Celanese

The chemistry inside innovation™

SUSTAINED, CONTROLLED DRUG DELIVERY TO THE EYE

Here, Harsh Patel, PhD, Senior Scientist, Cyonna Holmes, PhD, Global Senior Manager, Marketing, and Brian Wilson, PhD, New Business Development Partner, all at Celanese, consider the challenges and advances in sustained-release ocular drug delivery.

Chronic eye diseases are the primary drivers of blindness and low vision, and the prevalence of these diseases is only expected to increase over the next five years due to an increased incidence of underlying conditions and the ageing population. Yet, there are still unmet needs in treating these diseases effectively. Innovative treatment approaches are needed to address the patient treatment burden and ineffective therapeutic delivery. As a result, improving efficacy and providing sustained delivery options for small molecules, biologics and RNA are critical for improving treatment options for chronic eye conditions. The ocular drug delivery market is expected to grow at a compound annual growth rate[1] of 6–9% as innovative approaches enter the market to address growing patient populations with glaucoma, chronic inflammation, diabetic retinopathy and macular degeneration.

> "Improving efficacy and providing sustained delivery options for small molecules, biologics and RNA are critical for improving treatment options for chronic eye conditions."

CHALLENGES WITH CURRENT DOSE FORMS AND TRENDS TOWARDS SUSTAINED DELIVERY

Traditional topical formulations and intravitreal injections dominate the ophthalmic drug market. However, topical formulations have been associated with a low estimated patient adherence rate of 40–50%[2] and poor bioavailability due to ocular barriers such as tear turnover, blinking and corneal and conjunctival barriers. Similarly, frequent intravitreal injections have negative side effects such as retinal toxicity, aggregation from injected materials, damage to the retina and lens, elevated intraocular pressure and inflammation due to repeated scleral puncturing.[3] To overcome these challenges, sustained, controlled delivery of small molecules and large biologics is needed, and these approaches are gaining traction over current dose forms when treating chronic eye diseases.[4] Successful application of such systems can significantly reduce the treatment burden to patients and, in turn, facilitate lower overall cost to the healthcare system.[5]

POLYMERIC IMPLANT FOR OCULAR DRUG DELIVERY

Polymeric implantable drug delivery systems remain a promising option for sustained, controlled delivery of therapeutics in the eye. The controlled, continuous release of therapeutic (Figure 1) from a polymeric implant removes the variability of patient compliance,

Dr Harsh Patel
Senior Scientist
T: +1 859 372 3256
E: harsh.patel@celanese.com

Dr Cyonna Holmes
Global Senior Manager, Marketing
T: +1 972 443 3748
E: cyonna.holmes@celanese.com

Dr Brian Wilson
New Business Development Partner
T: +1 616 286 7457
E: brian2.wilson@celanese.com

Celanese Corporation
222 West Las Colinas Boulevard
Suite 900N
Irving
Texas 75039
United States

healthcare.celanese.com

Copyright © 2022 Frederick Furness Publishing Ltd

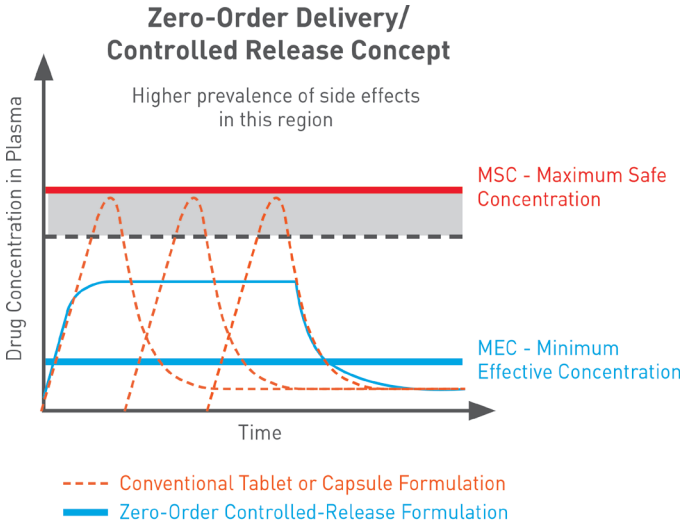


Figure 1: EVA is a biostable polymer offering better control of drug dosing, and eliminating undesirable bursts, with a zero-order controlled-release profile.

improves bioavailability and may mitigate issues associated with repeated injections. Sustained drug release is achieved by the adjustable diffusion of the drug from such a system, which improves the half-life of the molecule, delays degradation and reduces elimination.

