Quotient Sciences

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Strategies for Accelerating the Development of Modified Release Oral Forms

Introduction

Oral modified release (MR) formulations enable control over the rate and location of drug release in the gastro-intestinal (GI) tract, in order to achieve specific therapeutic benefits in comparison to immediate release (IR) formulations, including:

- Maintenance of drug plasma concentrations over a prolonged period to reduce dosing frequency
- Attenuation of peak to trough ratios to reduce the incidence of peak-related adverse events (AEs) and potentially improve efficacy
- Deliver drug to specific, targeted regions of the gastrointestinal (GI) tract to improve absorption or for localized treatment

MR drug delivery can also have commercial benefits and is prevalent as part of product life-cycle management (LCM). Modest reformulation of an already approved drug from an IR to MR format allows both line and patent extension opportunities and continued market exclusivity. Examples of marketed MR products are shown in Table 1.

Table 1: Example marketed MR formulations

Category	Therapeutic Area Features	Example Product
CNS medicines	> CNS product space very competitive > Multiple products in each class so product differentiation is key	Wellbutrin XL® Belvic
Opioids	> MR improves pain management significantly > Risks of dose-dumping and need for Abuse-Deterrent MR driven by this class	OxyContin®
ADHD	> Patient compliance a big factor for pediatrics > Interesting clinical requirements to have different PK in day-time vs night-time	Focalin XR™ Concerta®
GI products	> Targeted or locally acting technologies important	Lialda®, Pentasa® (mesalamine)
Over the counter	> Product differentiation important > MR products provide marketing opportunities	Prevacid®24HR Claritin-D® 24-Hour

An impressive variety of MR formulation technologies are available eliciting a wide range of control on drug release and delivery. Careful selection of appropriate excipients and delivery technologies is key to the design of MR formulations fulfilling specific performance requirements, from gastro-retention (GR) to sustained or pulsatile release.

Challenges in successful MR formulation development

GI physiology and implications for selecting an MR technology

Successful oral MR formulation development requires consideration of the multiple environments the formulation will encounter across different anatomical regions during GI transit. Factors such as transit time, absorptive surface area, permeability, fluid volumes and composition, pH, enzyme and transporter expression must all be considered (Table 2).

Table 2: GI regions, typical adult physiology and key features

GI Region	Length (m)[a]	Surface area (m2)[a]	pH (fasted)[a]	Transit time (hrs)[a]
Oesophagus	0.25	0.1	6 - 7	Rapid
Stomach	0.15	0.1	1 - 2	0 - 2
Small intestine - duodenum	0.25	2	4 - 6	rapid
Small intestine - jejunum	2.5	100	6 - 7	0.5 - 2
Small intestine - ileum	3	150	7 - 7.5	0.5 - 2.5
Large intestine	1.5	0.35	5 - 7	20

[a] Approximate values presented however large individual variations can occur

As a general rule of thumb drug absorption from more distal regions of the GI tract can become more problematic. MR formulations are specifically challenged when they reach the large intestine due to limited liquid volume and high bacterial content, resulting in dissolution, solubility and stability challenges in-vivo[1].

Whilst a formulation scientist would be highly cognisant of the need for drug solubility under different intestinal conditions as a driving force for absorption, permeability considerations are also crucial. Drugs pass through cells lining the gut wall, either by a passive transcellular or paracellular process down a concentration gradient, or an active process via a transmembrane protein and energy which, in turn, can be absorptive (influx) or exsorptive (efflux). Understanding permeability can help to define the rate limiting process for absorption in a MR formulation strategy.

The GI tract also has luminal (e.g. peptidases esterases), bacterial, and mucosal/gut wall enzymes impacting on oral drug metabolism, absorption, and bioavailability. Expression gradients have been evaluated for many, such as the cytochrome P450 enzyme CYP3A4, which has high expression in the upper small intestine but limited large intestinal expression. Large intestinal delivery of a CYP3A4 substrate drug could bypass this and increase bioavailability[2]. MR release rates may result in local drug GI concentrations below saturation thresholds for enzymes and transporters. This can lead to suboptimal PK and requires careful consideration.

In addition understanding potential food effects, both positive (increasing drug exposure) or negative (decreasing drug exposure) is also important, particularly for MR formulations such as hydrophilic matrices. Food effects on GI physiology including increased pH, slower gastric emptying, altered contractile forces, induction of bile and altered transit rates, can impact formulation performance (e.g. premature loss of integrity due to contractile forces), or the drug itself (e.g. improved solubilisation in meal lipids). The extent of food effects is meal dependent and clinical MR fed investigations are important to consider as part of the MR formulation development strategy.

Physicochemical properties of the API

Physicochemical properties and dose of the API can have a significant impact on the performance of MR formulations. Highly soluble drugs normally show a relatively fast release rate, which can be difficult for the formulation to control. If the drug has pH dependent solubility, in-vivo drug release rates can vary throughout the GI tract. In this case a pH modifier can be used to create a microenvironment within the dosage form, and smooth the drug release profile. Alternatively, a pH independent formulation technology such as an osmotic pump could be considered. For soluble drugs, for which the diffusion is the main driving force for drug release, the molecular weight is also important as it will affect the diffusion coefficient. Depending on the drug properties, drug loading in the formulation can also affect the drug release profile, and therefore further adjustment may be required to maintain the same drug release profiles for different formulation strengths.

