Powerful Microscopy solutions for the Pharmaceutical Industry

Electron Microscopy imaging & Electron Diffraction

Advanced studies of pharmaceutical API compounds involve high resolution imaging and crystal structure analysis with electron diffraction at very small scale (micron to nm) using state of the art Electron Microscopes. **NanoMEGAS SPRL** is a leading Company established in the field of advanced imaging and electron diffraction in Transmission Electron Microscopy (TEM) and **we provide Electron Microscopy based services for the Pharmaceutical Industry for Risk & Cost Reduction during Drug Development and Manufacturing.**

ELECTRON MICROSCOPY SOLUTIONS AND SERVICES

Electron Microscopy Imaging of very small (nm scale) crystals ("X- Ray amorphous")

TEM-EDS microanalysis at nm scale of phases present in API

Trace analysis : detection and structure analysis of very small size (< 10 nm) & very low amount of crystallites (< 0.01%)

Electron Crystallography -3D Precession Electron Diffraction Tomography solution for cell parameter determination of APIs and their polymorphs

Electron Crystalllography- 3D Precession Electron Diffraction Tomography solution for crystal structure determination of APIs and their polymorphs

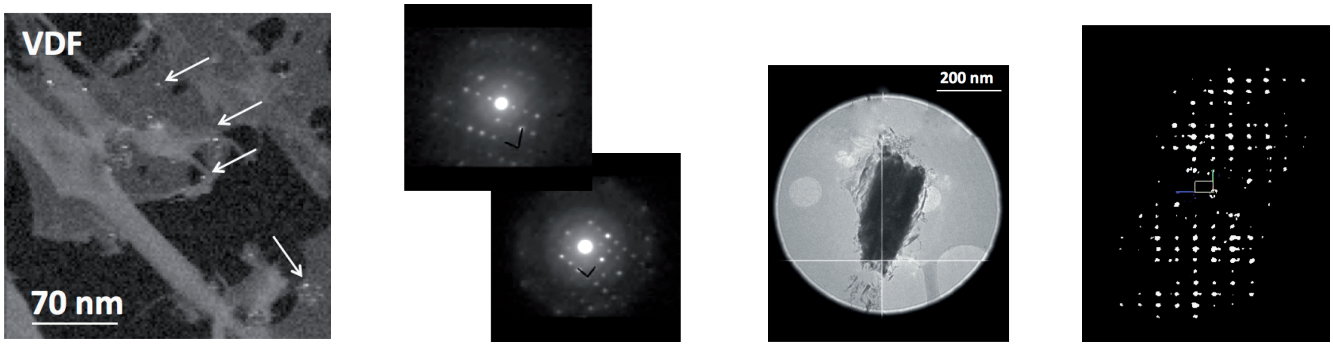
Analysis of amorphous pharmaceuticals using Electron Diffraction Techniques (ePDF - Pair Distribution Function)

Nanoscale mapping of amorphous/crystalline areas for Amorphous Solid Dispertions (ASD) using TEM electron diffraction & imaging techniques

NanoMEGAS
Advanced Tools for electron diffraction

contact: info@nanomegas.com

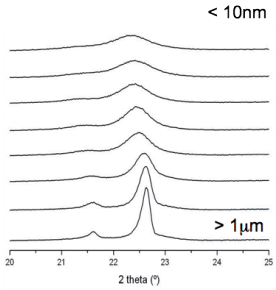
Trace analysis with TEM high resolution imaging and electron diffraction



From left to right : Virtual Dark Field (VDF) TEM high resolution image showing 10 nm resorcinol crystals (arrows) on amorphous background; corresponding ED patterns for crystallites ; individual Nicotinic acid API nanocrystal and its corresponding ED pattern

High Resolution Virtual Dark Field (VDF) in TEM is a technique that enables detection of very small trace of crystalline material; in the example shown above, trace crystals of very small sizes (eg 10nm) can be observed at very low quantity (< 0.01%). **Structure characterization (like phase confirmation) of such small crystals can be done using Electron Diffraction on individual crystallites.**

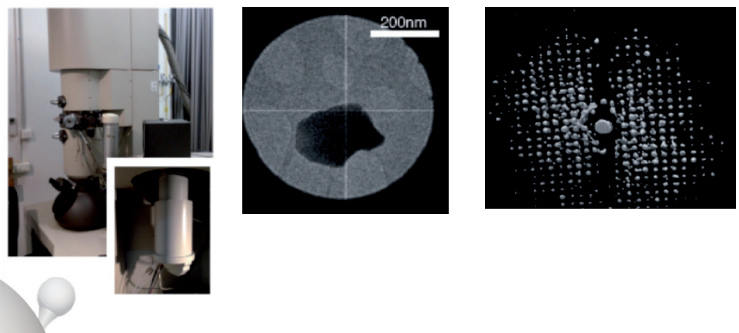
Drug polymorph structure analysis with TEM 3D electron diffraction tomography



X-Ray "amorphous"

Electron Crystallography is considered as the method of choice for structure determination of nanocrystalline compounds (crystals as small as 20 nm to several microns). Such nano-crystallites reveal typically "X-Ray amorphous" powder diffraction patterns (for sizes < 10nm) where is very difficult to identify and characterize their structures using X-Ray diffraction techniques.

Use of precession 3D **electron diffraction (PED) with TEM makes possible unit cell and structure determination on individual nanocrystals**. Using 3D diffraction tomography , a 3D reconstruction of the reciprocal space can be performed by tilting the sample and recording ED patterns (Fig. 1) (typically ±45° every 1°) . Collected electron diffraction (ED) patterns can be processed to precisely determine the unit cell and reveal the space group symmetry of the API crystal. Full atomic crystal structure can also be performed after collection and precise measurement of ED intensities.



From left to right: CM30 (300 KV) Transmission electron microscope (TEM), individual Carbamazepine (CBZ) API crystal, 3D reciprocal space reconstruction of CBZ crystal, CBZ Structure solved from 3D electron diffraction data (50° continuous tilt, 3823 reflections, 0.8° resolution). Cell parameters: a =7.53 Å; b =11.14 Å; c =14.06 Å; β = 92.80 °, P21/n (monoclinic). In blue structure solved by Single crystal X-Ray diffraction, in red structure solved by Electron Diffraction.