

Characterising Solid Dosage Forms of Proteins and Vaccines



XstalBio Ltd is an advanced drug delivery company specialising in the formulation of therapeutic proteins, peptides, DNA and vaccines.

XstalBio can provide biotechnology, pharmaceutical and vaccine companies interested in the delivery and stabilisation of proteins or vaccines an immediate competitive advantage by offering a significant advancement in Circular Dichroism (CD) analysis.

Conventional CD is used to elucidate the structural aspects of protein conformation in solution but cannot be applied to particles.

An innovative, yet simple, rotating CD cell holder has been developed by XstalBio to provide rapid, reliable information on the secondary and tertiary structure of proteins in the **solid-state**, for example:

- bound onto particles such as **alhydrogel or encapsulated into lipid membranes**.
- as solvent suspensions of lyophilised powders.
- in solution in the presence of scattering particles or aggregates.

This powerful tool enables faster and more cost-effective analysis of formulations, yet can be easily slotted into existing CD systems and used with freely available software packages. XstalBio has already completed **successful technology transfer of this technique to a major pharmaceutical company active in vaccine development and a large biotechnology company**.

How can solid-state CD analysis improve your protein/antigen formulation development programs ?

- **Speeds up the development process:**
 - Analysis time for **CD is typically 20 minutes per sample; ELISA requires 1 day**
 - **Sooner understand and quantify effects** of process/formulation changes on your protein formulation
- **Helps you to understand unexplained potency decreases** often related to protein/antigen structure changes in the solid-dosage form, but impossible to measure using currently available solution-based analysis techniques.
- **Reduces uncertainty** of the choice of formulations for advanced testing, *e.g. in vivo*

"Application of the Drug Product CD analysis technique to our drug product has fundamentally changed our understanding of the formulation. This has resulted in the identification of technology options for formulation improvement."
Dr Allan Watkinson, Head of Formulation Development, Avecia Biotechnology

Your organisation can evaluate and utilise the XstalBio CD technology in a two stage process:

Evaluation: Send XstalBio some of your solid protein formulations for analysis by CD. We will analyse these samples for you and respond with a short report, summarising the data produced on the structure of the proteins provided.

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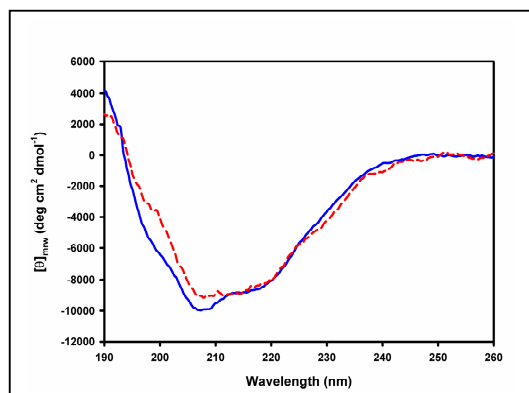
Technology Transfer: Following satisfactory evaluation, XstalBio will undertake a straightforward technology transfer programme and tailor the methodology and cell design for the research requirements of the individual organisation. Full training by a XstalBio senior scientist, will be given until each client is confident of running an analysis and the data outputs on their own solid dosage formulations.

Example: Drug Product spectra and information obtained from solid-state CD

This example shows a CD study of a recombinant protective antigen of *Bacillus anthracis* (rPA). The data provides valuable insights into the conformational stability of rPA in the adsorbed state, *i.e.* in the final formulation.

Secondary structure of rPA in the free form and adsorbed onto a common adjuvant, alhydrogel, are very similar as can be seen from the far UV CD spectra shown below:

Figure Far UV CD spectra of rPA solution (solid line) and rPA-adjuvant vaccine formulation (dash line).



Near UV CD spectra of the rPA formulation (data not shown), shows sharp bands with the appearance of two new bands in the region of 270- 280 nm. This is due to a more rigid structure of the antigen in the adsorbed state.

Table Estimated secondary structure of rPA Drug Substance (DS) in solution and rPA Drug Product (DP), in the solid-state obtained from the analysis of far

UV CD spectra using a commonly used algorithm: CDSSTR.

Sample	Method	Helix	Sheet	Other
PA ₈₃ crystal	X-ray diffraction	13	31	56
rPA solution (DS)	CD	11	29	60
rPA vaccine formulation (DP)	CD	10	31	59

FOR MORE INFORMATION OR TO INITIATE ANALYSIS/TECHNOLOGY TRANSFER

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