Selecting an appropriate MR formulation technology

Whilst the development of MR formulations has historically been a part of late stage development or LCM strategies, there are increasing examples of where MR technologies are being utilized in the development of new chemical entities (NCEs). In all cases a clear definition of the Target Product Profile (TPP) is important, to outline the desired characteristics of the drug product required to deliver the desired in vivo performance. The TPP is based on the drug product requirements including the intended clinical use, dosage strength(s), drug release characteristics, stability and other product quality criteria.

There are many MR formulation technologies which can be used to control the rate and time of drug release to achieve a particular TPP. A developer is therefore faced with the need to select the strategy that will provide optimal results in the most efficient and cost-effective manner. Table 3 outlines these formats, their objectives, and the types of formulations used to ensure appropriate release.

Table 3: A selection of MR formats, their behaviours and technologies they represent

MR format	Objective	Technologies	Formulation types
Sustained or extended release	› Extend the in vivo release profile of the drug or enable 1-2x daily dosing	Matrix or film coated tablets or multiparticulates	Matrix tablets, coated tablets or multiparticulates
Delayed release	› Release the drug at or near the intended site of absorption or action such as upper small intestine or colon › Deliver time, pH and/or microbially-triggered release	pH or time dependent coating	Tablets, capsules or multiparticulates
Gastro-retention	› Delay gastric emptying from the stomach to deliver the drug over a prolonged timeframe to the upper GI tract when an absorption window exists	Swellable raft, floating and bioadhesive systems	Tablets or capsules
Gastric bypass	› Prevent release of the drug in the stomach › Overcome gastric irritation or instability of the drug	Enteric coating	Enteric coated tablets or capsules
Biphasic release	› Eliminate the need for repeat dosing. › Provide rapid therapeutic effect from an immediate release layer and extended dosing via a sustained release layer	Bilayer tablets or multiparticulates with different release profiles	Bilayer tablets or multiparticulates
Pulsatile release	› Drug release as a pulse after a predetermined lag time – designed according to the body's circadian rhythm › Beneficial release mechanism for time-dependant dosing or for drugs that undergo first-pass metabolism.	Bilayer tablets or multiparticulates with different release profiles	Bilayer tablets or multiparticulates
Zero order release	› Provide zero order drug release with the release rate independent to the pH variation throughout the GI tract	Elementary, controlled-porosity or push-pull osmotic pump system	Coated tablet

Sustained or extended drug delivery is possible using various approaches to control release of drug from the dosage form by diffusion or erosion mechanisms. Incorporating the API into a hydrophilic, slow erosion or inert polymer matrix can retard drug release and extend drug delivery. The drug release mechanism can either be drug diffusion through the polymer layer or eroding of the matrix or, in most cases, a combination of the two. Barrier coatings can also modify the drug's dissolution profile by controlling access of biological fluids to the drug itself, which will dissolve and then release through the barrier via diffusion. A variation on this theme is a mechanism that utilized the osmotic pressure generated by osmogenes or the drug itself as the driving force to pump the drug out of the core through an orifice or controlled porosity coating.

Formulation technologies can also be used to target drug delivery to a preferred site of absorption. Gastro-retentive (GR) dosage forms for example can be

retained in the stomach for longer allowing a sustained release of drug to the upper small intestine when a narrow absorption window in this region of the GI tract has been defined. Delayed release systems are crucial for drugs designed to target the colon for treatment of both local and systemic disease. Colonic delivery is effective for targeting inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, as well as bowel cancer. The colon can also be an effective portal of entry for some systemic therapies. Lower levels of luminal and mucosal digestive enzymes present in the colon compared with those of the small intestine reduces the chances of drug degradation. Susceptibility to distinct colonic environmental conditions such as pH levels, pressure or the presence of particular bacteria are all potential dissolution triggers to achieve a delayed release profile.

In a pulsatile or biphasic formulation, time-dependant delivery controls drug plasma concentrations. These systems incorporate a specific lag-time based on GI transit. As it usually takes about 3-4 hours for ingested matter to pass through the small intestine, a time delay of 5 hours is a common target for drugs designed for colonic absorption for example. Based on therapeutic requirements, immediate, delayed or sustained release can follow time-lagged, pulsatile or biphasic release, multiplying the number of possible bioavailability profiles.

Development of Analytical Methods

Establishing suitable analytical methodologies is of paramount importance to the successful development of all MR formulations. The critical quality attributes such as assay, related substances and dissolution release rate are critical to ensure that not only are the required safety aspects adhered to i.e. potency and purity, but to ensure that the desired performance and drug release of the MR formulation is obtained.

Perhaps the most important aspect of MR formulation characterization is the dissolution test which will be used to confirm and validate the MR characteristics of the formulation. The development of an appropriate dissolution methodology should be based on the physiochemical in-vitro and in-vivo characteristics of the drug substance and the TPP of the drug product.
A dissolution method needs to be able to:

a. Discriminate between formulations based on critical process parameters and formulation composition.

b. Assess batch to batch consistency.

c. Determine the stability of relevant release characteristics.

