Molecular Structure Analysis of Active Pharmaceutical Ingredients

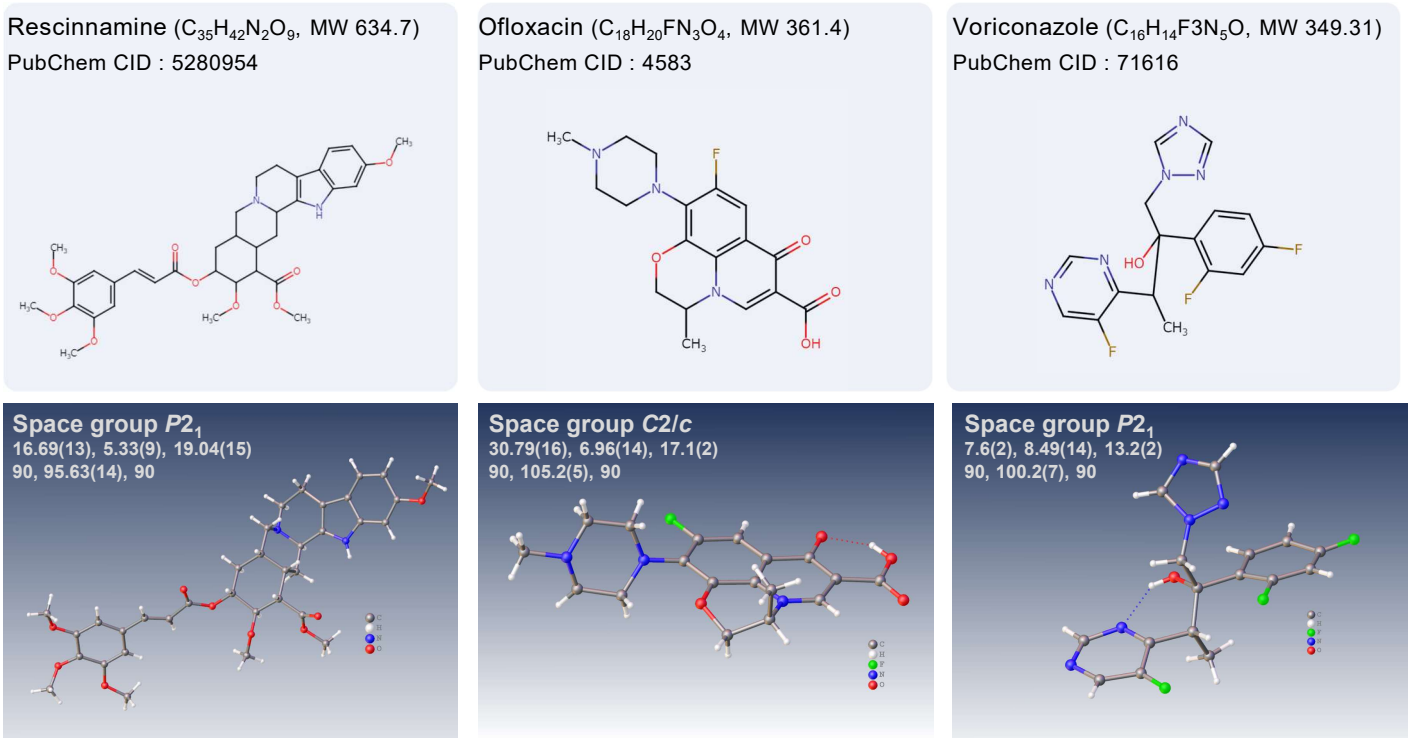
Product used：Electron Diffractometer

Structure analysis of active pharmaceutical ingredients with XtaLAB Synergy-ED and JEOL MS and NMR

Electron diffraction structure analysis of Reserpine, XtaLAB Synergy-ED

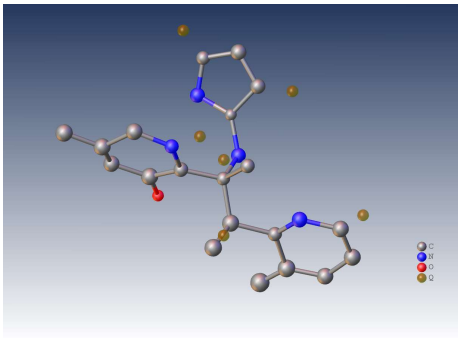
XtaLAB Synergy-ED is a fully optimized electron diffractometer for microcrystals analysis. The key feature of this product allows molecular structural analysis of pharmaceutical raw materials such as active pharmaceutical ingredients with powder. In addition, JEOL mass spectrometer (MS) and nuclear magnetic resonance (NMR) spectrometer provide detailed information for determining the molecular structure.

