pharmaceutics

# Supplementary Materials: Stabilisation and Growth of Metastable Form II of Fluconazole in Amorphous Solid Dispersions

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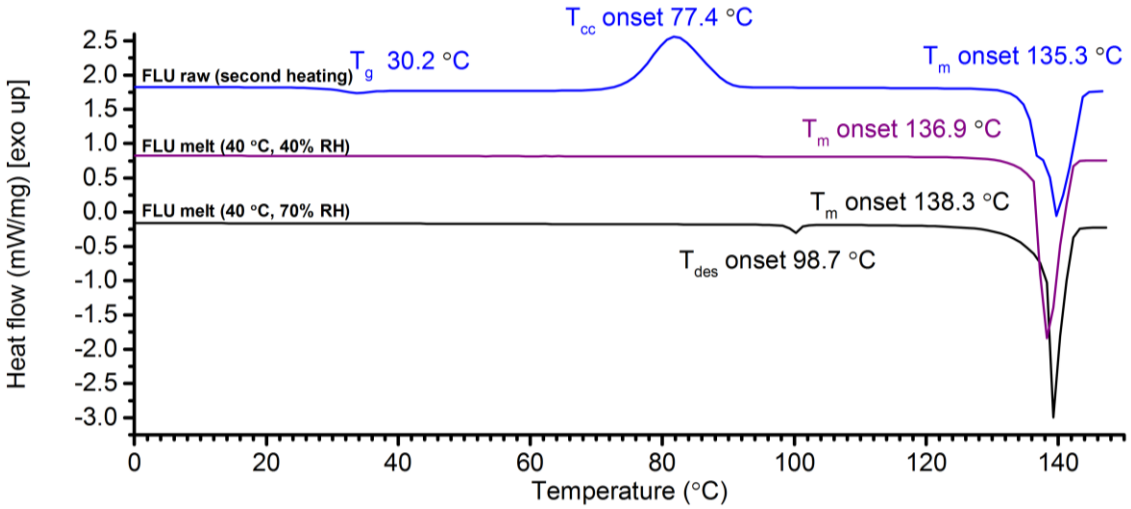


**Figure S1.** DSC curves of raw FLU (blue, second heating) and FLU crystallised from supercooled amorphous glass after 14 days of accelerated ageing at 40 °C, 40% RH (purple) and at 40 °C, 70% RH (black).

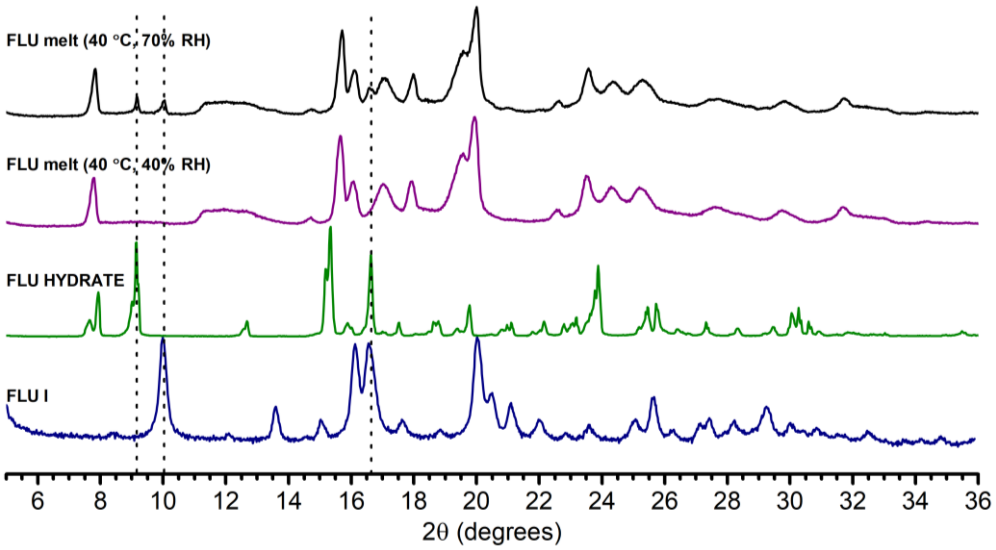


**Figure S2.** PXRD patterns of FLU form I (blue), FLU hydrate (green) and FLU recrystallized from supercooled amorphous glass after 14 days of accelerated ageing at 40 °C, 40% RH (purple) and at 40 °C, 70% RH (black).

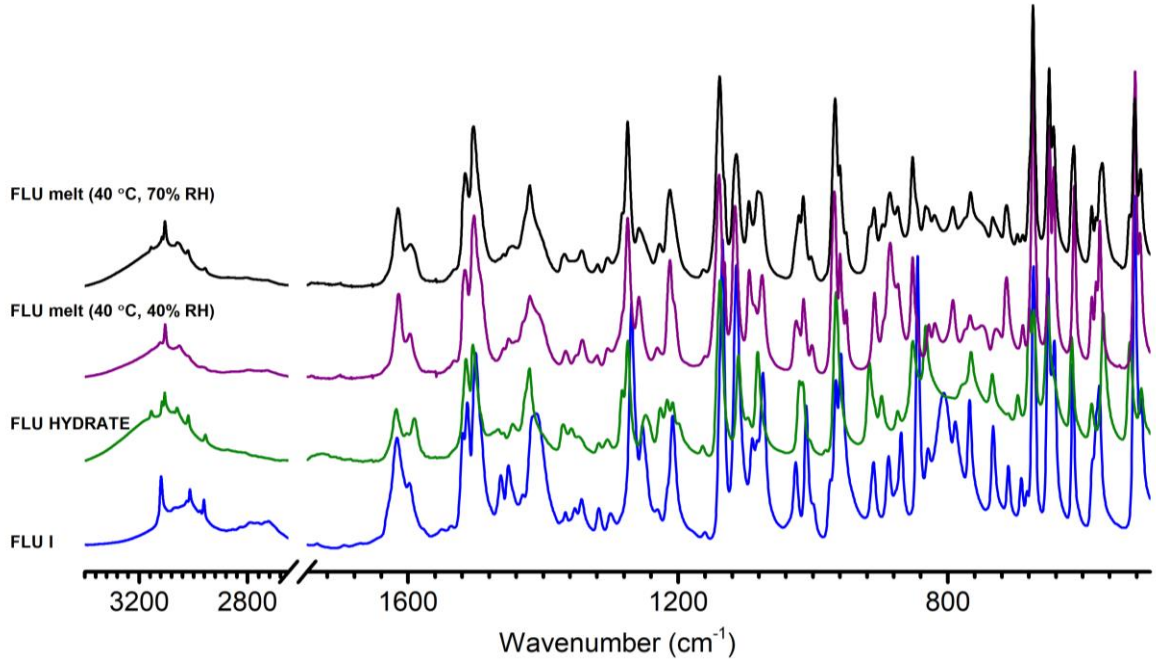


**Figure S3.** FTIR spectra of FLU form I (blue), FLU hydrate (green) and FLU samples recrystallized from supercooled amorphous glass after 14 days of accelerated ageing at 40 °C, 40% RH (purple) and at 40 °C, 70% RH (black).

