viatel™ bioresorbable polymers

Long-acting injectables (LAI): microsphere design and development using lactide/glycolide-based polymers

David Zermeño Pérez, Ph.D.
Business Development Manager
Ashland, Life Sciences, Pharmaceuticals

David.zermenoperez@ashland.com

Microsphere Summit 2025
15th & 16th October 2025, Liverpool, UK

agenda

intro to LAI's based on bioresorbable polymers

controlling drug release via viatel™ polymer chemistry

how Ashland can help

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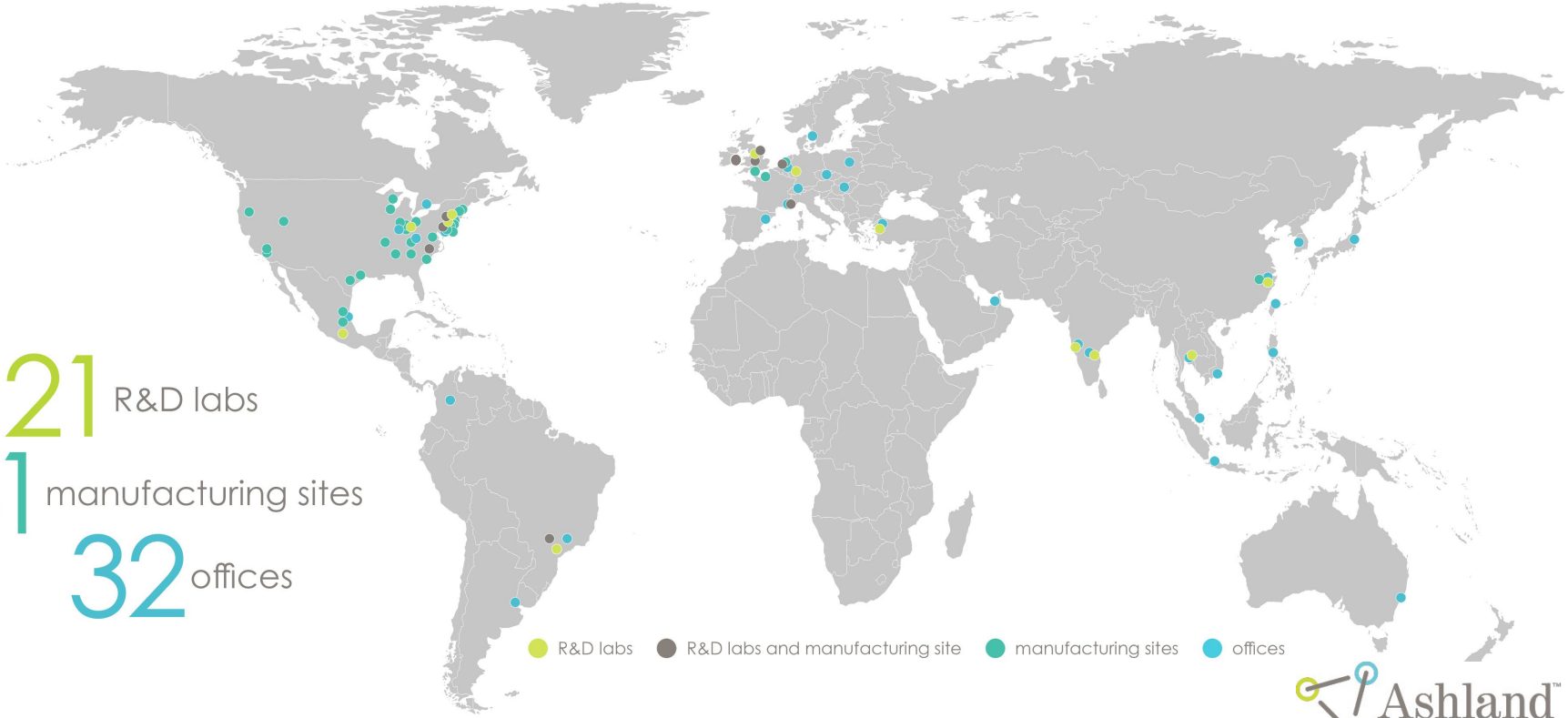
global footprint



21 R&D labs

41 manufacturing sites

32 offices

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Ashland's core strengths in pharma

tablet binding

Ashland produces binders for wet granulation, dry granulation, direct compression and roller compaction, as well as hot-melt extrusion.

modified release

Our extensive product lines offer various degrees of both hydrophilicity and molecular weights, providing you with a host of options.

tablet disintegration

Polyplasdone™ crospovidone provides a rapid disintegration and dissolution of oral solid-dosage forms, even at low use levels.

drug solubilization

High-quality excipients that improve the solubility of your Active Pharmaceutical Ingredient (API).

film coatings

Fully formulated film-coating systems, easily dispersed and provides a range of functions to suit almost any tablet core.

parenteral applications

Ashland provides a suite of products that are be suitable for use in parenteral, controlled release drug delivery systems.

