Supplementary Information

Effect of solvent evaporation on the liquid-crystalline order of itraconazole

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Supporting X-ray scattering (diffraction) patterns of solvent-evaporated itraconazole

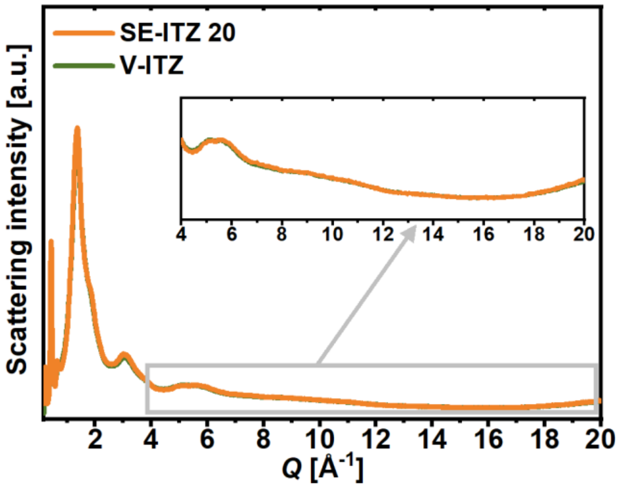

Fig. SI1 X-ray scattering patterns of SE-ITZ and V-ITZ in the full probed Q range of 0.17 – 20 Å^{-1}, with insets highlighting the Q region of 4 – 20 Å^{-1}, used for intensity normalization.

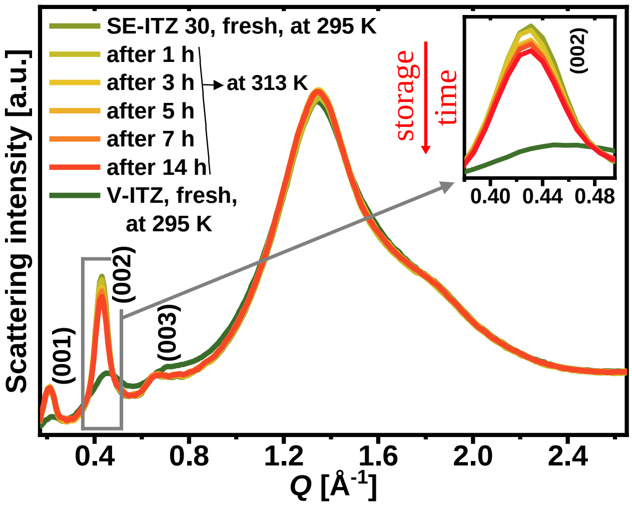

Fig. SI2 X-ray scattering patterns of fresh V-ITZ and SE-ITZ 30: fresh and stored at 313 K for 1, 3, 5, 7, and 14 hours. The inset presents the gradual decrease in the (002) diffraction peak’s amplitude for SE-ITZ 30 over the storage time.

Infrared spectra of the itraconazole-dichloromethane mixture

Firstly, we measured ATR-FTIR spectra of the commercial systems, ITZ and DCM, at 295 K and the assignment of particular molecular motions to the vibrational frequency of molecules is shown in **Fig. SI3**. The FTIR spectrum of V-ITZ showed a series of bands between 3200 and 2600 cm^{-1} assigned to the aromatic (3126 and 3066 cm^{-1}) and aliphatic (2967, 2936, 2878, 2827, and 2764 cm^{-1}) C-H stretching vibrations. The signal observed at 1697 cm^{-1} is related to the stretching vibrations of carbonyl groups. As reported in the literature [1,2], four peaks located at 1612, 1586, 1552, and 1509 cm^{-1} correspond to the aromatic C-C stretching, and the bands at 1450, 1379, and 1330 cm^{-1} are associated with the stretching vibrations of the N=N and C-N triazole moieties. The signals observed at 1271 and 1182 cm^{-1} are assigned to the aromatic C-H in-plane bending, while that at 1226 cm^{-1} can be connected with the asymmetric C-O-C stretching. The C-Cl stretching modes appear as a weak peak at 1106 cm^{-1}. The asymmetric (cyclic ether) and symmetric (alkyl-aryl ether and cyclic ether) C-O-C stretching vibrations are visible at 1039 and 974 cm^{-1}. The peaks occurring at 820, 794, 735, and 676 cm^{-1} can be assigned to the out-of-plane bending of the C-H benzene and triazole rings. On the other hand, in the DCM IR spectrum, two peaks detected at 3054 and 2987 cm^{-1} are assigned to the asymmetric and symmetric stretching of C-H bonds, respectively. The signals located at 1422 and 1264 cm^{-1} correspond to the bending vibrations of C-H groups, whereas the doublet visible at 732 and 703 cm^{-1} is related to the asymmetric and symmetric stretching of C-Cl groups.

