Amorphous Spray Dried Dispersions for Drug Delivery

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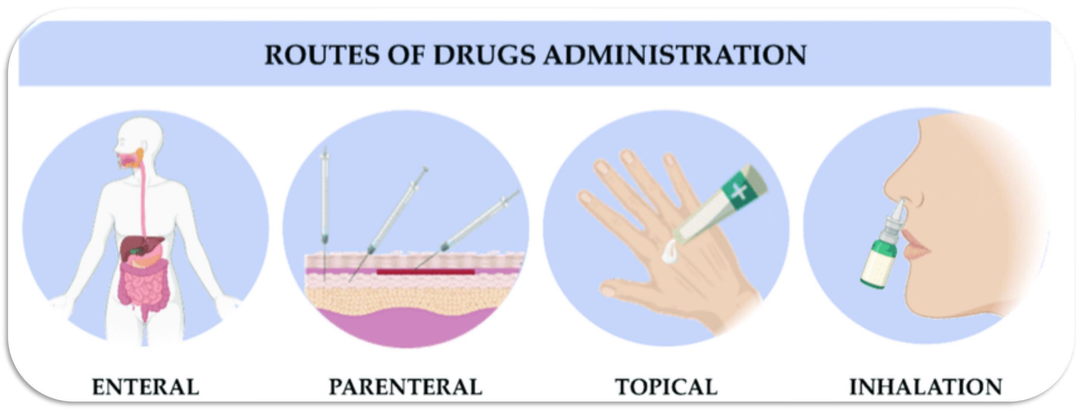
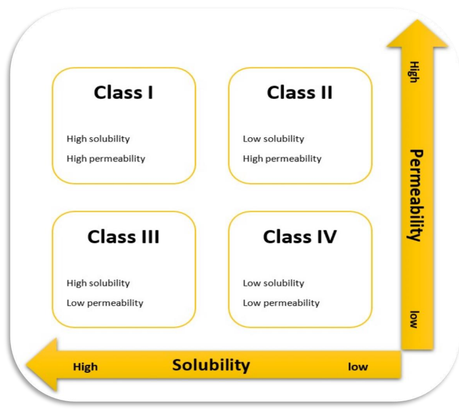
Collaborating with a CDMO to develop a spray dried dispersion for a large pharmaceutical company

Amorphous solid dispersions offer the benefits of increased bioavailability for poorly soluble drugs and improved formulations for biologic formulations. They also offer the potential for novel formulations that exploit multiple routes of administration.

However, they can suffer from physical instability and are often subject to regulatory requirements to demonstrate physical stability upon storage.

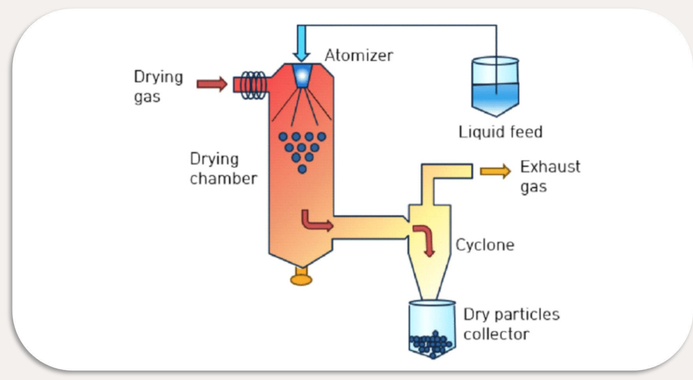
RSSL have the capabilities and expertise to develop methods, validate and perform GMP release testing on amorphous solid dispersions to demonstrate physical stability of the formulation.





Amorphous solid dispersion manufacture

There are numerous methods available to produce amorphous solid dispersions. These include spray drying, freeze drying and hot melt extrusion. A CDMO is developing a spray dried dispersion on behalf of a large pharmaceuticals company. This technique was chosen because it is reliable and reproducible. It allows for particle engineering with respect to the dispersion particle size and physical stability to be developed.



