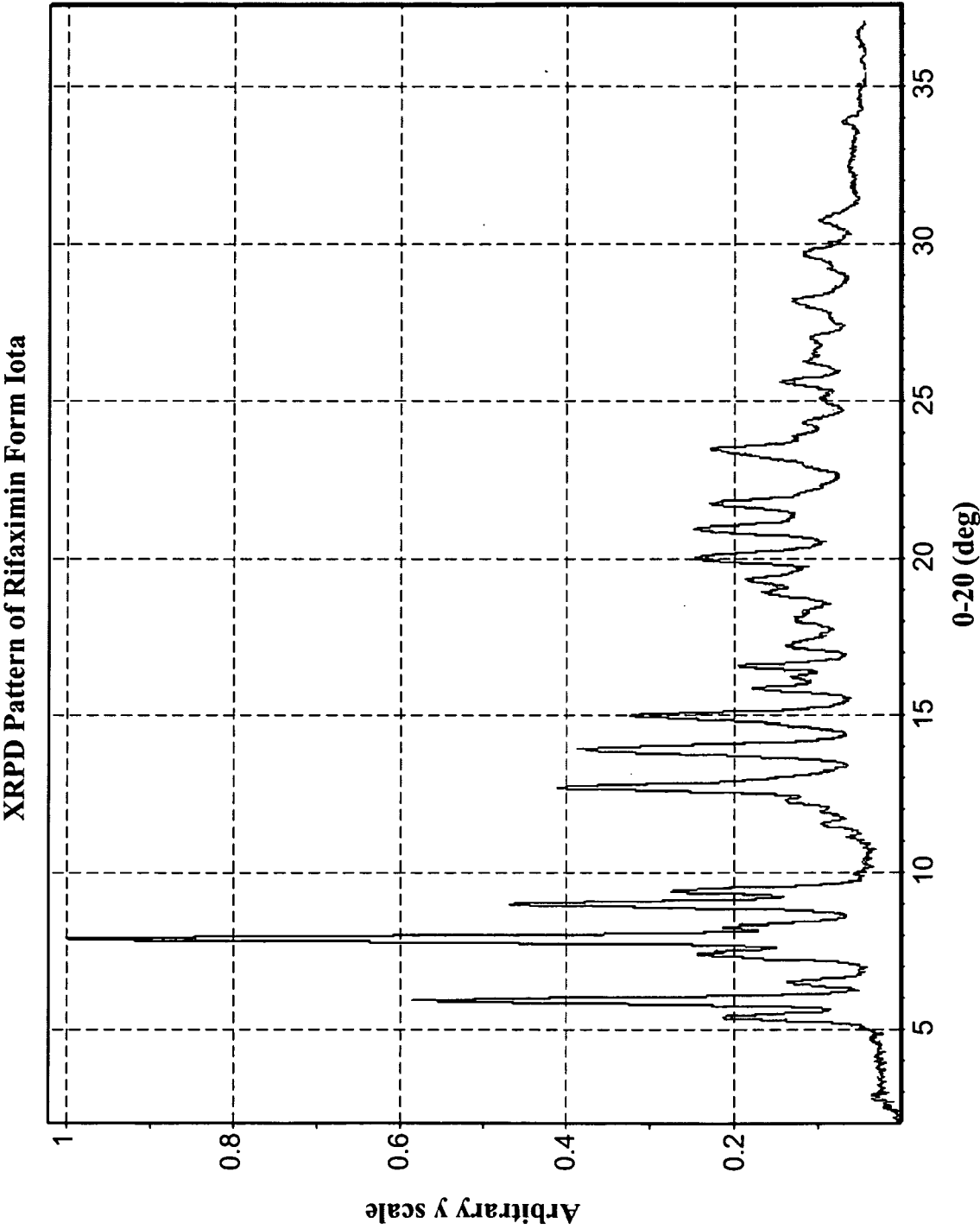