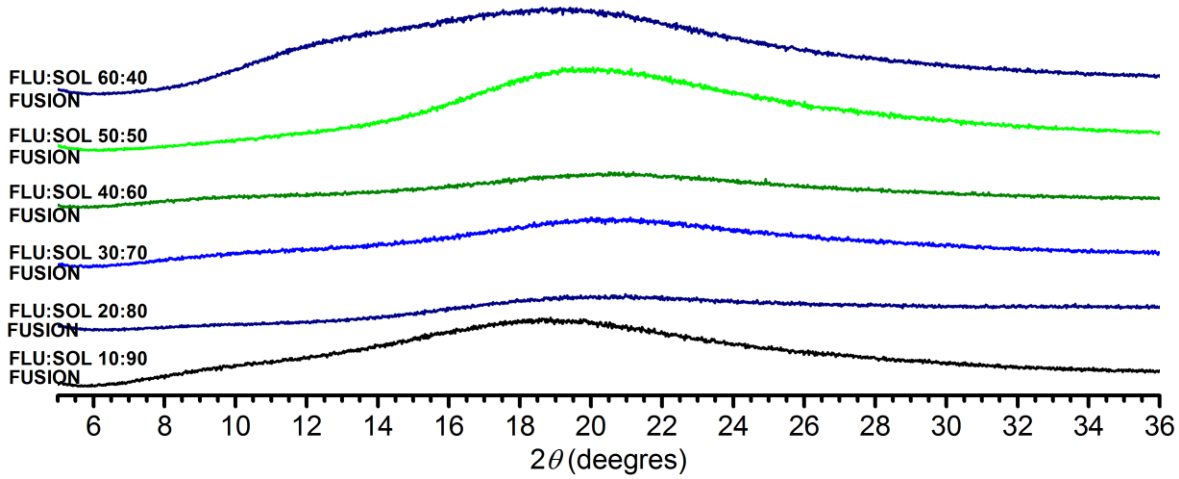


**Figure S4.** PXRD patterns of FLU:SOL solid dispersions obtained using fusion method recorded immediately after preparation.

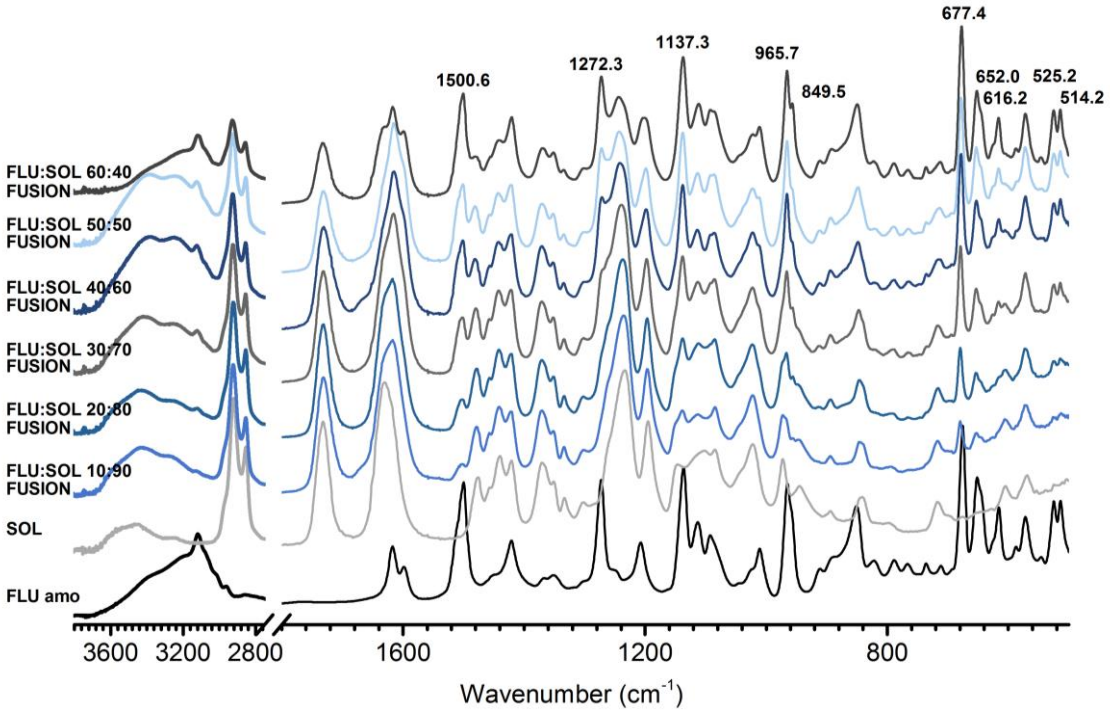


**Figure S5.** FTIR spectra of FLU:SOL solid dispersions obtained using fusion method recorded immediately after preparation.