Dissolution methods for MR formulations are typically developed using USP I or II apparatus (baskets or paddles) depending on the type of formulation.

Additionally, dissolution methods utilizing USP III apparatus maybe considered for GR formulation types. Solubility experiments need to be performed to assist with identifying suitable dissolution media as sink conditions are required. In addition to this, solubility assessments of the API and formulation across the physiological pH range need to be performed; Often, a 2-stage dissolution test is developed, which consists of a low pH and high pH dissolution media and simulates more closely with the environment of the GI tract. For sustained release, if the API is found to have good solubility that is pH independent then it may be possible to develop a single-stage dissolution method. The length of the dissolution test should allow greater than 80% of the formulation to be released with regular sampling intervals so that the shape of the dissolution profile can accurately be determined.

Use of in silico tools

In vitro and preclinical data can also be used to identify potentially suitable MR formulation strategies during early stages of development through the use of modelling and simulation, using physiologically based PK (PBPK) and physiologically based biopharmaceutics modelling (PBBM) models in software such as GastroPlus®. This type of software provides in silico predictions of the impact of MR input parameters on PK profiles, in addition to regional drug absorption impacts, food effects and many others.

Translational Pharmaceutics®

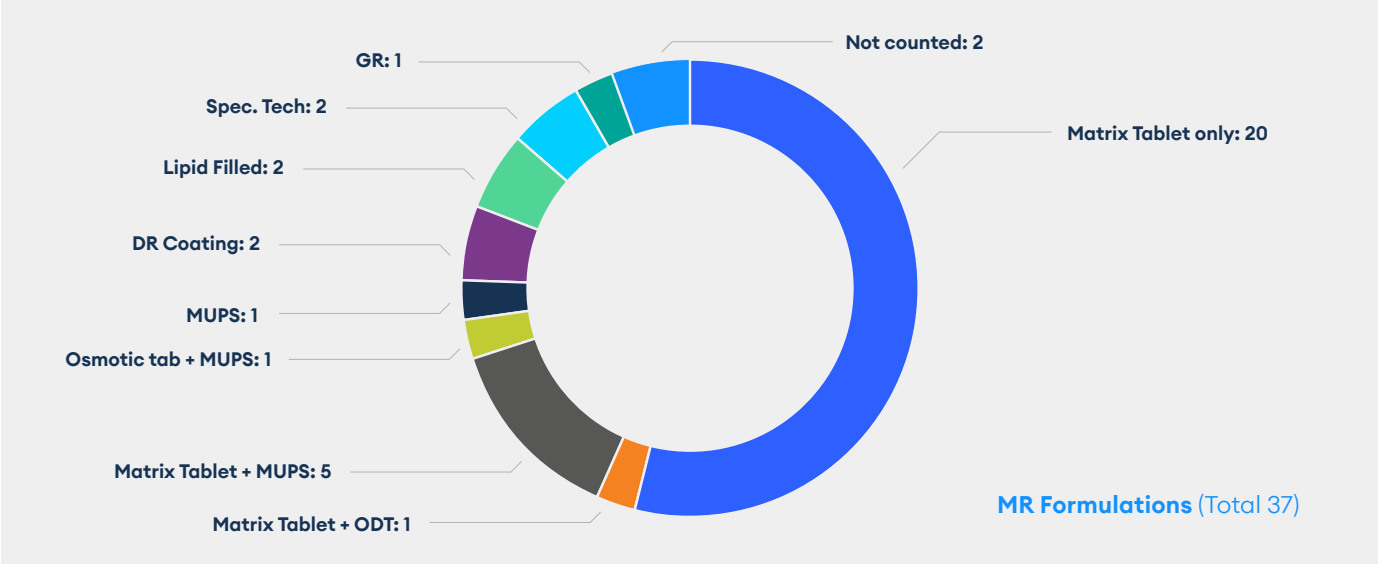
Conventional approaches to optimizing a drug product typically focus on a range of in vitro formulations which are screened in one or more preclinical in vivo models prior to selecting a small number of lead prototypes for testing in humans. However, translation of bioavailability between preclinical species and humans is poor[3,4,5,] the process is linear and rigid such that, if the formulations tested in the clinic fail to meet the target criteria, the project must retrench to the in vitro/preclinical phase. Since one cycle of this process can take up to 18 months and cost more than $1.5 million, the time and financial penalties on the development project are significant. In order to move away from this paradigm, alternative approaches are required to reduce the reliance on in vitro and preclinical methodology and to allow the rapid in vivo optimisation of MR formulations.

Translational Pharmaceutics® offers a new development paradigm in which the screening and selection of drug products is driven based on human data. This technology platform is unique to Quotient Sciences and integrates formulation development, real-time adaptive GMP manufacturing and clinical testing. A recent publication by Tufts CSDD shows that biotech/pharma companies save on average>12 months of development time compared to traditional development models. This

translates into R&D cost savings of >$100 million as well as the benefit of getting products to market much sooner[10].