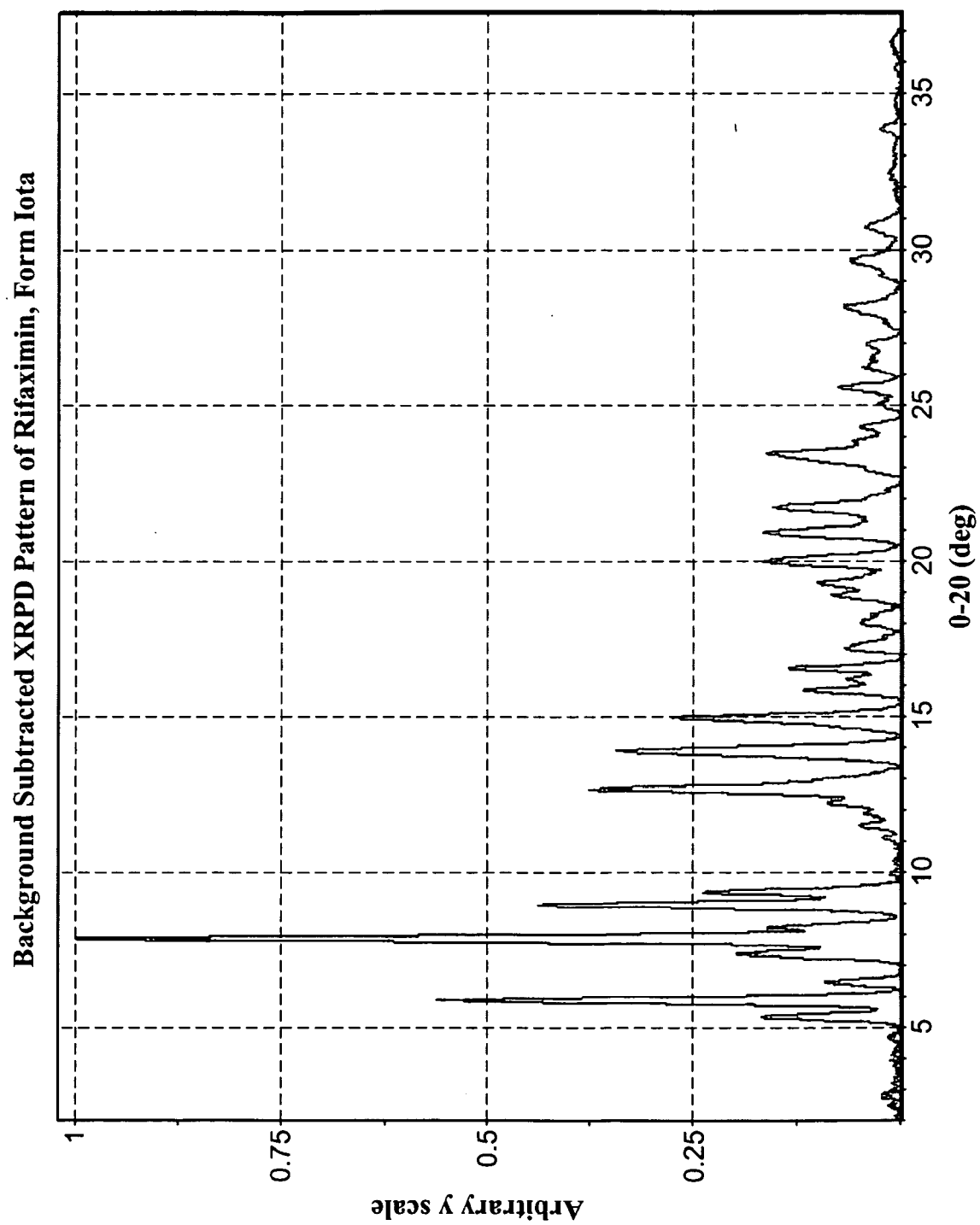