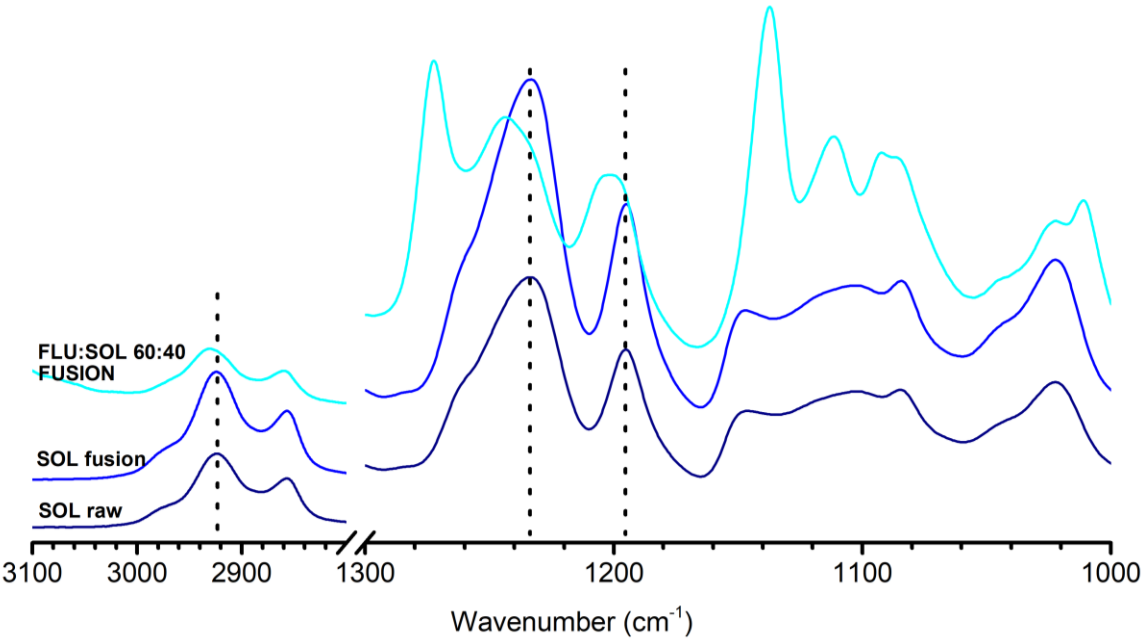


**Figure S6**. FTIR spectra of raw Soluplus, Soluplus heated to 145 °C and cooled to RT (SOL fusion) and 60:40 FLU:SOL solid dispersion obtained using fusion method.

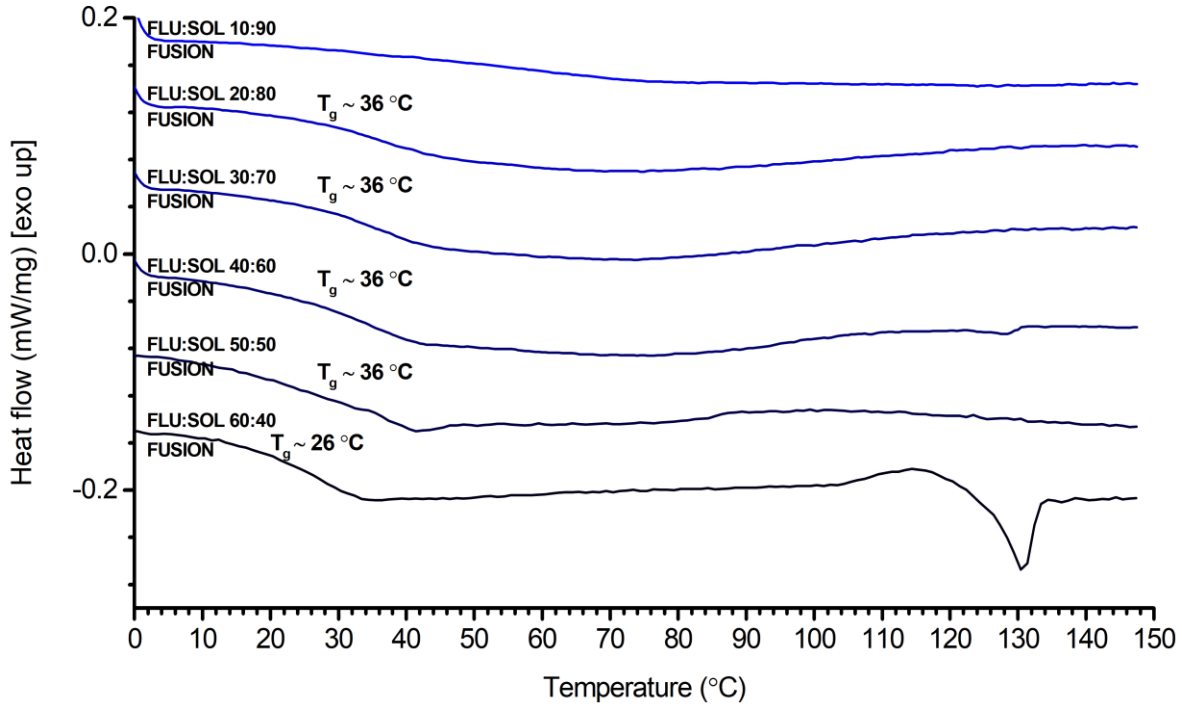


**Figure S7.** DSC curves of FLU:SOL solid dispersions obtained using fusion method recorded immediately after preparation.

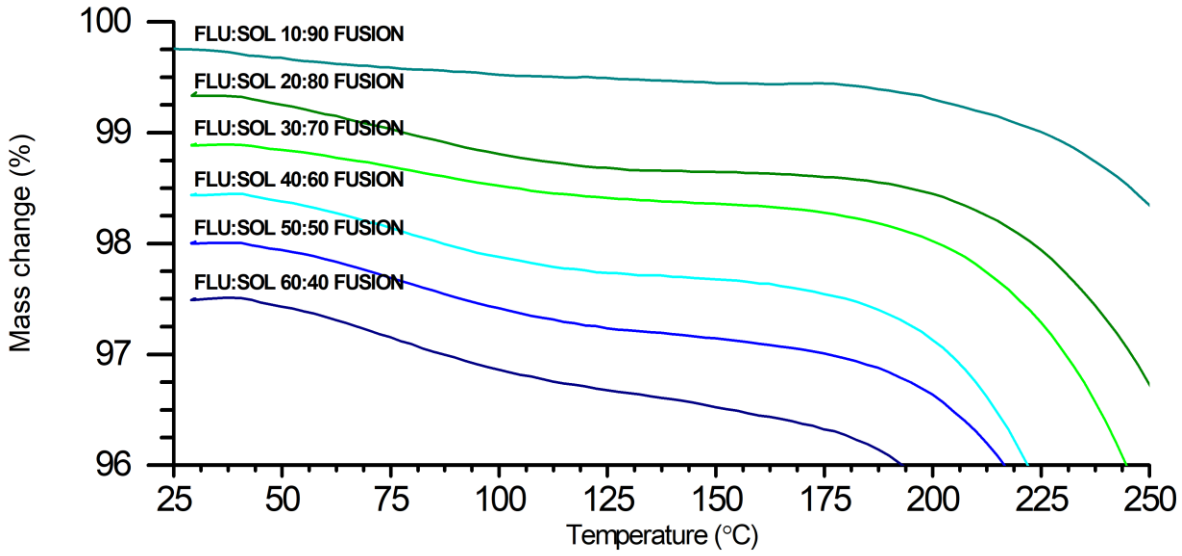


**Figure S8.** TGA curves of FLU:SOL solid dispersions obtained using fusion method recorded immediately after preparation.