Next, FTIR spectra of the ITZ:DCM mixtures were recorded to obtain more information about the interactions between solute and solvent molecules. As illustrated in **Fig. SI3**, the bands characteristic for ITZ in ITZ:DCM mixtures essentially exhibit only minor shifts (about 1-2 cm^{-1}) compared to those in V-ITZ. The peaks that shifted to a more significant degree under the influence of solvent (max. 6 cm^{-1}) are that of the aliphatic CH

(2936-2827 cm^{-1}) and the C=O stretching (1750-1650 cm^{-1}) vibrations (highlighted in light pink). Thus, the ITZ signal located at 2936 cm^{-1} after the introduction of solvent is blue-shifted to 2941 cm^{-1} (ITZ:DCM 20), and the further addition of ITZ leads to the red-shift of this band (2938 and 2939 cm^{-1} for the mixtures ITZ:DCM 30 and ITZ:DCM 40). The same effect is detected for the ITZ signal occurring at 2878 cm^{-1} (2884, 2883, and 2882 cm^{-1} for the mixtures with ITZ:DCM 20, ITZ:DCM 30, and ITZ:DCM 40). In the case of the ITZ peak located at 2827 cm^{-1}, a blue shift occurs in the presence of the solvent, which continues with the addition of ITZ. These C-H band shifts are probably related to the weak intermolecular interactions of hydrogen bond type existing between ITZ and DCM molecules (the aliphatic C-H groups as the donors) or the interactions of dipole-dipole type. Moreover, the carbonyl band of ITZ is blue-shifted from 1697 cm^{-1} to 1702 cm^{-1} ($\Delta\nu$ = 5 cm^{-1}) which can be associated with van der Waals interactions between ITZ and DCM. It should also be noted that the peak positions of the DCM molecule in the mixtures (highlighted in light yellow) exhibit only insignificant shifts (about 1-2 cm^{-1}) compared to those in DCM, resulting from the impact of ITZ (solvent polarity effect).