Figure 47



List of observed peaks for Rifaximin, Form Iota. Note that the peak labels in this image are meant as a visual aid.

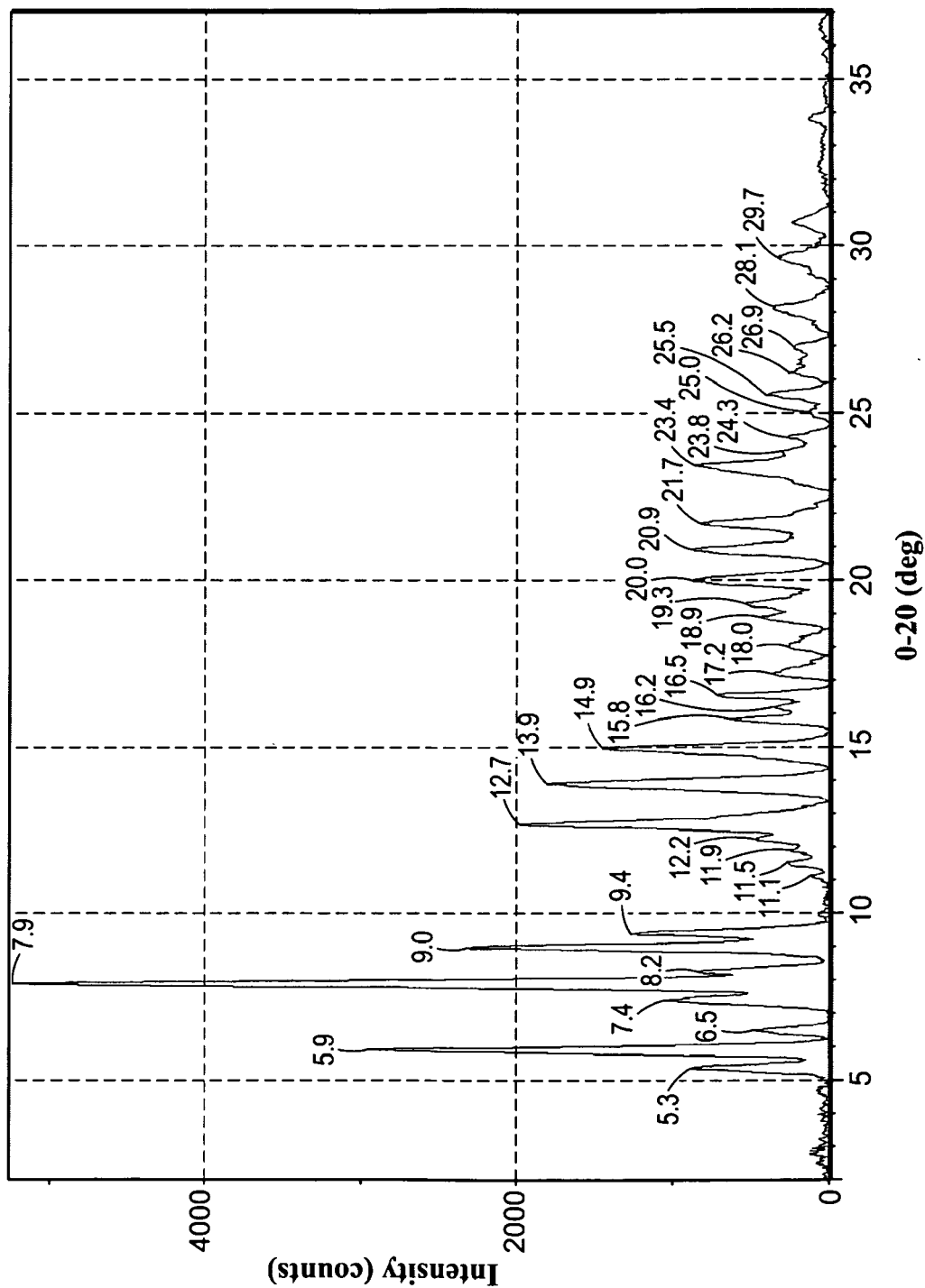


Figure 48

Figure 49A

## Observed peaks for Rifaximin, Form Iota

| $2\theta$      | $d$ space (Å)      | Intensity (%) |
|----------------|--------------------|---------------|
| $5.3 \pm 0.1$  | $16.550 \pm 0.316$ | 17            |
| $5.9 \pm 0.1$  | $15.031 \pm 0.260$ | 54            |
| $6.5 \pm 0.1$  | $13.683 \pm 0.215$ | 9             |
| $7.4 \pm 0.1$  | $12.011 \pm 0.165$ | 20            |
| $7.9 \pm 0.1$  | $11.220 \pm 0.144$ | 100           |
| $8.2 \pm 0.1$  | $10.757 \pm 0.132$ | 16            |
| $9.0 \pm 0.1$  | $9.870 \pm 0.111$  | 44            |
| $9.4 \pm 0.1$  | $9.449 \pm 0.102$  | 24            |
| $11.1 \pm 0.1$ | $7.957 \pm 0.072$  | 2             |
| $11.5 \pm 0.1$ | $7.695 \pm 0.067$  | 5             |
| $11.9 \pm 0.1$ | $7.450 \pm 0.063$  | 5             |
| $12.2 \pm 0.1$ | $7.231 \pm 0.059$  | 9             |
| $12.7 \pm 0.1$ | $6.992 \pm 0.055$  | 37            |
| $13.9 \pm 0.1$ | $6.371 \pm 0.046$  | 34            |
| $14.9 \pm 0.1$ | $5.930 \pm 0.040$  | 27            |
| $15.8 \pm 0.1$ | $5.602 \pm 0.035$  | 12            |
| $16.2 \pm 0.1$ | $5.478 \pm 0.034$  | 7             |
| $16.5 \pm 0.1$ | $5.360 \pm 0.032$  | 14            |
