DIFFERENTIATING ORAL SUSPENSIONS WITH VERSATILE EXCIPIENTS

In this article, Mariona Venceslao Molins, Marketing Manager for Europe and Global Market Manager for Oral Treatment, and Liliana Miinea, PhD, Technology Manager, both at Lubrizol, discuss how excipient-based approaches can facilitate patient-centric formulations and transform oral suspensions.

In today's crowded pharmaceutical market, drug developers increasingly need to consider how their products can align with patients' preferences and improve compliance. Certain patient populations – such as paediatric and geriatric, or those with neurodegenerative conditions – often struggle with taking oral solid dosages. One possible cause of this is difficulties with swallowing large tablets and capsules (dysphagia). In a large population-based survey, one in six adults in the US was found to struggle with dysphagia.[1] Furthermore, approximately 1% of children in the US experience swallowing difficulties,[2] and dysphagia can also be a common symptom of neurodegenerative disorders.[3] This challenge will only be further exacerbated by the global demographic shift to an ageing population, with the number of people aged 80 years or older expected to triple to 426 million by 2050.[4]

When it comes to improving patient compliance with medication, oral suspensions are a useful option. They are much easier to swallow than solid dosage forms, which is crucial for those who suffer from dysphagia. Using the right excipients, oral suspensions can also be developed in palatable, no-spill and shake-free formats, which are more convenient for patients suffering from the tremors symptomatic of conditions such as Parkinson's disease and multiple sclerosis.[5] These factors can be crucial for helping patients stick to their vital medication regimens.

However, the pharmaceutical landscape is complex and, alongside patient compliance, there are a host of other factors that drug developers need to consider. First and foremost, formulators are looking to create products that stand out in a crowded and competitive market. At the same time, pharmaceutical manufacturers are increasingly looking to streamline their processes to reduce complexity and cost. Developers need to balance these competing demands while delivering patient-friendly products. This is where pharmaceutical excipients shine.

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GIVING DRUGS A NEW LEASE OF LIFE

Over the years, the excipient market landscape has transformed. Drug developers are no longer looking for simple binders and fillers to package their APIs, but for functional excipients that can help them to bring highly differentiated products to market. This can be achieved by formulating an entirely new drug product with a novel API as part of an NDA or through the reformulation of a pre-existing API through the US FDA's 505(b)(2) approval pathway.

The 505(b)(2) pathway allows for the use of safety and efficacy data from previous studies to streamline approval.[6] It is possible to capitalise on the 505(b)(2) route by reformulating approved drugs using versatile excipients that facilitate more patient-centric dosage forms. Ultimately, this allows for the creation of differentiated products, including opportunities for over-the-counter (OTC) drugs that are more convenient and comfortable for patients, which can give them a competitive edge.

EXCIPIENT-BASED APPROACHES FOR TRANSFORMING ORAL SUSPENSIONS

Whether developing a new drug product or reformulating a pre-existing one, the choice of excipient is crucial. With oral suspensions, the key excipients are the suspending agents. These are a class of

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excipients added to dispersed systems to ensure that solid particles in the formulation are kept uniformly distributed within the continuous phase, thereby maintaining the physical stability of the product.

The importance of the suspending agent cannot be understated. When dispersing an API in the liquid phase, formulators need to overcome an array of challenges, including (but not limited to) creaming, sedimentation, caking, particle growth and adhesion to the container.[7] To counteract these processes and formulate a shelf-stable oral suspension, a high-quality suspending agent is critical. Suspending agents can bring other benefits too, such as helping manufacturers to optimise texture and mouthfeel, improving the patient experience.

Suspending agents come in many forms, and formulators must select the option that is right for their drug development project. One popular class of suspending agents is natural polysaccharides and their derivatives (such as starch, pectin and xanthan gum), which work by increasing the viscosity of the aqueous systems in which they are dispersed. Cellulose-based suspending agents are a subset of these natural polysaccharides and include water-soluble ethers, such as methylcellulose and hydroxyethyl-cellulose. Another alternative used in the market is hydrated silicates, which are naturally occurring siliceous clays that form colloids in water (e.g. bentonite and hectorite).[7]

Carbomers – synthetic high molecular weight cross-linked polyacrylic acid polymers that swell in water to form hydrogels – are another important class of suspending agents that can confer significant advantages to a formulation.