Polymeric approaches are being considered to leverage the versatility of biocompatible thermoplastics to:

1. Provide tunable drug release of molecules ranging from small molecules to large biologics
2. Provide innovative shapes and designs for customised implant delivery options
3. Incorporate drug elution to existing medical devices to provide dual functionality.

BIODURABLE IMPLANT ADVANTAGES

Polymer-based, biodurable ocular implants offer distinct advantages in ocular delivery and have demonstrated versatility in the delivery of small molecules to large biologics. Biodurable ocular implants can be designed with high drug loading without compromising mechanical integrity or long-term release kinetics. High drug loading is critical in achieving drug-release profiles of 6+ months that are relevant to the treatment of chronic eye diseases that use a combination of drugs or a high molecular weight API.

> "Biodurable ocular implants can be designed with high drug loading without compromising mechanical integrity or long-term release kinetics."

Additionally, a reliable drug-release profile can be achieved with a biodurable implant as this approach does not rely on a bulk degradation mechanism with less predictable drug release. Biodurable implants also reduce the risk of drug molecule instability that may be caused by polymer degradants from erodible materials. As a result, release and accumulation of these degradants does not occur, thus mitigating inflammatory risk.

> "An EVA implant in the suprachoroidal space serves as a unique approach to deliver therapeutic agents with various molecular weights."

TUNABILITY FOR PRECISE DELIVERY

Biodurable implants using polymers such as ethylene-vinyl acetate (EVA) can achieve tailored release profiles over a wide range of molecules. Tunability can be further achieved through the pairing of drug-filled cores and customisable porous membranes. This approach adds another layer of adjustability as both the core and membrane properties can be modified to achieve a range of release profiles for small molecule, biologic and RNA delivery. Additionally, these two tunable components of an EVA implant – the core and membrane – also allow for dual release of more than one molecule through separate mechanisms, resulting in a fixed-dose combination implant.

TARGETED DELIVERY

Nearness of an implant to a targeted region can increase the therapeutic bioavailability of a molecule. As a result of localised biodurable implant delivery, lower drug concentrations are needed to elicit the desired therapeutic effect within the eye.

Due to the high compartmentalisation within the eye, unique locations for biodurable implant placement exist. As an example, suprachoroidal administration appears to be a promising and less-invasive technique for treatment of ocular posterior segment diseases. A polymeric implant must provide flexibility to mould into various shapes and sizes that may fit spaces such as the suprachoroidal space while maintaining mechanical integrity. As a result, an EVA implant in the suprachoroidal space serves as a unique approach to deliver therapeutic agents with various molecular weights.

Sustained delivery of molecules to treat chronic eye diseases can be achieved through polymeric implants, and biodurable implants offer an innovative approach to achieve desired therapeutic release profiles. As prevalence and patient needs continue to increase, ocular therapeutics need to adopt newer dosage forms to overcome challenges associated with traditional routes of administration. Biodurable implants address this growing unmet need and are ideal for the treatment of chronic eye disorders.

CELANESE SUSTAINED-RELEASE DRUG DELIVERY SOLUTIONS

Celanese has extensive expertise as a solutions provider for the pharmaceutical and medical device industry. Through collaboration with its customers, the company solves challenging drug delivery problems with innovative solutions that improve patient care. VitalDose® EVA, a pharmaceutical-grade polymer, is in pipeline and commercialised products and can be manufactured and designed to address a wide range of therapeutic areas and molecule types. VitalDose is a registered trademark of Celanese. Additionally, the Celanese Pharmaceutical Laboratory offers formulation support for early-stage pharmaceutical research and development.

Copyright © 2022 Frederick Furness Publishing Ltd

ABOUT THE COMPANY

Celanese Corporation is a global chemical leader in the production of differentiated chemistry solutions and speciality materials used in most major industries and consumer applications. The company's businesses use the full breadth of Celanese's global chemistry, technology and commercial expertise to create value for its customers, employees, shareholders and the corporation. Celanese partners with its customers to address their most critical business needs, and strives to make a positive impact on communities and the world through The Celanese Foundation. Based in Dallas (TX, US), Celanese employs approximately 8,500 employees worldwide and had 2021 net sales of US$8.5 billion (£6.3 billion).