| $17.2 \pm 0.1$ | $5.162 \pm 0.030$  | 7             |
| $18.0 \pm 0.1$ | $4.928 \pm 0.027$  | 5             |
| $18.9 \pm 0.1$ | $4.700 \pm 0.025$  | 8             |
| $19.3 \pm 0.1$ | $4.604 \pm 0.024$  | 10            |
| $20.0 \pm 0.1$ | $4.448 \pm 0.022$  | 17            |
| $20.9 \pm 0.1$ | $4.250 \pm 0.020$  | 17            |
| $21.7 \pm 0.1$ | $4.099 \pm 0.019$  | 15            |
| $23.4 \pm 0.1$ | $3.795 \pm 0.016$  | 16            |
| $23.8 \pm 0.1$ | $3.733 \pm 0.015$  | 6             |
| $24.3 \pm 0.1$ | $3.663 \pm 0.015$  | 5             |
| $25.0 \pm 0.1$ | $3.559 \pm 0.014$  | 3             |
| $25.5 \pm 0.1$ | $3.488 \pm 0.013$  | 8             |
| $26.2 \pm 0.1$ | $3.401 \pm 0.013$  | 5             |
| $26.9 \pm 0.1$ | $3.310 \pm 0.012$  | 4             |
| $28.1 \pm 0.1$ | $3.176 \pm 0.011$  | 7             |
| $29.7 \pm 0.1$ | $3.010 \pm 0.010$  | 6             |

Figure 49B

## Prominent peaks for Rifaximin, Form Iota

| $2\theta$      | $d$ space (Å)      | Intensity (%) |
|----------------|--------------------|---------------|
| $5.9 \pm 0.1$  | $15.031 \pm 0.260$ | 54            |
| $7.9 \pm 0.1$  | $11.220 \pm 0.144$ | 100           |
| $9.0 \pm 0.1$  | $9.870 \pm 0.111$  | 44            |
| $12.7 \pm 0.1$ | $6.992 \pm 0.055$  | 37            |
| $13.9 \pm 0.1$ | $6.371 \pm 0.046$  | 34            |
| $14.9 \pm 0.1$ | $5.930 \pm 0.040$  | 27            |