Why did a CDMO partner with RSSL?

This company is a Contract Development Organisation (CDMO) with expertise in developing stable amorphous solid dispersions. Whilst they have a wide variety of in-house analytical instrumentation (including the same equipment as RSSL) they do not have the capabilities to develop and validate the physical characterisation methods required for regulatory approval. RSSL were able to develop methods to determine the physical form of the solid dispersion drug product by two complimentary techniques.

Differential Scanning Calorimetry (DSC)

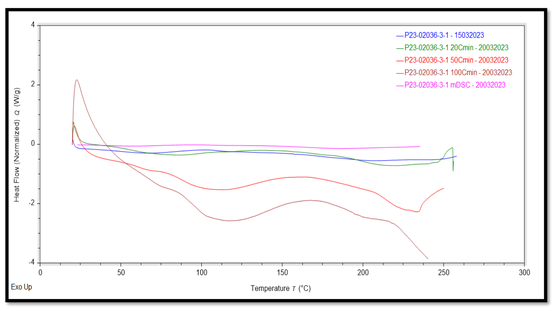
DSC is a thermal analysis technique in which the heat flow of a sample is measured as a function of temperature or time.

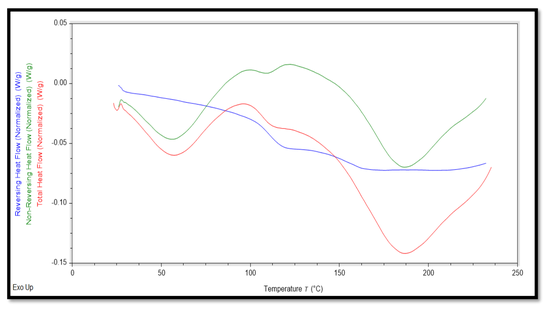
RSSL's analysis showed that both the API and excipient had melting endotherms that overlapped. To try and resolve the peaks faster heating rates were employed.

Heating rates of 20°C, 50°C and 100°C per minute were examined on the SDD intermediate which did not resolve the melting endotherms.

An alternative DSC approach was employed; modulated DSC analysis utilises a slower oscillating heating Rate which can separate thermal events.

The presence of a glass transition (Tg) with a mid-point of ~110°C in the reversing heat flow thermogram indicated that the API was amorphous.



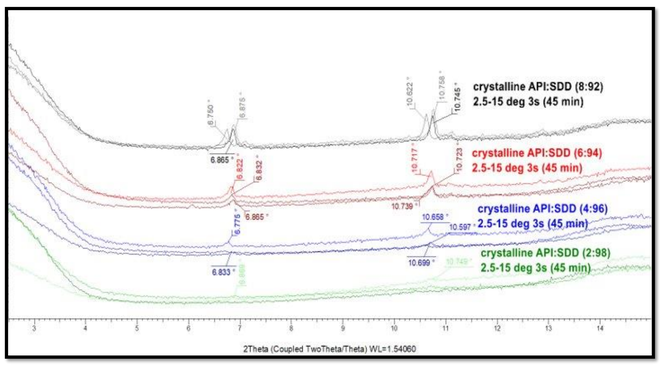


X-Ray Powder Diffraction (XRPD)

XRPD is a powerful technique for the characterization of crystalline material within amorphous solid dispersions. RSSL's initial testing determined the range and sensitivity available by XRPD.

RSSL were able to develop a method suitable to identify any crystalline material within the SDD. Additional analysis using crystalline API spiked into the SDD determined a suitable limit of the technique was 4% crystalline API.

The method has now been developed by RSSL to incorporate additional crystalline excipients within the drug product (SDD excipient blend).



Success story

RSSL's expertise in physical characterisation have successfully demonstrated that RSSL are able to support the development and characterisation of amorphous solid dispersions with the ability to perform DSC and XRPD analysis for GMP release testing.

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