Celanese offers the VitalDose® EVA drug delivery platform, providing controlled drug release through implants and inserts. Compared with traditional dose forms, the VitalDose® platform reduces treatment burden, addresses patient adherence issues and improves bioavailability. The company partners with clients to enable innovative drug delivery of small molecules, biologics and RNA within the desired release profile. With decades of experience in medical and pharmaceutical applications, Celanese seeks to improve product development and elevate patient care.

REFERENCES

1. *"Ocular Drug Delivery System Market". Fact.MR (2021), Research Report for Celanese.*
2. *Tapply I, Broadway DC, "Improving Patient Adherence to Topical Medication in patients with Glaucoma". Patient Prefer Adherence, 2021, 15, pp 1477–1489.*
3. *Nayak K, Misra M, "A review on recent drug delivery systems for posterior segment of eye". Biomed Pharmacother, 2018, 107, pp 1564–1582.*
4. *Kim HM, Woo SJ, "Ocular Drug Delivery to the Retina: Current Innovations and Future Perspectives". Pharmaceutics, 2021, Vol 13(1), p 108.*
5. *Wittenborn JS et al, "The economic burden of vision loss and eye disorders among the United States Population Younger than 40 Years". Ophthalmology, 2013, Vol 120(9), pp 1728–1735.*

ABOUT THE AUTHORS

Harsh Patel earned his PhD in Biomedical Engineering from the University of Alabama (Birmingham, AL, US). He has extensive technical experience in parenteral drug delivery across multiple polymers. At Celanese, Dr Patel serves as a Senior Scientist for Pharma and Medical, and holds patents and has numerous published articles in peer-reviewed journals.

Cyonna Holmes earned her PhD in Biomedical Engineering from the University of Texas Southwestern Medical Center (Dallas, TX, US) and her BS in Bioengineering from Stanford University (CA, US). At Celanese, Dr Holmes serves as Global Senior Manager for Ophthalmology Marketing. She has experience in the areas of drug delivery, lifecycle management strategy, new product development and market entry strategy. She has published articles in peer-reviewed journals.

Brian Wilson earned his PhD in Biochemistry from the University of Notre Dame (IN, US). He has 11 years of API experience in the areas of formulation development, drug delivery and new product development. At Celanese, Dr Wilson serves as a New Business Development partner for the pharma and medical businesses. He holds patents and has numerous published articles in peer-reviewed journals.

SUBSCRIBE TODAY!

PRINT SUBSCRIPTION £99/YR + POSTAGE

for 12 (minimum) high-quality topic-specific magazines per year.

NOW SUSTAINABLY PRINTED*

www.ondrugdelivery.com/subscribe

ON drugDELIVERY

RECYCLED Paper made from recycled material FSC® C022819

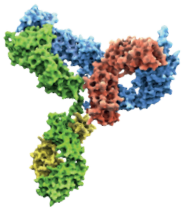
WORLD LAND TRUST™ www.carbonbalancedpaper.com

*using Forestry Stewardship Council® certified recycled paper, vegetable-based inks, biodegradable laminates and carbon balanced materials offset via the World Land Trust™ following ISO140001 processes

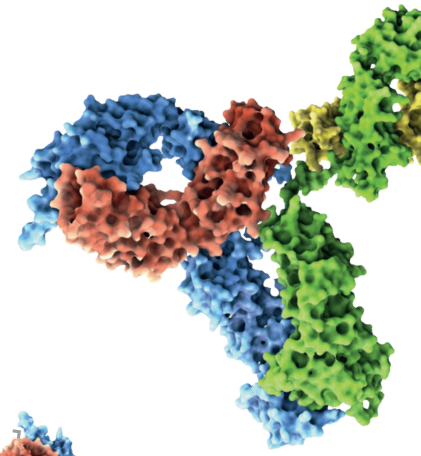
Copyright © 2022 Frederick Furness Publishing Ltd