Quotient has significant experience in the development and optimisation of MR products using Translational Pharmaceutics®, having conducted more than 50 formulation optimization programs in last 5 years across a wide variety of therapeutic areas. A breakdown shows that 68% of the project involved a single technology platform and 32% incorporated two or more technology platforms. 54% of the total projects are were based on the use of matrix tablets and 27% involved coated systems including MR multiparticulates (MUPs), tablets and osmotic pumps for sustained and delayed release.

Figure 1: Different technologies used for MR formulation development



As discussed previously, there are numerous potential formulation strategies available for MR dosage forms. Selecting a specific platform and the quantitative levels of critical-to-performance excipients in that formulation can be challenging based on surrogate nonclinical, in vitro or in silico data. In-study protocol flexibility using Translational Pharmaceutics can enable optimization of key variables based upon actual clinical data and/or the assessment of multiple technology platforms to achieve the desired TPP. Offering potential benefits in terms of PK variability and bimodal release combination flexibility, could be compared to a matrix MR tablet, which could be easier to commercialize if performance was sufficient.

How design space can be incorporated into this within an adaptive clinical study

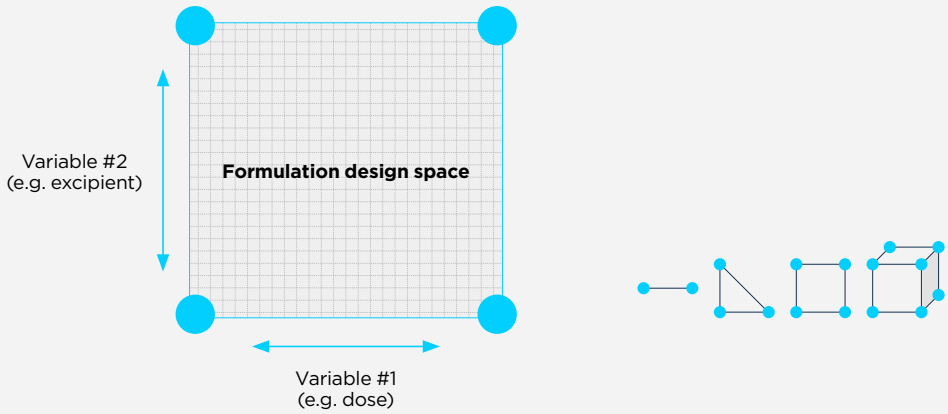
The principles of Translational Pharmaceutics® are ideally suited to the development of MR formulations. Benefits are maximized by utilization of the concept of 'design space' as described in ICH Q8[6]. In this legacy context, design space is linked to a Quality-by-Design (QbD) development paradigm, where the intention is that a formulation or processing space will be defined within which in vivo product performance will not be affected. Formulation design space within a Translational Pharmaceutics program adapts this concept to a space in which it is fully expected that in vivo product performance will vary as compositions are changed. This allows critical-to-performance formulation components to be utilized as continuous variables during the conduct of the clinical study, enabling enhanced precision in selection of the formulations to manufacture for dosing.

The design space concept can be applied to any formulation, drug product, or dosage form. The goal in MR formulations is to address all the adjustable, critical-to-performance parameters that can influence release rate and PK profile. While mapping two variables is common, it is possible to define the design space for as many as are relevant[7]. For example, any of these following parameters could be considered as part of the design space:

- API Dose/Concentration
- Functional Excipient Content
- Drug: Polymer Ratio
- Surface Area Volume Ratio
- Coating Composition/Thickness