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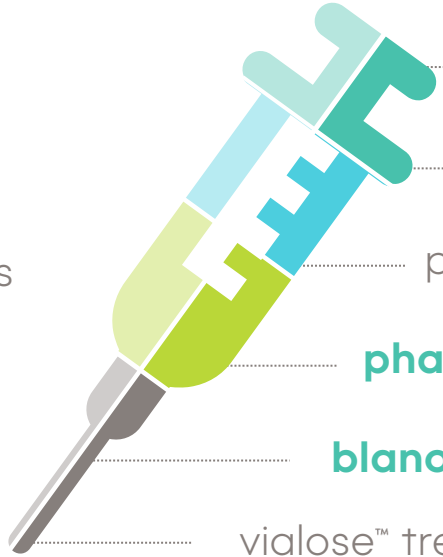
excipients for parenteral use

parenteral applications require excipients of the highest quality

Ashland's high-purity excipient portfolio meets industry standards



excipients for LAI formulations

plasdone™ povidone – C grades

viatel™ bioresorbable polymers

parenteral-grade cavitron™ cyclodextrins

pharmasolve™ n-methyl-2-pyrrolidone (NMP)

blanose™ CMC grades

vialose™ trehalose dihydrate

+ custom polymers

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Ashland's viatel™ portfolio

comprehensive platform of bioresorbable polyesters produced from lactide, glycolide, ε-caprolactone, and PEGylated chemistries

for drug delivery

- poly D,L-lactide-co-glycolide (PDLGA)
- poly D,L-lactide (PDLLA)
- poly D,L-lactide-b-methoxy polyethylene glycol (PDLLA-mPEG)

for medical devices

- poly L-lactide-co-glycolide (PLGA)
- poly ε-caprolactone (PCL)
- poly L-lactide (PLLA)
- poly D-lactide (PDLA)
- poly L-lactide-co- ε-caprolactone (PLCL)

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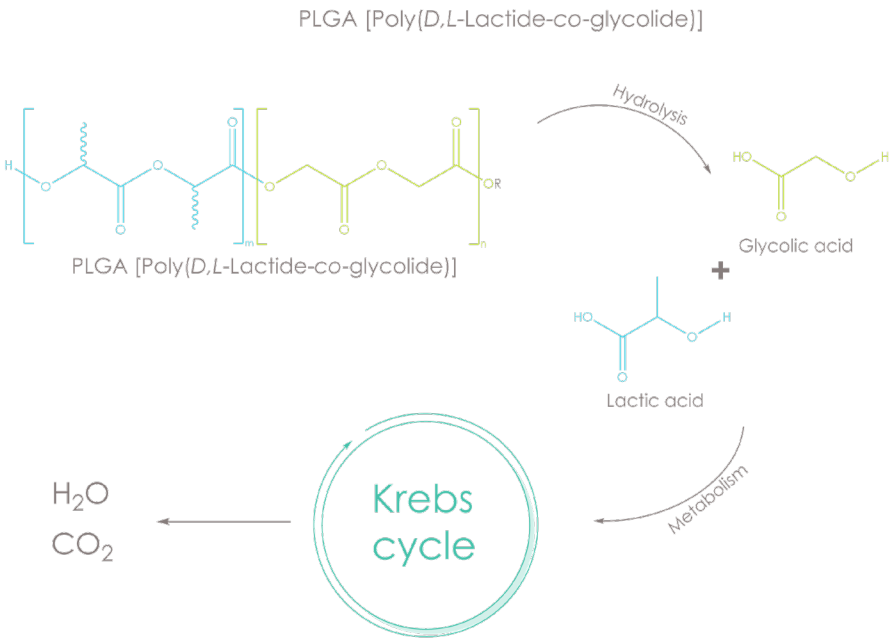
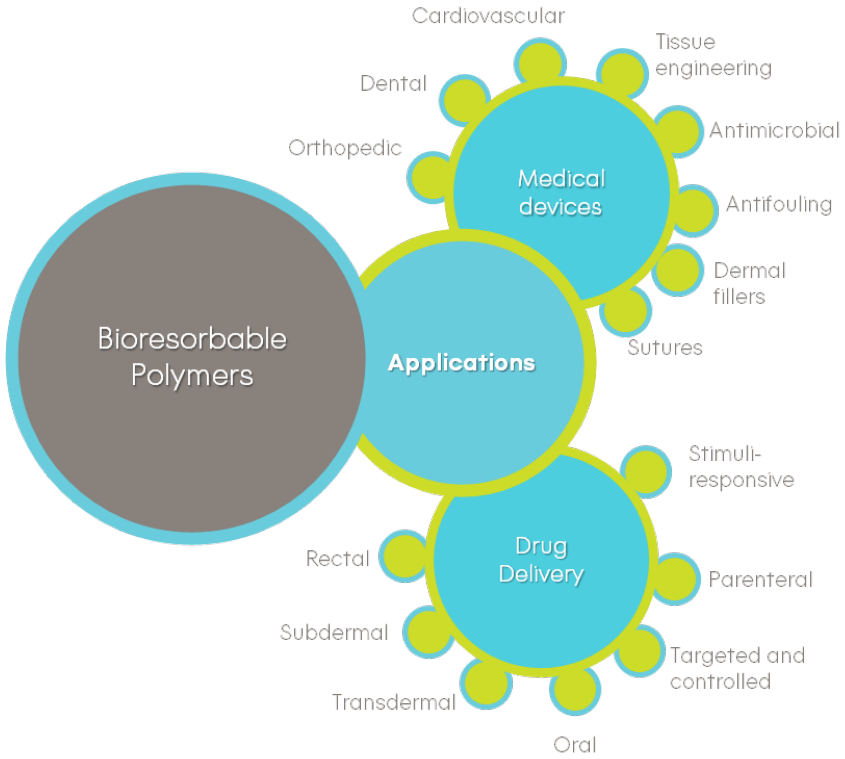
bioresorbable polymers in the body





