KEEPING UP WITH THE DEMAND FOR EFFECTIVE OPHTHALMIC DRUGS

In this article, Robert Lee, PhD, President of the CDMO Division of Lubrizol Life Science Health, explores the growth of the ophthalmic drug market and discusses the challenges that pharma companies may face when creating drugs to treat some of the most common ocular indications.

With rising public awareness of eye-related diseases and an ageing population, the demand for treatments for ocular conditions has dramatically increased. The global ophthalmic drug market has seen significant growth as a result. Its value was estimated to be US $28,400 million (£20,800 million) in 2020 and is expected to increase further to $36,300 million by 2025.[1–3] The rising incidence of glaucoma and age-related macular degeneration (AMD) in particular have been identified as key factors driving the predicted expansion.

Of the 2.2 billion people affected globally by ocular conditions, AMD (170 million), cataracts (94 million), glaucoma (7.7 million) and diabetic retinopathy (DR) (3.9 million) are the most common.[4] Some common ophthalmic conditions, including glaucoma, impact the front portion (anterior) of the eye, whereas others, such as DR and AMD, affect the rear portion (posterior) of the eye. Drugs used to treat these conditions will therefore need to reach the target area of the eye, resulting in different delivery requirements.

More and more pharma companies are keen to develop new ocular drugs as a result. However, developing effective ophthalmic products is no simple task; challenges often come in the form of formulation issues and the need to identify suitable delivery methods. Pharmaceutical companies will need to find a way to navigate these challenges throughout product development to ensure market success.

Fortunately for pharma companies seeking to take advantage of the growth in the sector, there is no need to face the challenges of ophthalmic drug development alone. One of the keys to success is identifying and partnering with contract development and manufacturing organisations (CDMOs) that have extensive ophthalmic drug development experience and expertise to support pharma companies on their manufacturing journey.

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UNDERSTANDING ANTERIOR EYE TREATMENT NEEDS

Drug delivery methods targeting the anterior section of the eye are often topical, commonly relying on dosage forms such as eye drops and topical ointments. Anterior delivery treatments are easy to administer and are the most widely available ophthalmic treatments. Despite their popularity, however, there are many challenges surrounding topical ophthalmic treatments, such as their ability to penetrate the cornea or stay on the eye long enough to achieve efficacy.

The bioavailability of APIs delivered in the form of eye drops has been reported to be as low as 5–10%.[5,6] One reason for this is that the conjunctival sac capacity is typically lower than the treatment volume, leading to a large proportion of the liquid running off from the eye area. Blinking and innate solution drainage also mean that the drug is often removed from the target area before it can be absorbed. The corneal and conjunctival epithelia additionally act as natural barriers, further limiting drug absorption.

Frequent administration to achieve the desired effect may be needed to compensate for low efficacy of the drug product. However, this has the potential to lead to toxicity, reduced patient compliance and increased costs. With careful formulation, residence time on the eye can be prolonged.

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This can be achieved using delivery systems that offer muco- or bioadhesive properties, such as solid lipid nanoparticles, micelles and liposomes. Excipients such as carbomers, polycarbophil or sodium alginate can also establish bioadhesion.

INJECTIONS OR IMPLANTS FOR POSTERIOR EYE TREATMENT

Compared with anterior eye treatments, drugs requiring delivery to the posterior of the eye are often even more challenging. Posterior-targeting medicines generally need to reach the retina – a layer of cells critical for sight. As this currently cannot be achieved via topical administration, injections or implants are often used to deliver drugs to the back of the eye.

One of the main challenges associated with parenteral ophthalmic drugs is maintaining an effective concentration within the vitreous humor for a significant portion of time. Fluid clearance mechanisms limit the duration of the effect of drugs, necessitating further injections. However, treatments are invasive and uncomfortable for patients, so any method that can reduce frequency is highly desirable.

CONSIDERATIONS WHEN DEVELOPING IMPLANTS

Implantable drug delivery to the eye is highly attractive, due to sustained release potential, but can pose many challenges in development.[7] Implants can either be bioresorbable (absorbed by the body over time) or biodurable (do not break down and typically require removal and/or refilling following initial treatment). Careful consideration must be paid as to which polymers to use to provide these properties.

"The methods used to manufacture implantables vary considerably and include solvent-based methods, injection moulding and hot-melt extrusion."

The methods used to manufacture implantables vary considerably and include solvent-based methods, injection moulding and hot-melt extrusion. However, not all APIs are compatible with these methods. Throughout hot-melt and injection-moulding methods, APIs are often exposed to high temperatures and shear. Some drugs cannot tolerate these stresses without degradation occurring. Determining the best method for the API will require a thorough understanding of these manufacturing techniques.

Expert formulation could also allow for processing temperatures to be lowered to reduce API stress or switching to solvent-based processes to reduce degradation. However, solvent-based methods are not without their challenges and care must be taken to ensure that the API is compatible with the selected systems to minimise degradation.

THE BENEFITS OF EXPERT SUPPORT

The many challenges involved in designing both anterior and posterior ophthalmic treatments, and the rising complexity of their delivery systems, necessitate development and manufacturing by experts. Therefore, it is essential to partner with a CDMO with extensive experience of working with ophthalmic drug products. An ophthalmic drug development partner should be able to offer the expertise, capabilities and facilities necessary to help overcome the obstacles involved. A CDMO partner should also provide access to a portfolio of polymers, including implantable, biodurable polymers and mucoadhesive excipients, and have robust sterile manufacturing facilities.

ABOUT THE COMPANY

The Lubrizol Corporation, a Berkshire Hathaway Company, leverages its unmatched science to unlock immense possibilities at the molecular level, driving sustainable and measurable results. Founded in 1928, Lubrizol owns and operates more than 100 manufacturing facilities, and sales and technical offices around the world and has approximately 8,600 employees.

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Robert Lee, PhD, President, Lubrizol Life Science Health, CDMO Division, is responsible for product and business development along with providing the company's strategic direction. Before joining Lubrizol, Dr Lee held senior management positions at Novavax, Lyotropic Therapeutics and Imcor Pharmaceutical Co. He holds BSc degrees in Biology and Chemistry from the University of Washington (Seattle, WA, US) and a PhD in Physical Bio-organic Chemistry from the University of California (Santa Barbara, CA, US). Dr Lee has published more than three dozen articles and five book chapters, as well as holding 11 issued patents and 15 provisional or PCT patent applications. He has over 30 years of experience in pharmaceutical research and development of both therapeutic drugs and diagnostic imaging agents. Dr Lee maintains strong academic ties, including an appointment as Adjunct Associate Professor of Pharmaceutical Chemistry at the University of Kansas (Lawrence, KS, US) in the early 1990s, serving as a reviewer for both the International Journal of Pharmaceutics and Journal of Pharmaceutical Sciences, and serving on the Editorial Board for the journal MOJ Bioequivalence & Bioavailability, The Scientific Pages of Nanotechnology and the Journal of Analytical and Pharmaceutical Research.