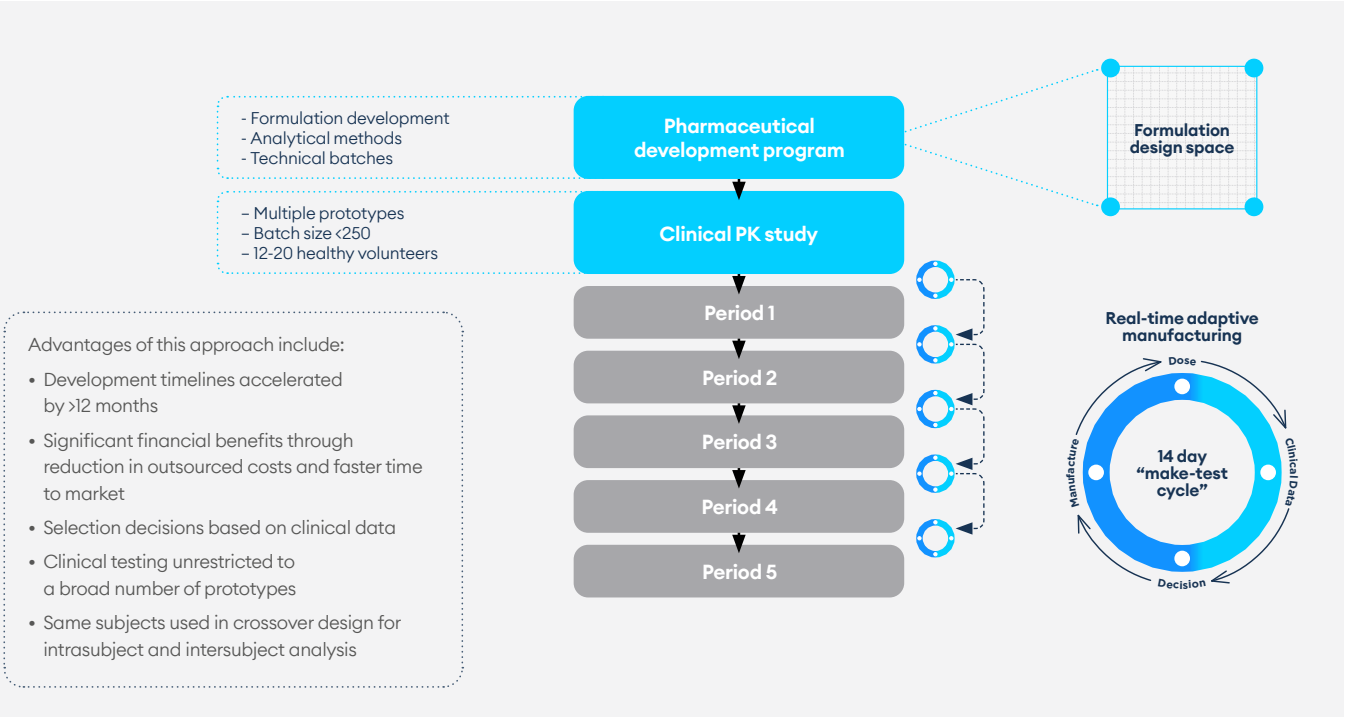
Extremes of release rate can be developed in vitro, and the corresponding critical parameter values may be used as the minimum and maximum values to define the design space - the corner points (Figure 2). Any formulation within this map may be manufactured and dosed without any regulatory amendment or notification. As clinical results develop, trial medications will be adjusted accordingly to optimize the drug-release pattern and increase or decrease the dose as required.

Figure 2: Formulation design space. Initial data will be generated using the corner points. The large, square diagram represents the use of two variables, but other numbers of variables may be considered simultaneously. For example, from left to right, the small diagrams represent 1, 2 interdependent, 2, and 3 variables



The flexibility a design space concept affords is only beneficial to the extent that manufacturing can keep pace with clinical trial dosing modifications. Seamlessly integrating a manufacturing facility with the clinical testing organization running the study can shrink the time between decision points and restart the trial with the next iteration of drug product (Figure 3).

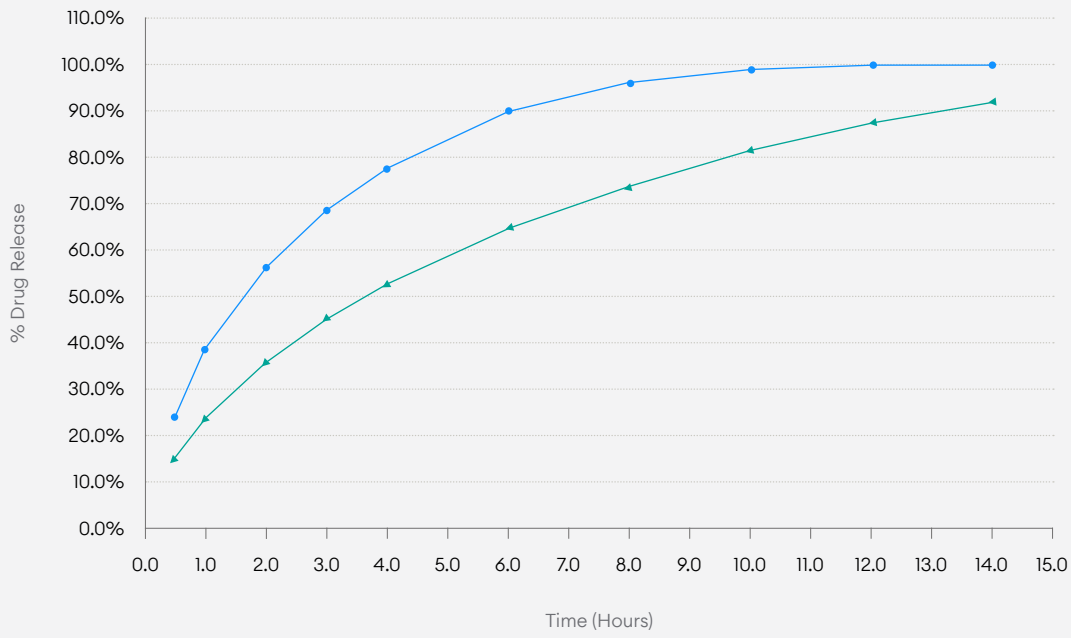
Figure 3: Design-space-based development followed by real-time adaptive manufacturing with a 14-day make-test cycle, for example, sharply cuts the overall trial time by shrinking the intervals between test periods.



Radiolabelling of MR dosage forms for scintigraphic imaging can allow direct in vivo visualisation of drug product location which can be incorporated into a design space study to help define factors that influence PK, such as changes in the absorption profile with site of delivery (Case study 2).