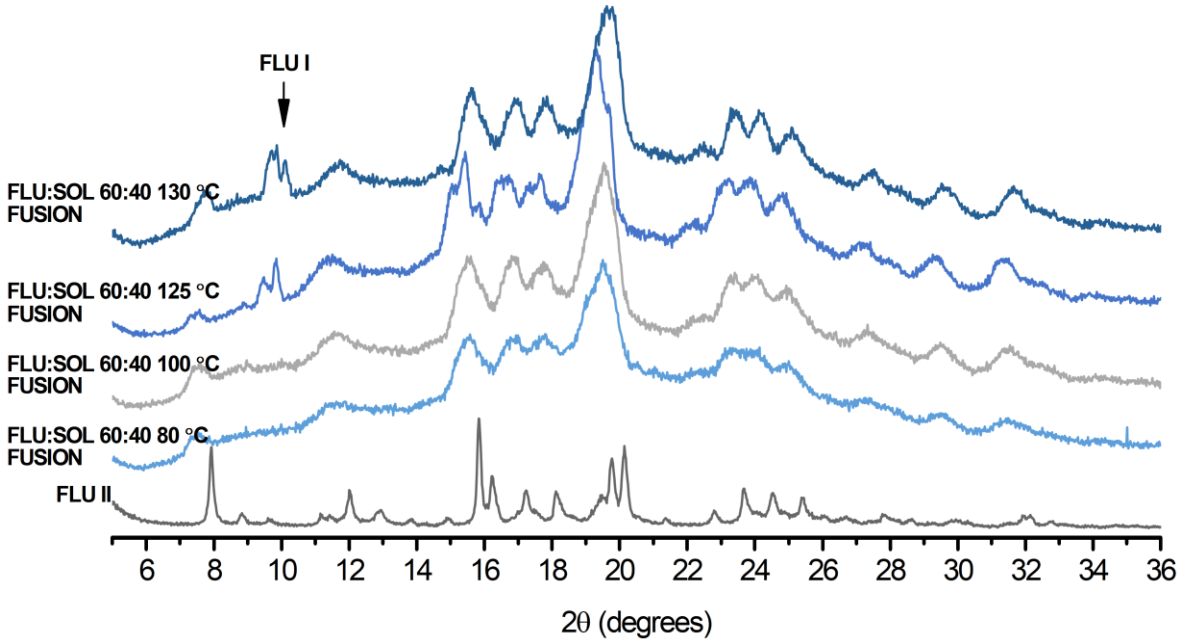


**Figure S9.** PXRD patterns of FLU:SOL 60:40 solid dispersion prepared using fusion method after heating at 80, 100, 125 and 130 ± 2 °C for 15 minutes. The PXRD pattern of FLU form II is provided for comparison.