CARBOMERS IN ORAL SUSPENSIONS

Of the vast array of suspending agents, carbomers are emerging as a popular choice for creating differentiated oral suspensions, thanks to their unique chemistry. Carbomer particles swell when they are hydrated and neutralised, forming a colloidal dispersion. These swollen, close-packed microgels can hold the solid API particles permanently within the gel structure, helping to provide excellent suspending properties – even at very low inclusion levels.

The suspending ability of carbomers is due to their high yield value. This helps to prevent sedimentation and maintain uniformity. Carbomers also impart shear thinning properties, which means that they flow more easily when under stress,[8] allowing for easier filling and dosing and making them more amenable to cold processing during manufacture.

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Carbomers are unique in that they provide a wide range of viscosity profiles and have high yield values, even at low concentrations. These combined features make carbomers more efficient as a suspending agent than cellulose-based excipients or natural gums such as xanthan.

Using these polymers, formulators can impart properties that make the final product easier to use for the consumer, such as improved pourability, ease-of-swallowing and no-spill properties. Carbomers can also impart mucoadhesive properties to a formulation. This mucoadhesion can improve the sensorial experience by providing a soothing effect for a cold and cough formulation, for example, while simultaneously enhancing bioavailability and tissue protection. Furthermore, due to their long history of use within the pharmaceutical industry, formulators can be confident that carbomers are safe and effective.

BRINGING IT ALL TOGETHER: A CASE STUDY OF CARBOMERS IN ACTION

Paracetamol is one of the most well-known and popular OTC analgesics in the world.[9] Using a popular carbomer available on the market,[10] formulators were able to take this common drug and reformulate it into a differentiated oral suspension with improved patient-centric and manufacturer-friendly properties.

Firstly, the inclusion of the carbomer polymer imparted no-spill properties to the oral suspension compared with a reference formulation, allowing for greater ease-of-use for patients who suffer from neurodegenerative disorders. Furthermore, the polymer imparted mucoadhesion, allowing for protective tissue coating and greater bioavailability. Lastly, by facilitating cold processing, the resulting oral suspension allowed for superior scalability and ease of manufacturing. This effectively illustrates how incorporating the right excipient can transform a drug formulation and facilitate crucial patient-centric properties while also addressing manufacturing needs.

FACTORS TO CONSIDER WHEN CHOOSING AN ORAL EXCIPIENT

Innovation in the excipient landscape means that there is a wide range of variables to consider when seeking out the right excipient for a drug development project beyond functional ability. Formulators should seek out multifunctional excipients, such as carbomers, that can simplify formulations and streamline manufacturing, as well as increase the potential for product differentiation.

Another aspect to consider is that natural thickeners and suspending agents are often derived from plants and, in recent years, crop shortages have led to challenges in sourcing these ingredients. These difficulties can hinder vital R&D work and disrupt commercial production, so using synthetically derived excipients, such as carbomers, from a provider that has a strong supply chain is critical. The chosen excipient supplier should also be able to provide comprehensive expertise and technical support, which will help to facilitate the development of effective and differentiated oral suspensions using their excipients.

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THE POWER OF EXCIPIENTS

In a crowded and competitive market that needs to serve an increasingly ageing population, and with a significant proportion of patients struggling with dysphagia and neurodegenerative disorders, patient-centric oral suspensions will continue to be in demand. Whether for 505(b)(2) reformulations or NDA projects, excipient-based strategies are key to helping drug developers to bring enhanced oral suspension products to market.

In particular, carbomer-based suspending agents offer an array of advantages due to their unique chemistry. Ultimately, by incorporating effective excipients that facilitate patient-centric formulations and streamline manufacturing, pharma companies can bring differentiated products to market while driving improved quality of life for patients – a win for everyone.

ABOUT THE COMPANY

The Lubrizol Corporation, a Berkshire Hathaway company, is a specialty chemical company whose science delivers sustainable solutions to advance mobility, improve wellbeing and enhance modern life. Founded in 1928, Lubrizol owns and operates more than 100 manufacturing facilities, sales and technical offices around the world and has more than 8,000 employees.

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