Development of Dissolution Methods
Dissolution testing is key during the development phase of the program so that MR formulation composition can successfully be identified in order to obtain a desired release rate. For design space studies a slow and fast release formulation type is typically developed using common excipients to both formulations with a change being made to specific excipient ratios to alter the release rate. The dissolution testing performed can then be utilized to optimize this design space and allow successful MR formulations to be developed. An important key parameter during dissolution method development is to ensure that the method is capable of being discriminatory between composition types and as such allow optimum formulations to be developed.

Figure 4: Slow and fast release dissolution profile for MR formulations utilizing the design space concept



The dissolution profiles shown in Figure 4 show the extremes of fast and slow release MR tablet formulations that were developed by varying the amount of hydroxypropyl methylcellulose (HPMC) polymers present in the formulation. The key parameter assessed was the amount of drug released at 80%, which was at just over 4 hours for the fast release formulation and just under 10 hours for the slow release formulation. By utilising the design space approach and by setting a shelf-life on the formulation extremes it was possible to manufacture MR formulations anywhere within the MR formulation design space in the subsequent clinical study based on emerging PK data.

In vitro-in vivo correlations (IVIVCs)
An IVIVC is a tool for predicting the in vivo bioavailability of a drug based on its in vitro data. If an IVIVC can be developed and validated then it can be used to justify biowaivers, post-approval scale-up changes and establishing dissolution specifications. Three often-used approaches to perform IVIVC are the so-called Level A, Level B, and Level C approaches.

For Level A analysis, the fraction drug absorbed is plotted against the fraction drug dissolved in a generally linear correlation between in vitro dissolution and the in vivo input. MR products are the focus of IVIVCs since only products with dissolution rate-limited absorption should exhibit a Level A correlation. Level B IVIVC compares the mean in vitro dissolution time to either mean residence time or mean in vivo dissolution time and are used rarely. Level C IVIVC establishes a single point relationship between a dissolution parameter and a PK parameter and does not reflect the complete shape of the plasma concentration time curve but can be useful in early stage MR development.

Case study 1

Development of an optimized MR tablet formulation for initial proof-of-concept trials

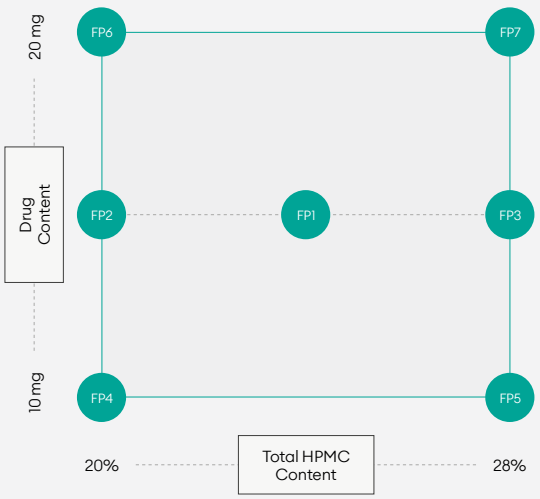
Background and objectives

SLx-2101, a novel PDE-5 inhibitor1 was being developed by Surface Logix as an antihypertensive agent. A Phase II pilot clinical study using an immediate release tablet had been conducted and the data determined it was necessary to develop a once-daily modified release formulation to reduce Cmax related adverse events and ensure the 24h PK profile remained within the therapeutic window.

Project scope

Using formulation design space concepts, a strategy built upon ICH Q8 Development Pharmaceutics and Quality-by-Design principles, HPMC based matrix SLx-2101 MR tablets were developed for assessment in an adaptive relative bioavailability Phase I study to and optimize the MR tablet formulation based on human clinical data. A two-dimensional formulation design space was established covering dose strengths between 10-20 mg and sustained drug release durations between approximately 12 and 20 hours (Figure 5). The relationship between key formulation variables and formulation performance were investigated. Representative formulations at the extremes and the mid-points of the design space were manufactured and characterized to demonstrate that the performance of the formulation can be controlled by varying the levels of drug loading and HPMC in the formulation (Figure 5).

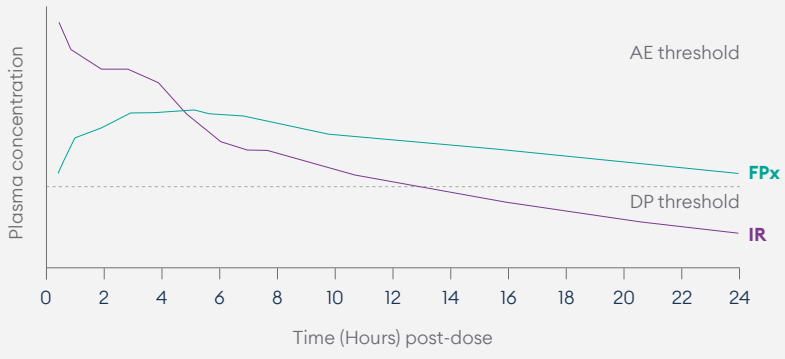
Figure 5



Outcome

SLx-2101 MR tablet formulations within the design space were manufactured real-time and evaluated in a flexible clinical study, avoiding the restriction of only dosing pre-defined formulation compositions. The formulation selection was driven by clinical data from the previous dosing period and the optimal MR formulation was identified in 6.5 months (Figure 6).