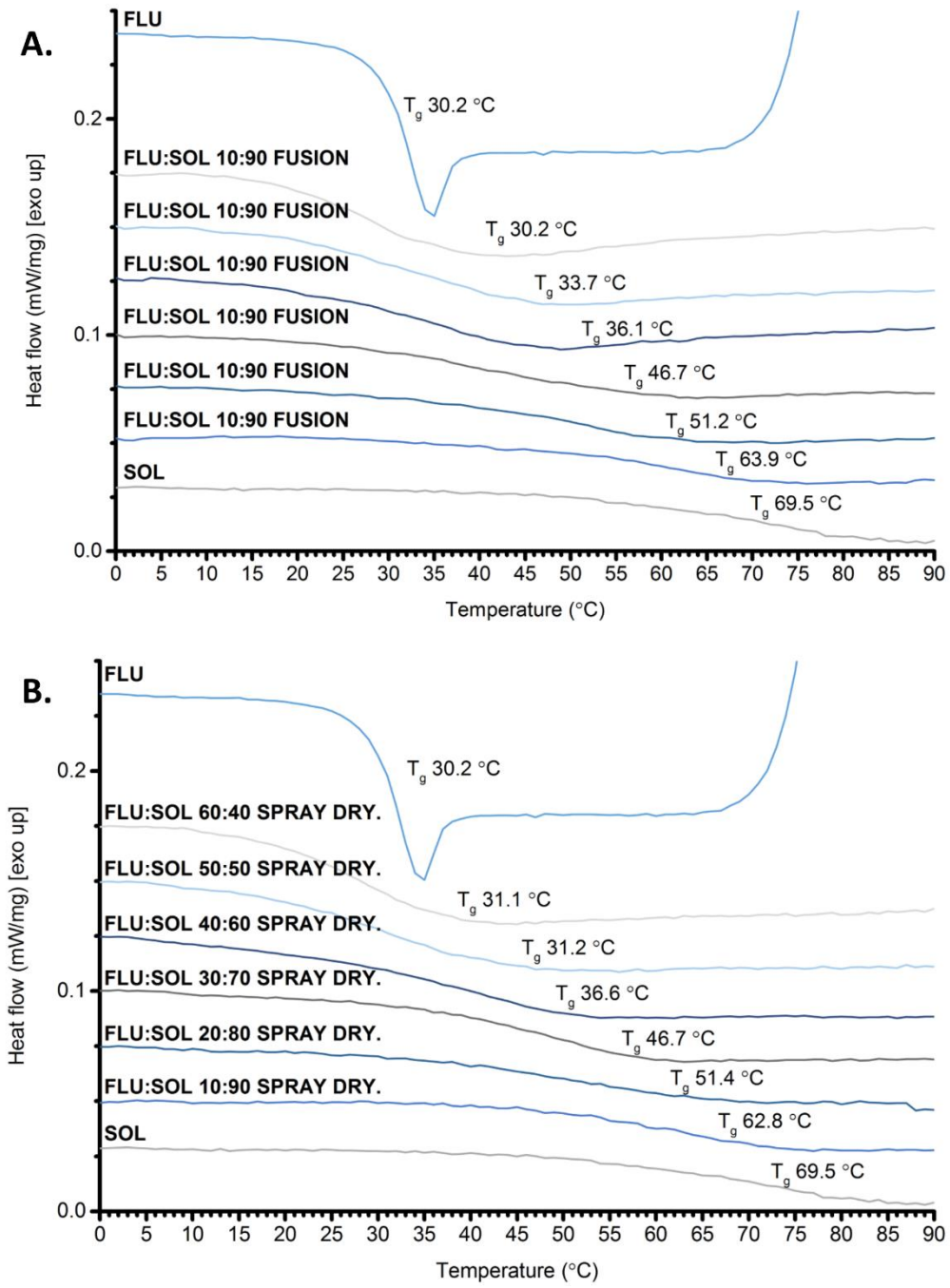


**Figure S10.** DSC curves (zoomed $T_g$ temperature region in the second heating cycle) of FLU, SOL and FLU:SOL solid dispersions prepared using fusion (**A**) and spray drying (**B**) method with determined $T_g$ of the obtained materials.

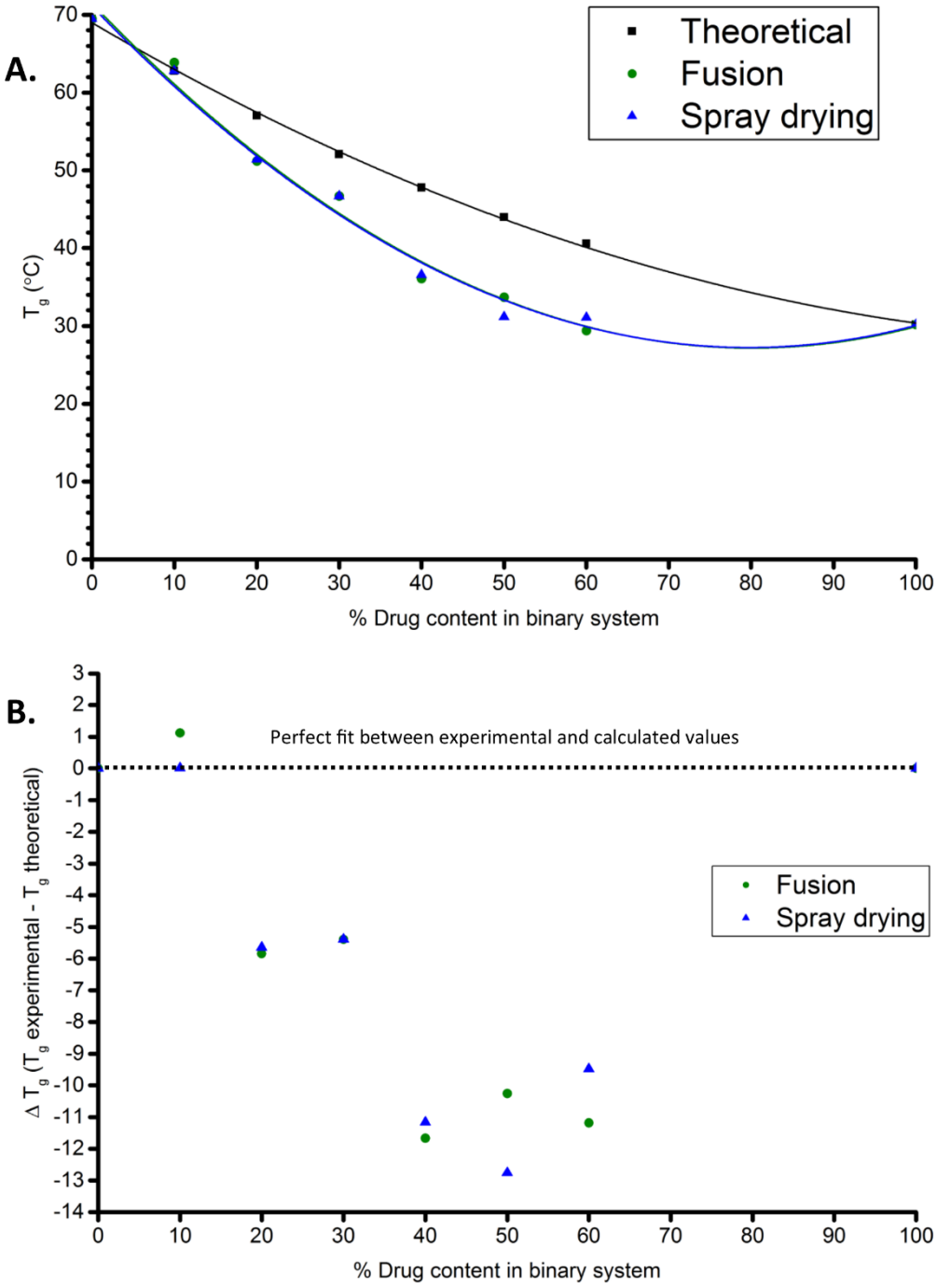


**Figure S11.** (**A**) Theoretical $T_g$ values calculated using Gordon-Taylor equation and experimental $T_g$ values of neat FLU, SOL and FLU:SOL solid dispersions obtained using fusion and spray drying methods. (**B**) The difference between experimentally obtained $T_g$ values of FLU:SOL solid dispersions and theoretically calculated $T_g$ of FLU:SOL binary mixtures using Gordon-Taylor equation.