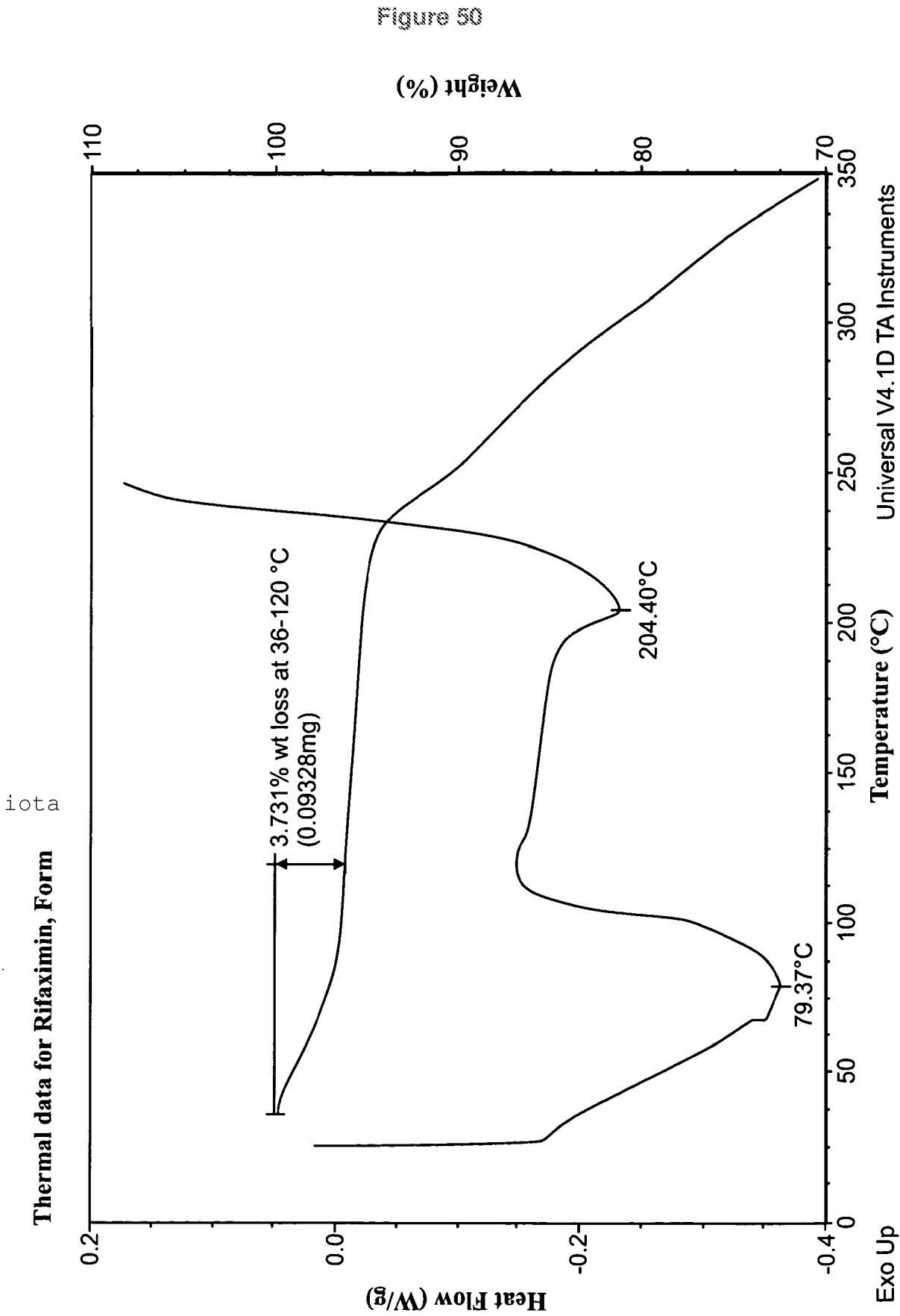
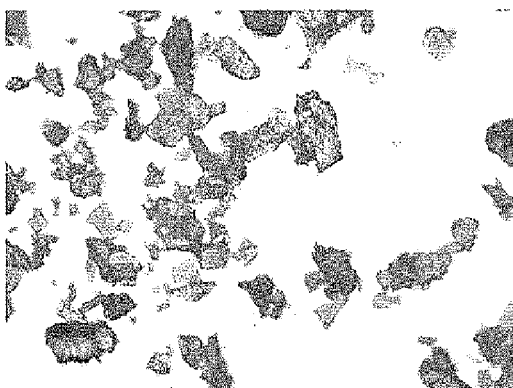
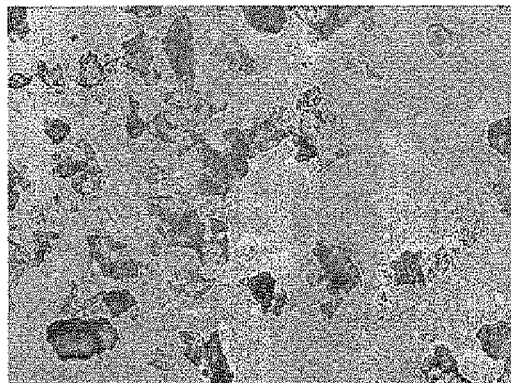


Figure 51A

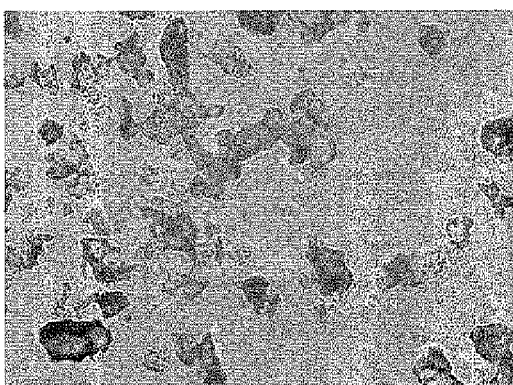
Hot Stage microscopy of Rifaximin, Form i.



