Recipharm



Balancing solubility and extended release through science-led OSD development

A complexation-enabled tablet case study combining cyclodextrin solubilisation with a pharmacokinetically rationalised release specification

Developing an extended-release tablet for an extremely poorly soluble active substance means solving two competing challenges: making the drug available in solution and controlling its release over time. Recipharm's formulation and analytical experts brought these requirements together, translating cyclodextrin complexation into a practical, manufacturable oral solid dose (OSD) formulation.

The strategy combined two elements: complexation of the active substance with a cyclodextrin to enhance its solubility, followed by optimisation of the extended-release profile against a specification designed rationally around the drug's pharmacokinetic characteristics, rather than a generic or empirical release target.

The full development scope, including a comprehensive data package, was completed within three to four months of actual project initiation. This followed a significant delay after proposal approval, primarily due to the time required to obtain the necessary licence, leaving a compressed window for delivery.

THE CHALLENGE: BALANCING SOLUBILITY AND PROLONGED RELEASE

The active substance is characterised by extremely low aqueous solubility, which limits dissolution and, in turn, the extent and consistency of absorption. For an extended-release product the difficulty is compounded: the dosage form must first make the drug available in solution at a sufficient rate and then sustain that availability over the intended dosing interval.

- Poor solubility limits the amount of drug that can dissolve, so simply slowing release from a conventional formulation risks incomplete release.
- Techniques that raise solubility often accelerate release, which must then be re-controlled to achieve an extended profile.
- The target release profile needed to be justified scientifically, not simply matched empirically, so that the resulting specification would be meaningful for in vivo performance.



FORMULATION STRATEGY: CYCLODEXTRIN COMPLEXATION

Addressing the solubility barrier first

Cyclodextrins are cyclic oligosaccharides with a hydrophilic exterior and a hydrophobic internal cavity. A poorly soluble molecule, or part of it, can be accommodated within this cavity to form a host-guest inclusion complex, which presents the drug to the aqueous environment in a form with substantially improved apparent solubility and dissolution behaviour.

Recipharm selected complexation as the enabling step to overcome the solubility limitation at the point of formulation, before applying the release-controlling elements of the extended-release system.

FROM CONCEPT TO A MANUFACTURABLE TABLET

- The team translated the complexation approach from a theoretical concept into a practical, manufacturable tablet formulation.
- The solubilised drug form was combined with an extended-release system so that the solubility benefit was retained while release was controlled over time.
- Formulation and process choices were made with manufacturability in mind, so that the concept could be reproduced as a practical tablet rather than remaining a laboratory demonstration.

DESIGNING THE RELEASE PROFILE AROUND PHARMACOKINETICS

Rather than adopting a release target by convention, Recipharm optimised the extended-release profile against a specification rationally designed around the pharmacokinetic characteristics of the drug.

- The pharmacokinetic behaviour of the active substance was used to define the release profile needed to support the intended exposure over the dosing interval.
- Dissolution testing was used to optimise the formulation towards that target profile, and the dissolution specification was set with reference to it.
- Linking the specification to the pharmacokinetic rationale gives the release limits a clear scientific basis, supporting meaningful quality control of the commercial product.

PROGRAMME DELIVERY: COORDINATING SCIENCE AND DOCUMENTATION

Development activities could only begin after a significant delay following proposal approval, primarily owing to the time required to obtain the necessary licence. This left a compressed window in which to complete the work.

- The entire development scope was completed within three to four months of actual project initiation.
- A comprehensive data package was generated within the same period, supporting the formulation and the rationale for the release specification.
- Close planning and parallel execution of formulation, analytical and documentation activities enabled the team to complete the scientific work and supporting documentation within the same timeframe.



OUTCOME: A MANUFACTURABLE FORMULATION AND COMPLETE DATA PACKAGE

Recipharm translated a complex theoretical concept into a practical, manufacturable extended-release tablet formulation. The programme combined a mechanistically sound solubilisation strategy with a pharmacokinetically rationalised release specification, supported by a comprehensive data package. The full scope was delivered within three to four months of actual project initiation, despite the delayed start.

CONCLUSION: CONNECTING FORMULATION SCIENCE WITH MANUFACTURABILITY

This case shows how Recipharm addressed an extremely poorly soluble active substance's solubility limitation first, through cyclodextrin complexation, then engineered an extended-release profile against a specification grounded in the drug's pharmacokinetics.

By connecting formulation expertise, analytical depth and manufacturability, Recipharm development team gave the programme a robust scientific foundation and delivered the full scope within a compressed development window. This science-led approach to OSD development brings practical problem-solving together with the product understanding needed to support later manufacturing and quality control.



About us

Recipharm is a leading Contract Development and Manufacturing Organisation (CDMO) employing over 4,500 employees. Recipharm provides expertise in development and manufacturing across oral dosage sterile, fill & finish, and biologics; clinical trial material development and manufacturing services; and, pharmaceutical product development. Its Biologics segment works with customers to develop and commercialise advanced therapy medicinal products (ATMPs): pre-clinical to clinical and commercial development and manufacture for new biological modalities. The company operates development and manufacturing facilities in France, Germany, India, Italy, Portugal, Spain, Sweden and the US.

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