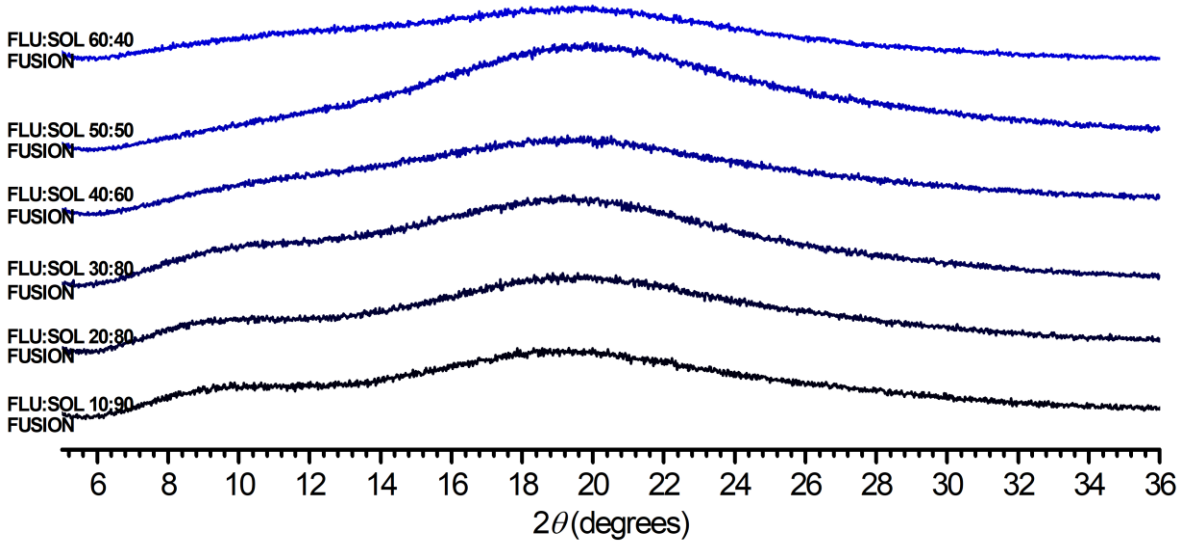


**Figure S12.** PXRD patterns of FLU:SOL solid dispersions prepared using fusion method after 14 days of stability studies (40 °C, 40% RH).

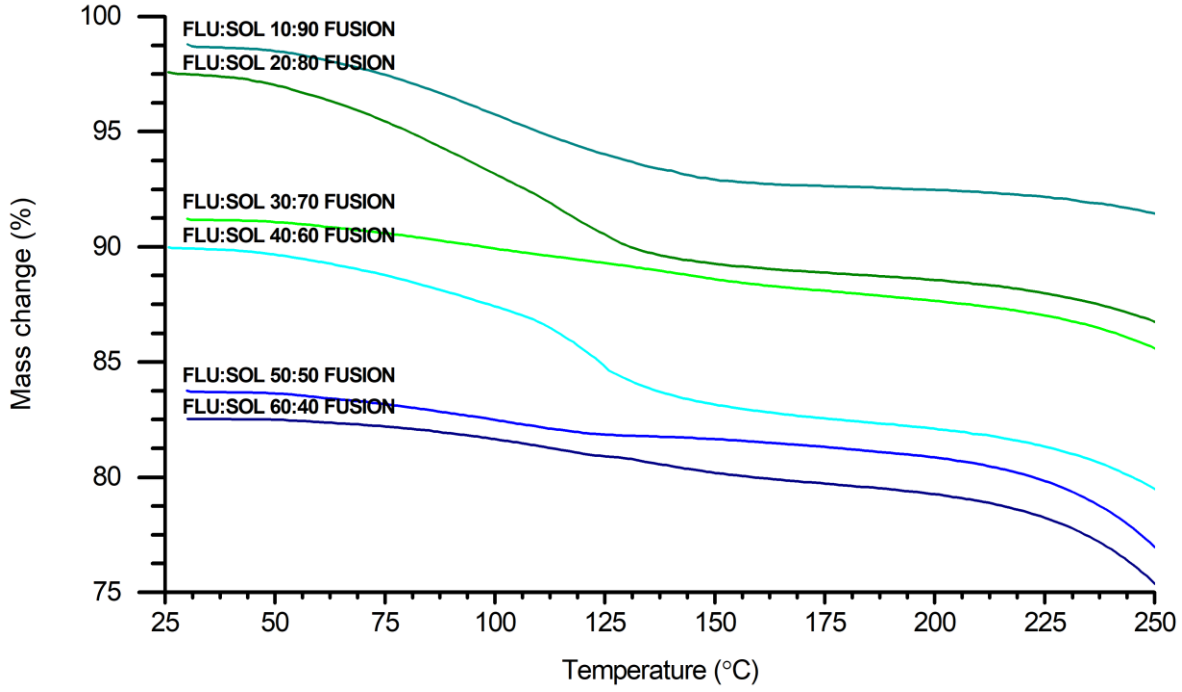


**Figure S13.** TGA curves of FLU:SOL solid dispersions obtained using fusion method recorded after 14 days of stability studies (40 °C, 70% RH).

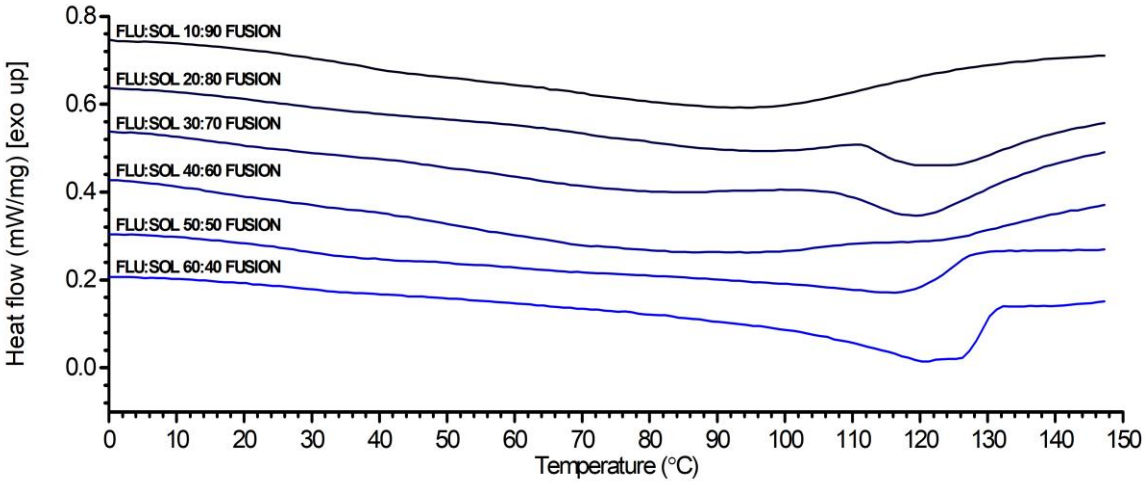


**Figure S14.** DSC curves of FLU:SOL solid dispersions prepared using fusion method after 14 days of stability studies (40 °C, 70% RH).