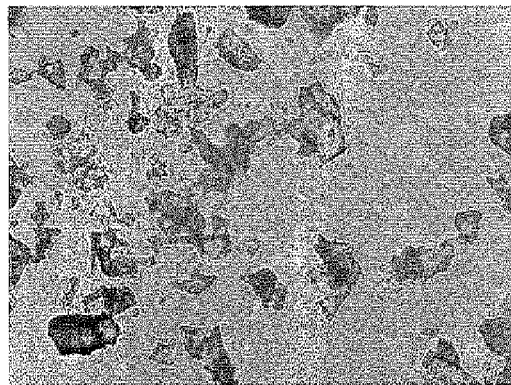
T= 30°C



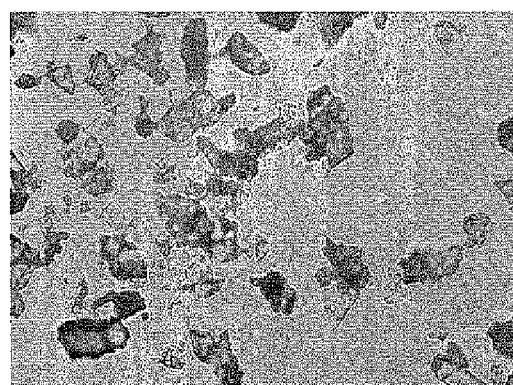
T= 30°C



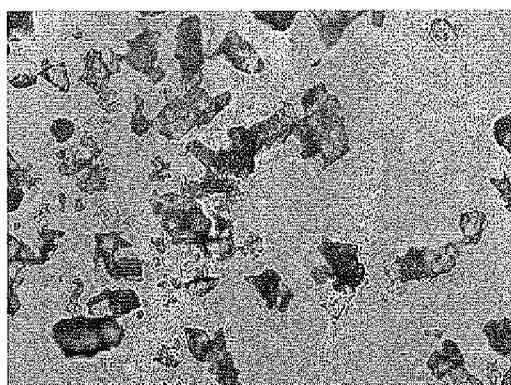
T= 80°C



T= 120°C



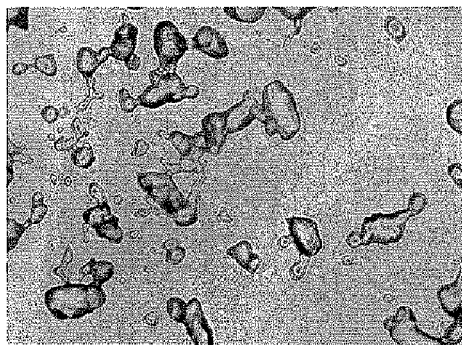
T= 190°C



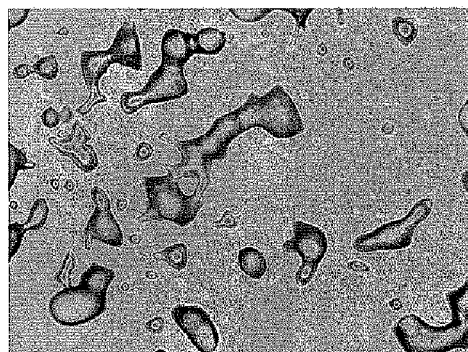
T= 204°C

Figure 51B

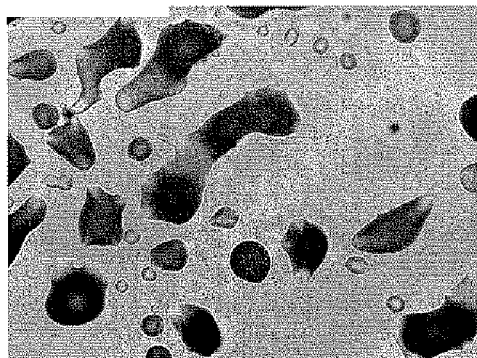
Hot Stage microscopy of Rifaximin, Form i.