Figure 6



Case study 2

MR formulation optimization using design space and scintigraphic imaging[8]

Background and objectives

Phase II trials for an MR formulation of LY545694 (glutamate receptor antagonist for persistent pain management) were performed by Eli Lilly. Results indicated that the preferred site of drug absorption was in the small intestine, and hence based on expected GI transit times, significant quantities of drug were being delivered to a non-absorptive region. The requirement was therefore to identify an optimized MR formulation capable of achieving the same exposure and plasma concentration–time profile, but with a lower dose, by a precise, optimal targeting of drug delivery to the small intestine.

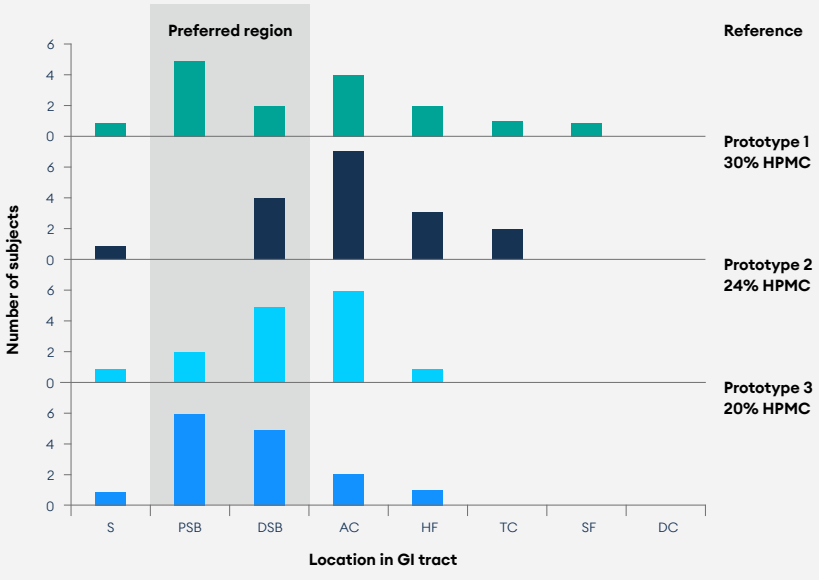
Project scope

A single dimension design space for a HPMC matrix MR tablet (2 to 8 hours release) was used complimentarily with scintigraphy. Tablets were radiolabelled to visualize the erosion and anatomical location. The clinical protocol was designed as a six-period crossover study, and polymer content was adjusted to target delivery to the absorption site.

Outcome

Based on in vitro dissolution data a 30% HPMC polymer formulation was predicted to give a faster release profile in vivo than the original, reference MR formulation, resulting in the desired improvement in relative bioavailability. However, the scintigraphic and PK data confirmed a slower completion of erosion, which was attributed to a higher mechanical strength in vivo than otherwise predicted from dissolution testing. Two additional formulations were subsequently selected and dosed (24% and 20% HPMC polymer respectively), with the 20% polymer level successfully giving the desired exposure profile. The optimal MR formulation provided comparable exposure to the reference MR formulation with 30% less drug in the dosage form. Scintigraphic data supported this observation, and showed that in all subjects, erosion was largely complete in the small intestine (Figure 8).

Figure 8: Anatomical location of complete erosion for the radiolabelled reference and prototype MR formulations. The light grey shaded area indicates the apparent regions available for absorption. Figure abbreviations are as follows: stomach (S), proximal small bowel (PSB), distal small bowel (DSB), ascending colon (AC), hepatic flexure (HF), transverse colon (TC), splenic flexure (SF), and descending colon (DC).



Overall, a new MR prototype targeted drug release to the absorption window, allowing a lower dose product to match AUC of the sub-optimal product and therefore providing a saving on cost of goods (COG). The study also confirmed the potential risks of using dissolution methodologies which are not clinically relevant to select formulation compositions.

Case study 3

Life Cycle Management: Development of an MR tablet formulation for once-daily dosing and generation of an IVIVC[9]

Background and objectives
Arena developed and commercialized Lorcaserin HCl (a 5-HT2c agonist for chronic weight management in obese adults) for twice-daily dosing as an IR tablet (BELVIQ®). Post launch, there was a commercial and clinical need for a once-daily, MR tablet to compliment the original formulation and rapid identification of an MR formulation was required as part of LCM.

Project scope
The formulation design space was based on the tablet coating composition to control release rate. The clinical protocol was designed as a five-period crossover study, initially dosing a mid-range prototype, and then faster or slower release based upon the emerging PK data. The fifth period of the study was an optional food-effect assessment on a lead prototype.

Outcomes
Extended release and good exposure were demonstrated in vivo, and with the ability to adjust formulation composition based on arising PK an MR formulation was identified that maintained a 24- hour efficacious plasma concentration (Figure 6). In addition the dissolution and PK data from this program were evaluated to identify a potential IVIVC (Figure 7).