Electron diffraction structure analysis of active pharmaceutical ingredient powders

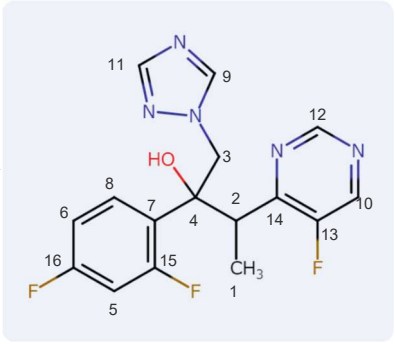


XtaLAB Synergy-ED allows electron diffraction structure analysis of powder samples less than few μm without sample preparation. CrysAlis^{Pro} for ED is an instrument control and single crystal analysis software platform for 3D ED/microED experiments. This system provides researchers a simple and effective platform for electron crystallography. The example above shows the results of electron diffraction structure analysis of active pharmaceutical ingredient powders. The measurement time required to complete the data collection is few minutes. It is possible to use Cryo-transfer holders for heat sensitive samples and hydrates.

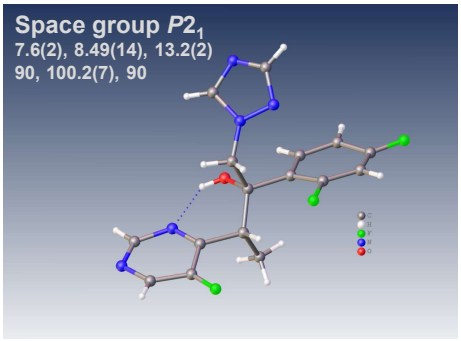
Structure analysis of Voriconazole powder



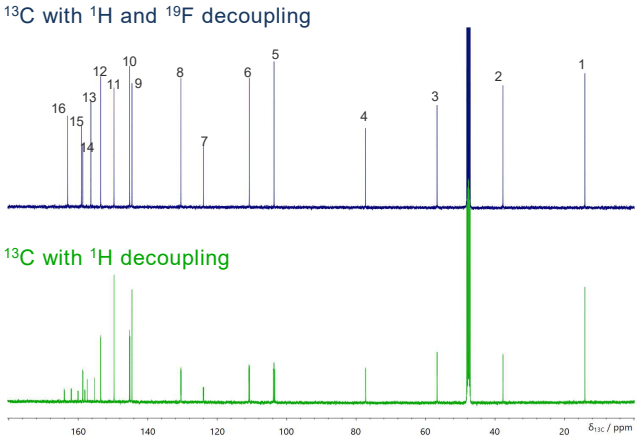
An initial model of Voriconazole determined by electron diffraction structural analysis