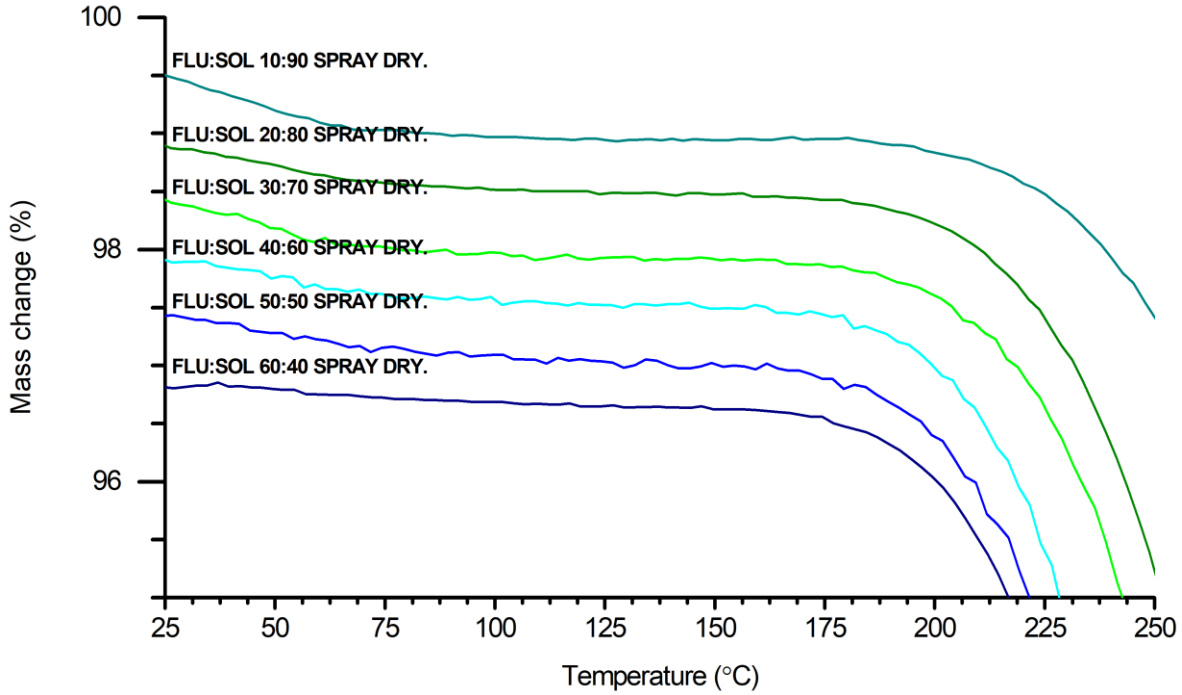


**Figure S15.** TGA curves of FLU:SOL solid dispersions obtained using spray drying method recorded after 14 days of stability studies (40 °C, 40% RH).

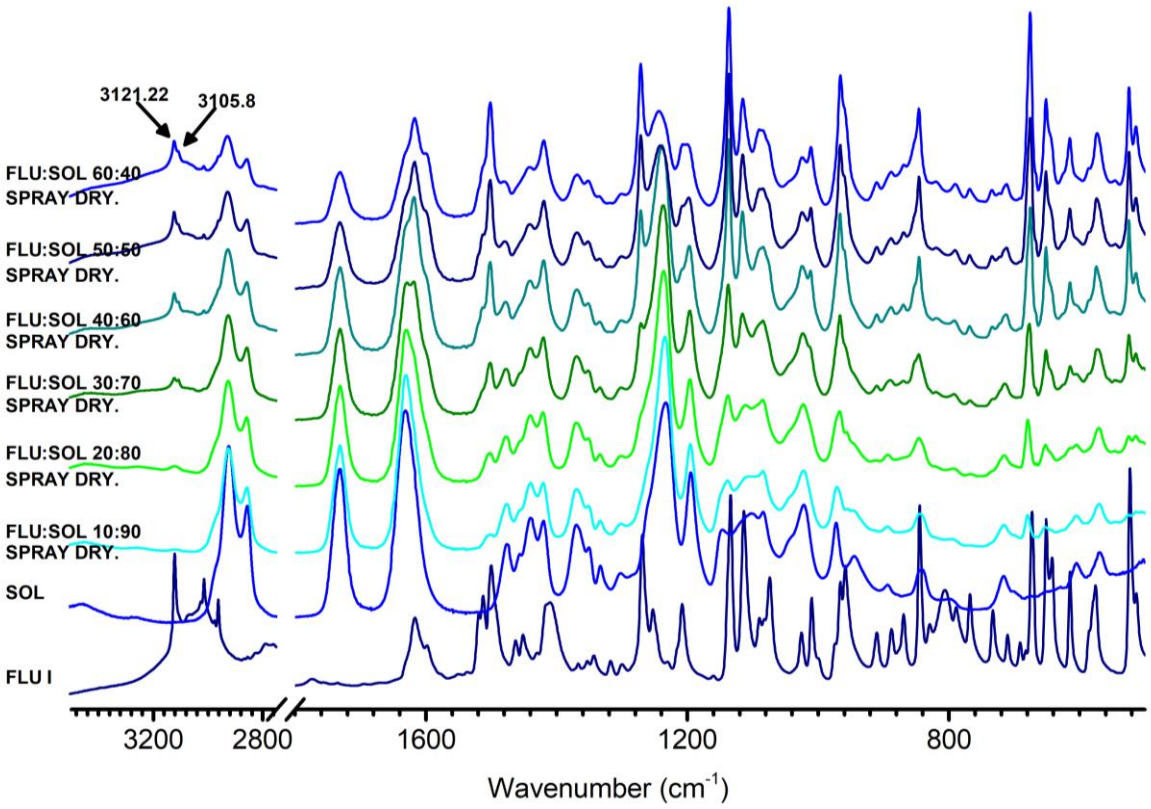


**Figure S16.** FTIR spectra of FLU:SOL solid dispersions obtained using spray drying method acquired immediately after preparing.