T= 218°C



T= 222°C



T= 250°C

Figure 52

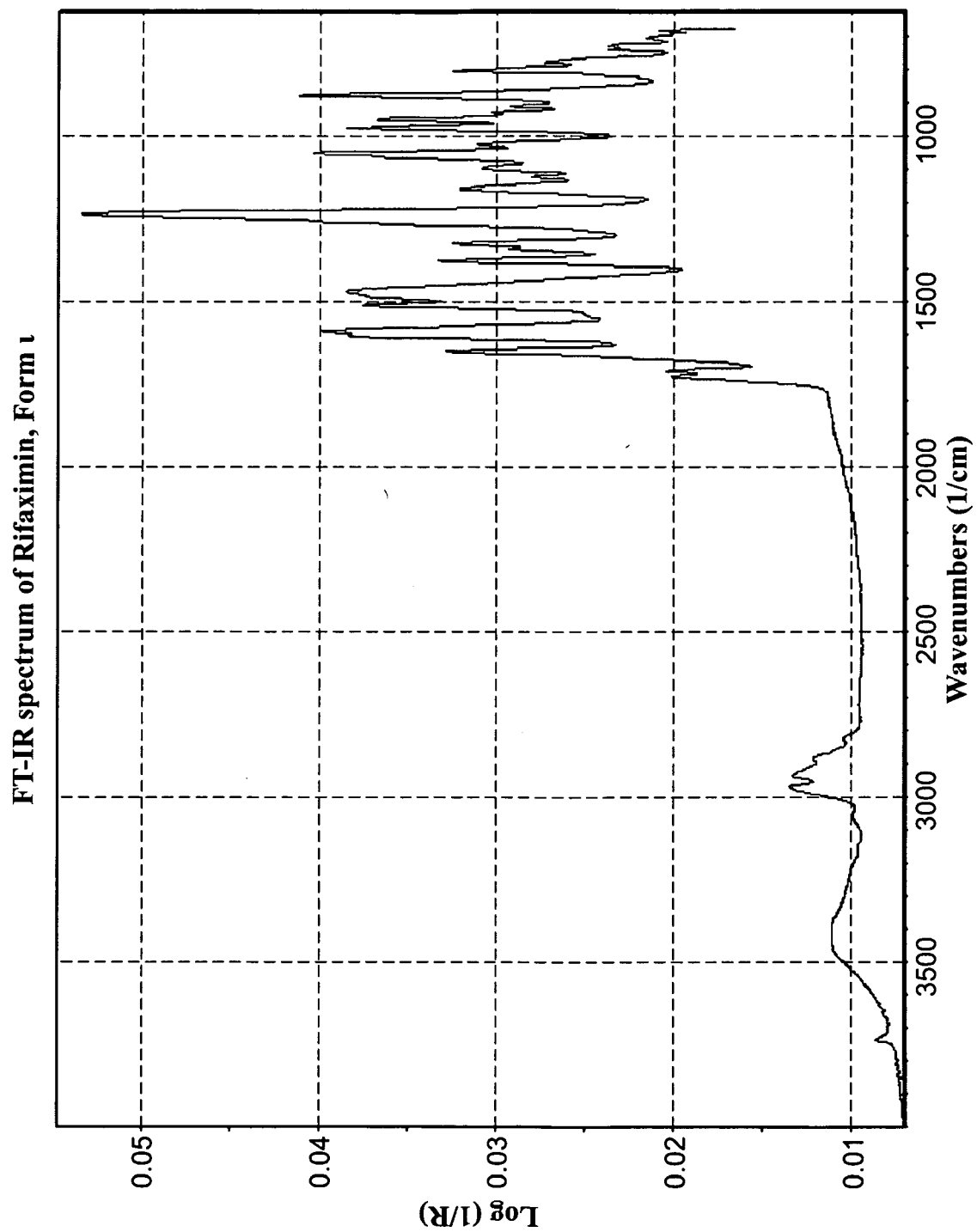


Figure 53