A structural formula of Voriconazole determined by NMR analysis



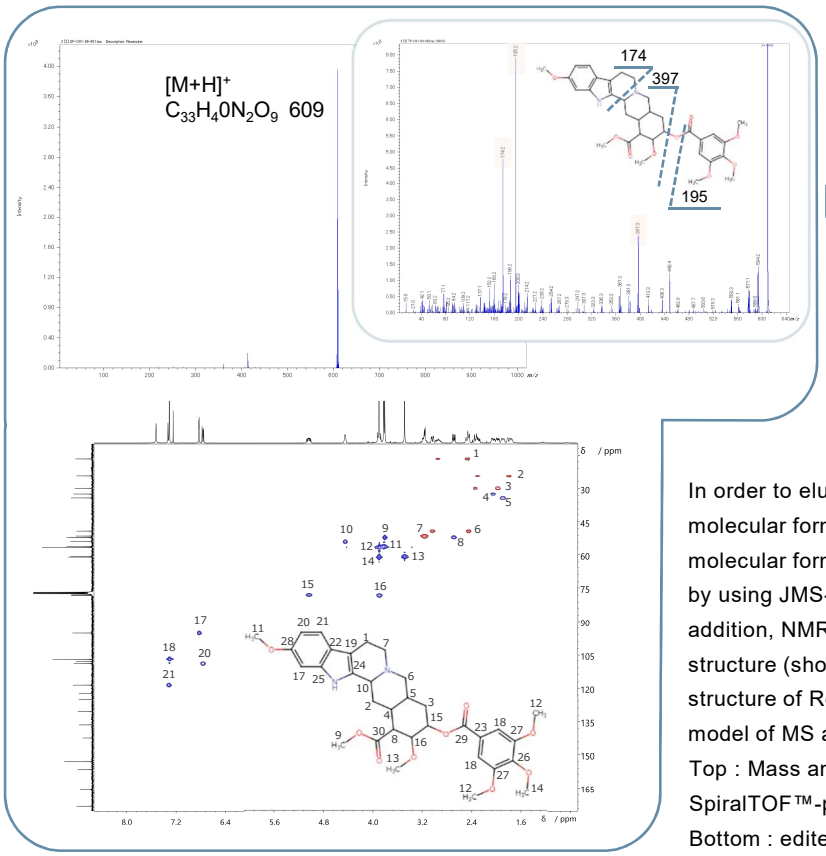
A refined structure of Voriconazole by using NMR analysis results

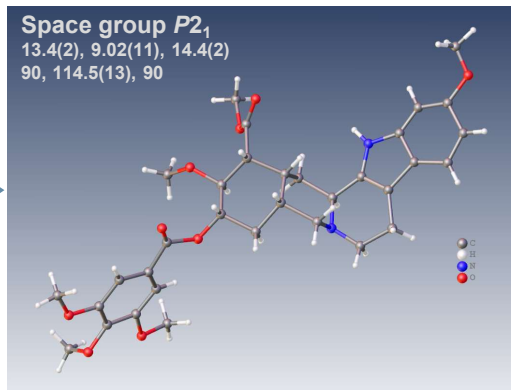


^{13}C NMR of Voriconazole, JNM-ECZL 500R
Blue: ^{13}C with ^{1}H and ^{19}F decoupling
Green: ^{13}C with ^{1}H decoupling

Structure refinement is a method of obtaining accurate atomic coordinates by using electron diffraction intensities. In the example above, this refinement is performed by the full matrix least-squares method of SHELXL. In this method, a local minimum model with incorrect, but not necessarily unrealistic geometries can be achieved during refinement (shown left). In addition, NMR analysis provides the details of Voriconazole chemical structure (shown center). An initial model of Voriconazole determined by electron diffraction structural analysis can be refined with the chemical model of NMR analysis result (shown right). The left figure is ^{13}C with ^{1}H and ^{19}F decoupling and ^{13}C with ^{1}H decoupling NMR spectra of Voriconazole by using JNM-ECZL 500R. ROYALPROBE™ HFX enables a wide variety of advanced ^{1}H and ^{19}F NMR experiments with dual tune mode. It is effective to simplify spectral assignments with ^{13}C with ^{1}H and ^{19}F decoupling and many unique correlation experiments for the analysis of organic compounds containing fluorine atoms, for example Voriconazole.

Structure analysis of Reserpine powder





Structure of Reserpine determined by XtaLAB Synergy-ED, JEOL MS and NMR

In order to elucidate the molecular structure of Reserpine, the molecular formula is determined by using MS. In the example, the molecular formula of reserpine is provided from the Mass spectrum by using JMS-S3000 SpiralTOF™-plus 2.0 (shown top left). In addition, NMR analysis provides details of Reserpine chemical structure (shown bottom left). The right-hand is the molecular structure of Reserpine which is refined by the chemical structure model of MS and NMR results.

Top : Mass and MS/MS spectra of Reserpine, JMS-S3000 SpiralTOF™-plus 2.0

Bottom : edited ^{1}H-^{13}C HSQC spectrum, JNM-ECZL 500R

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