Figure 6: Plasma concentration vs. time plot for Lorcaserin HCl formulations

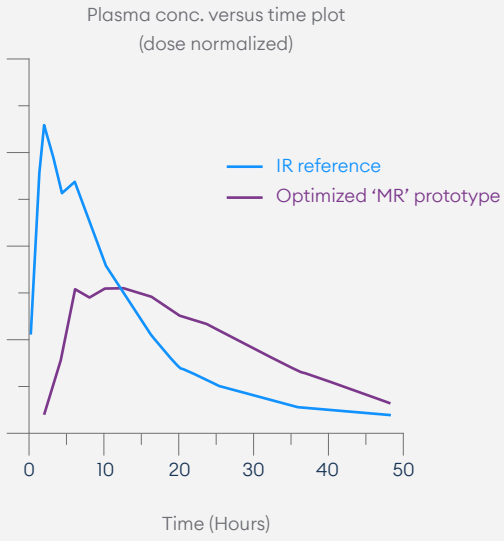
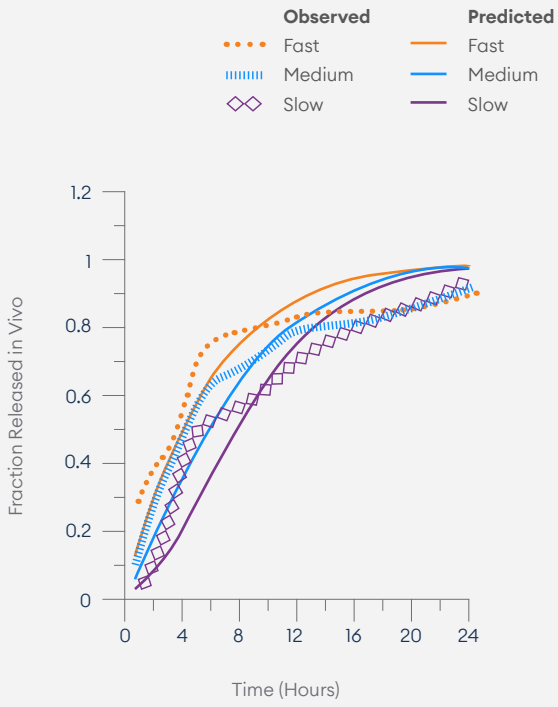


Figure 7: Predicted vs. Observed in vivo release profiles



A suitable once-daily formulation was identified within 6 weeks of commencing the program. Level A IVIVC was also established, providing valuable efficiencies for downstream project activities, including specification setting and change management. A new drug application (NDA) based on this formulation was submitted to FDA.

Considerations for cost of goods (COG) and scalability of MR Formulations

Even at an early stage of development it is important to consider COG, scale-up, robustness and product manufacturability. Manufacture of MR formulations may involve complex specialized technologies and excipients, as such the initial COG/manufacture maybe higher. However, owing to the reduced dosage regimen the number of units needed per patient may be reduced in comparison to a conventional IR dosage form, therefore, the long-term cost effectiveness is comparatively enhanced.

Over the past decade, there have been strong industry and regulatory drivers for companies to demonstrate a complete understanding of the impact of product or process change on product quality and performance through QbD. Implementation in the development and scale-up of MR formulations reduces the defects and product variability by setting up of quality target product profiles (QTPP), process and product design and its understanding, risk assessment by design of experiment (DoE), control strategy and continual improvement.

The impact of variability in these parameters is typically characterized by in vitro studies only (e.g. dissolution testing) which, in the absence of an IVIVC, may not provide assurance of in vivo performance. As such identification of “safe space” control strategies via process settings or product specifications carries risk. Translational Pharmaceutic® clinical studies also offer the potential to generate clinical PK data to underpin and interrogate QbD strategies. Examples of previous applications have included impact of excipient quantities (as previously outlined), wet granulation state and variation in tablet hardness on PK performance.

Summary

An effective MR formulation must deliver the drug at the right rate to the right place in the GI tract to maximize therapeutic benefit and/or reduce unwanted side effects. It must do this whilst moving through the GI tract, passing through a range of different environments, experiencing changes in environmental parameters such as pH, fluid volume, fluid composition, and physical forces, whilst also accounting for regional changes in drug absorption. This requirement, when coupled with the physicochemical and biopharmaceutics properties of molecules in development, presents a considerable challenge to the development team in identifying a drug product formulation capable of achieving the TPP.

Traditional formulation development strategies have proven to be suboptimal and time-consuming for the development of MR formulations and carry the “accepted risk” that in silico, in vitro, and preclinical testing methods are yet unable to provide categorical insights into the predicted in vivo performance in humans. A new development paradigm has emerged, Translational Pharmaceutics®, which provides development teams today the ability to optimize formulation compositions and production processes in real time based on arising human PK data.

Quotient Sciences has supported more than 100 modified release development programs over the past decade. Our extensive formulation know-how coupled with our agile and flexible approach to clinical and commercial manufacturing, makes us the ideal partner to provide an end-to-end solution for the development of modified release drug products.

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Who is Quotient Sciences?

Quotient Sciences is a drug development and manufacturing accelerator providing integrated programs and tailored services across the entire development pathway. Cutting through silos across a range of drug development capabilities, we save precious time and money in getting drugs to patients. Everything we do for our customers is driven by an unswerving belief that ideas need to become solutions, molecules need to become cures, fast. Because humanity needs solutions, fast.

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