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ASIA EDITION

Korea's Biortus facilitates drug development through its MicroED service

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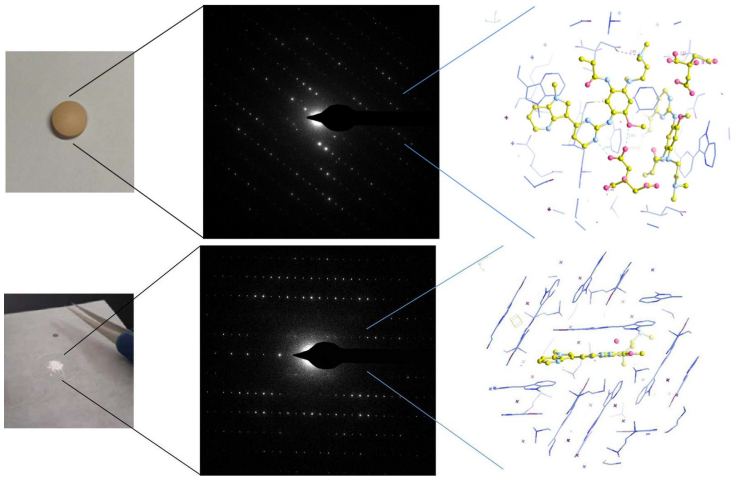
New crystal structure determination technique obtains diffraction patterns of small-molecule microcrystal in drug substance which can determine drug stability, process development, and bioavailability



Microcrystal electron diffraction (MicroED) is a new crystal structure determination technique for small molecules. It obtains diffraction patterns of small-molecule microcrystal from an electron microscope, and resolves the atomic-resolution structure (better than 1.0A) with the traditional crystallography approach. The emergence of MicroED technology has raised great interest within the pharmaceutical research and development community. This technology holds great prospects of identifying the crystal form of drug substance, determining the structure of a natural product, and analyzing impurity in CMC process.

The crystal form of a small molecule drug substance has a direct effect on drug stability, process development, and bioavailability. It is also patentable to extend the drug protection period. The traditional x-ray single crystal diffraction technology is the gold standard for the structure and crystal form identification, but its bottleneck resides in the required large size of single crystal, which can be difficult to obtain and time-consuming. Many APIs produce only nanoscale crystals, and x-ray single crystal diffraction fails at such small crystals, but it is perfect for MicroED technology. Many small molecules spontaneously form microcrystals in the process of production, and its structure and crystal form can be directly obtained through MicroED technology. The unique technical advantage of MicroED will enhance the drug development process. In addition, MicroED technology requires only a minimal amount of sample (~1 mg) and produces results fast, sometimes within a day. This is extremely useful for those low-yield small molecules, such as some natural products or impurities in CMC.

As one of the first microED service providers in the world, Bioruts has established a mature and efficient protocol and delivered many high-resolution small-molecule structures. For example, only in three days, we have determined the structures and crystal forms of an API (from a pill) and its impurity in the synthesis process (from trace amount of powder), respectively

Image Caption:

Top: Structure and crystal form of an API

Bottom: Structure and crystal form of an impurity