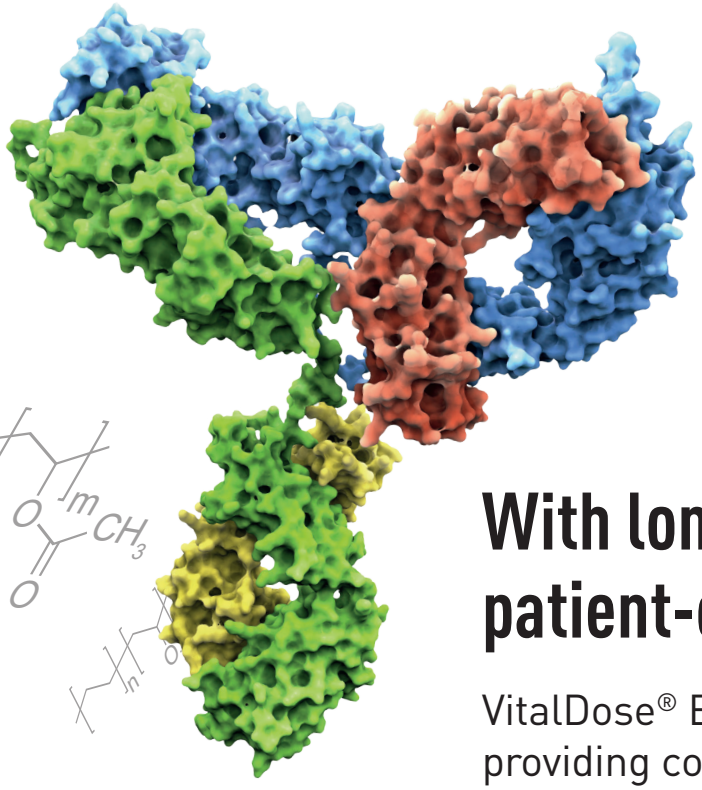
Celanese
The chemistry inside innovation™

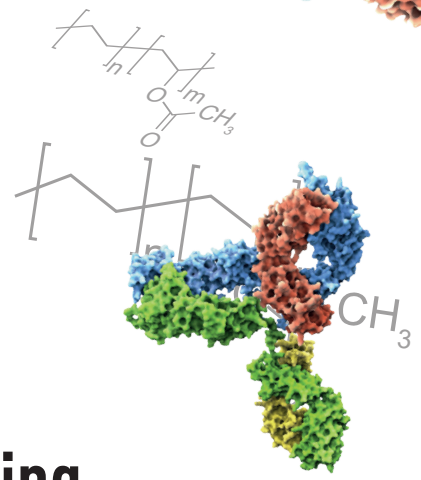
VITAL Dose®



Sustained Drug Delivery







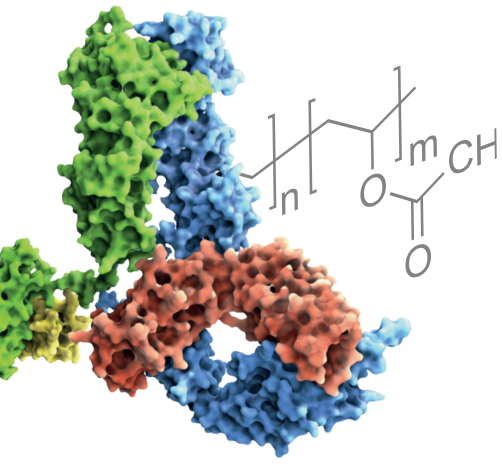
With long-acting, patient-centric therapeutics

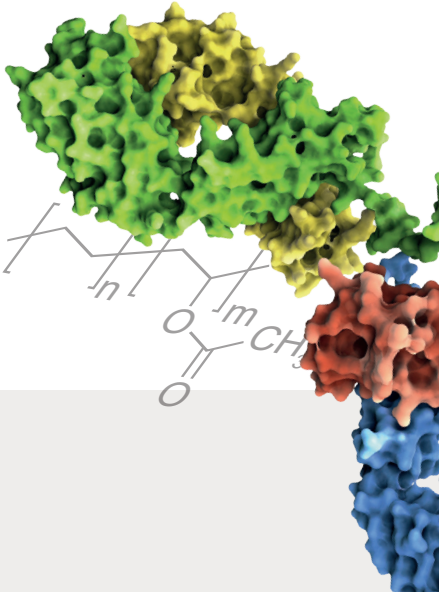
VitalDose® EVA is a copolymer drug-delivery platform providing controlled release through implant and insert dosage forms.

The VitalDose® platform is flexible and customizable with high drug loading capacity (⩽75%).

Our scientists and engineers will partner with you to create novel delivery systems for:

- Monoclonal antibodies
- Small molecules
- RNA





Collaborate with us
Email: Healthcare@Celanese.com
Website: Healthcare.Celanese.com

Celanese®, registered C-ball design and all other trademarks identified herein with ®, TM, SM, unless otherwise noted, are trademarks of Celanese or its affiliates.
© 2022 Celanese or its affiliates. All rights reserved.