**Table S1.** FTIR vibrational bands assignments of FLU forms I, II, amorphous FLU, FLU hydrate and melted FLU after accelerated stability studies at 40 °C and 40 / 70% RH.

| Vibrational Band Assignments | FLU Form I | FLU Form II | FLU Amorphous | FLU Hydrate | Melted FLU Stored at 40 °C and 40% RH | Melted FLU Stored at 40 °C and 40% RH |
|---|---|---|---|---|---|---|
| **Triazole C-H stretching** | 3019.8 | 3126.0, 3104.3 | | 3115.4, 3106.3 | 3122.7, 3104.6 | 3016.1, 3105.5 |
| **Difluorophenyl CH stretching, (involved C-H···O bonding)** | 3013.2 | 3051.8 | | 3060.9, 3020.0 | 3052.76 | 3060.2, 3020.9 |
| **Methylene C-H asymmetric stretching** | 2962.12 | | | 2956.8 | | 2956.3 |
| **Difluorophenyl ring C=C stretching** | 1617.0 | 1614.5 | 1617.0 | 1618.0 | 1614.4 | 1615.5 |
| **Difluorophenyl C=C stretching** | 1598.7 | 1598.2 | 1598.22 | 1591.0 | 1597.7 | 1597.0 |
| **Triazole C=N stretching** | 1519.6, 1512.8, 1500.3 | 1516.7, 1503.7 | 1499.6 | 1514.8, 1504.7 | 1516.7, 1502.7 | 1516.0, 1503.5 |
| **Difluorophenyl ring C-C stretching** | 1463.22 | | | 1467.1 | | |
| **Methylene scissoring** | 1451.6 | 1450.7 | | 1445.4 | 1451.4 | 1445.6 |
| **Methylene scissoring or triazole C-N stretching** | 1410.2 | 1420.3 | 1420.8 | 1420.3 | 1419.8 | 1419.8 |
| **Methylene wagging** | 1367.3, 1353.3 | 1367.3 | 1366.8, 1351.4 | 1370.6, 1358.6 | 1367.0 | 1368.7 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Triazole C-N stretching** | 1343.2, 1317.6, 1300.2 | 1341.7, 1321.0, 1304.6 | | 1348.0, 1317.6, 1305.1 | 1342.2, 1320.0, 1304.6 | 1343.2, 1319.5, 1304.8 |
| **O-H in-plane-bending (C-OH scissoring)** | 1269.4 | 1275.2 | 1272.8 | 1274.7 | 1274.9 | 1275.0 |
| **C-F stretching** | 1253.0 | 1258.3 | | 1248.2 | 1258.3 | 1258.3 |
| **C-C stretching, difluorophenyl in plane banding (H-C=C)** | 1230.8 | 1230.8 | | 1216.4 | 1231.0 | 1227.7 |
| **Triazole N-N stretching, Methylene twisting** | 1208.2 | 1212.5 | 1207.2 | 1208.18 | 1212.0 | 1212.3 |
| **Difluorophenyl ring C-H-in-plane bending** | 1133.9, 1113.7 | 1140.2, 1131.5, 1115.6 | 1136.3, 1113.2 | 1137.8, 1110.8 | 1139.5, 1131.3 | 1138.5, 1113.9 |
| **C-O-H bending, C-C-C trigonal bending** | 1025.9 | 1022.0 | | 1020.1 | 1025.0 | 1020.1 |
| **Triazole N=C-N bending** | 1010.0 | 1014.9 | 1011.0 | 1015.3 | 1114.1 | 1014.6 |
| **Triazole N-N stretching, methylene rocking** | 968.0 | 966.2 | 965.2 | 965.7 | 968,5 | 967.3 |
| **C-C-C ring breathing** | 959.9 | 958.9 | | | 959,9 | 960.4 |
| **Triazole C-N=C scissoring, difluorophenyl out-of-plane-bending** | 910.2 | 909.3 | 911.2 | 916.5 | 908,8 | 909.5 |
| **C-O bending, triazole in-plane-bending, methylene rocking** | 888.0 | 885.7 | 887.6 | 898.18 | 885.6 | 885.9 |
| **Triazole ring out-of-plane-bending** | 869.3 | 875.0 | | 874.6 | 874.1 | 874.3 |
| **Difluorophenyl C-H out-of-plane-bending** | 845.15 | 851.9 | 850.9 | 852.4 | 852.4 | 852.4 |
| **Triazole ring out-of-plane-bending** | 829.7 | 829.7, 819.6 | 822.0 | 833.1 | 828.5, 819.6 | 833.11, 820.8 |
| **Difluorophenyl C-H out-of-plane-bending** | 806.6, 789.2 | 792.6 | 788.7 | | 792.6 | 792.8 |
| **C-N asymmetric stretching (skeleton), C-C asymmetric stretching (skeleton), triazole bending N-C-C** | 768.0 | 766.0 | 766.5 | 766.1 | 767.3 | 766.5 |
| **C-N symmetric stretching (skeleton), triazole bending (N=C-N)** | 732.8 | 728.5 | 735.7 | 734.3 | 728.5 | 733.8 |
| **C-C-C in plane bending** | 710.6, 691.4, 673.0 | 713.0, 688.9, 674.0 | 711.1, 675.4 | 679.3, 673.0 | 713.0, 688.9, 674.0 | 713.1, 697.1, 688.9, 674.0 |
| **Triazole ring out-of-plane-bending** | 651.3, 642.2, 614.7 | 649.4, 643.1, 612.8 | 651.3, 615.7 | 652.3, 616.6 | 649.4, 643.4, 612.5 | 649.9, 643.6, 613.5 |
| **C-C-C in plane bending** | 585.3 | 586.7 | 587.2 | 587.2 | 586.7 | 587.0 |
| **C-F in-plane-bending** | 575.7 | 573.7 | 571.8 | 569.9 | 574.9 | 571.3 |
| **N-C-C bending** | 523.1 | 522.1 | 525.0 | 530.3 | 522.6 | 523.1 |
| **C-C-C out-of-plane-bending** | 513.5 | 515.9 | 513.9 | 513.5 | 515.4 | 514.4 |