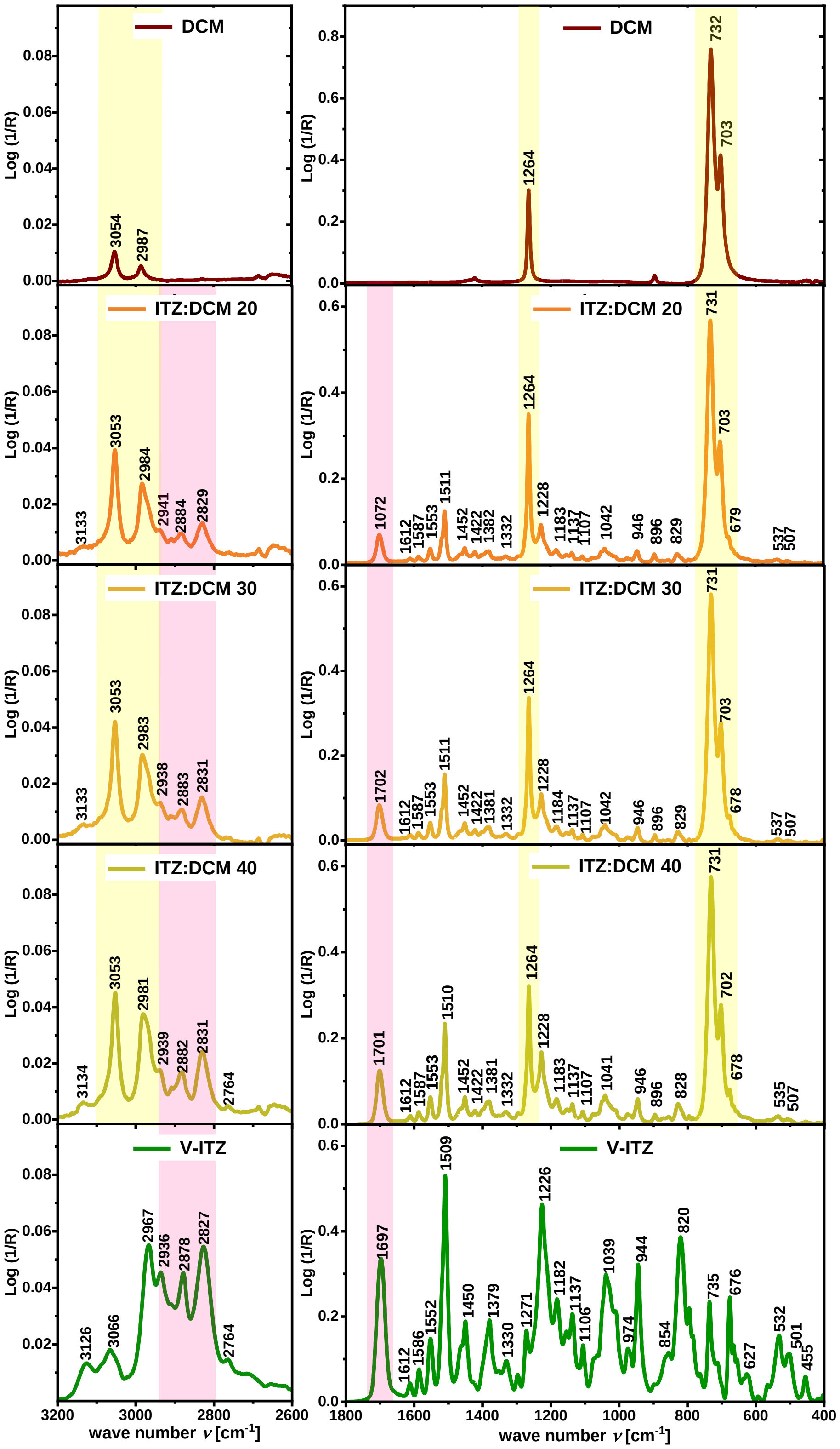

Fig. SI3 FTIR spectra of V-ITZ and DCM as well as ITZ/DCM mixtures. Data were presented in two spectral regions: (left) 3200–2600 cm^{-1} and (right) 1800–400 cm^{-1}.

Additionally, a comparison of the IR spectra of V-ITZ and the SE-ITZ samples prepared from ITZ:DCM mixtures of different concentrations (20, 30, and 40 mg/ml), in **Fig. SI4,** reveals no significant differences between them. This may suggest that there are no significant differences in the interaction patterns between ITZ molecules in these systems.

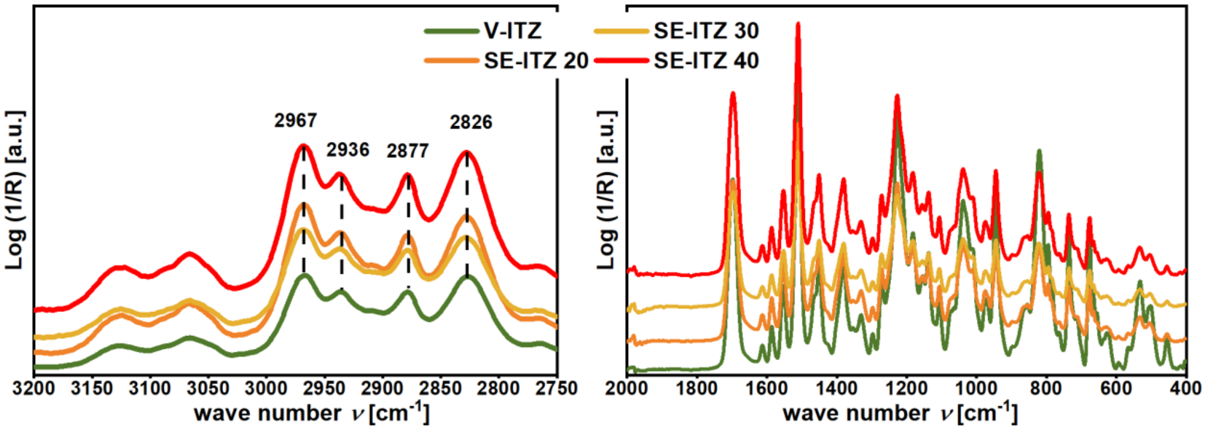

Fig. SI4 FTIR spectra of SE-ITZ samples, prepared from ITZ:DCM mixtures of different concentrations (20, 30, and 40 mg/ml), compared with that of V-ITZ, presented in two spectral regions: (left) 3200–2750 cm^{-1} and (right) 2000–400 cm^{-1}.

References

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1. Kujawski, J. et al. Structural and spectroscopic properties of itraconazole and ketoconazole–Experimental and theoretical studies. *J. Mol. Struct.* **1146**, 259–266 (2017).

2. Socrates, G. *Infrared and Raman characteristic group frequencies: tables and charts*. John Wiley & Sons (2004).