polyester material properties

Polymer	Tg (°C)	Tm (°C)	Tensile modulus (GPa)	Tensile strength (MPa)	Elongation at break (%)	Degradation time* (months)
PLGA (50% D,L-lactide)	45 – 50	Amorphous	1.4 – 2.0	35 – 55	2 – 10	**1 – 3**
PLGA (80% D,L-lactide)	55 – 60	Amorphous	3.3 – 3.5	50 – 70	2 – 10	**3 – 6**
PGA	35 - 45	220 – 233	6.0 – 7.0	60 – 100	1 – 20	**6 – 12**
PLLA	60 – 65	170 – 200	2.7 – 4.1	15 – 150	3 – 10	**12 - 24**
PDLLA	45 – 55	Amorphous	1.7 – 3.4	27 – 55	2 – 10	**12 – 18**
PCL	-65 – -60	58 – 65	0.2 – 0.35	20 – 34	300 – 1000	**12 - 36**
PLCL (70% L-lactide)	10 – 20	135 – 155	0.02 – 0.04	17 – 22	300 – 700	**12 – 24**

*dependant on concentration, shape, formulation and site of implantation

Duffy, P et al. "Synthetic bioresorbable poly-a-hydroxyesters as peripheral nerve guidance conduits; a review of material properties, design strategies and their efficacy to date". *BIOMATERIALS SCIENCE*, 2019, 7, 4912-4943

solubility of polyesters

polymer	acetone	ethyl acetate	chloroform	methylene chloride	tetrahydro -furan	N-methyl-2-pyrrolidone	hexafluro-isopropanol	dimethyl formamide
PLGA 50:50	~	~	+	+	~	+	+	+
PLGA 75:25	+	+	+	+	+	+	+	+
PDLLA	+	+	+	+	+	+	+	+
PLLA	-	-	+	+	-	~	+	-
PGA	-	-	-	-	-	-	+	-
PCL	+	+	+	+	+	+	+	+

+ = fully soluble
~ = partially soluble
- = insoluble

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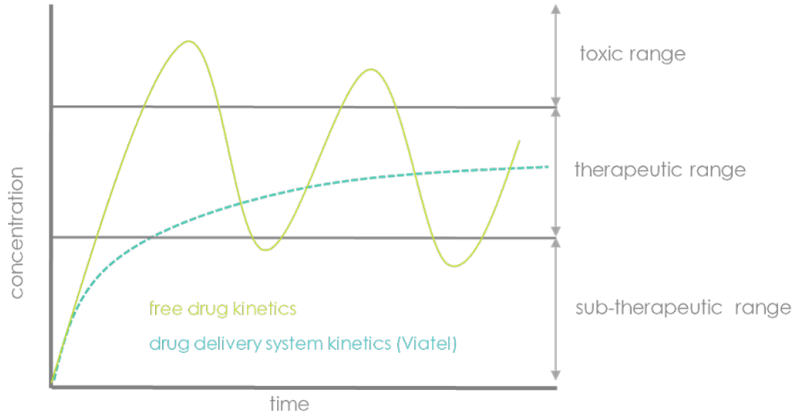
purpose of LG polymers in pharma

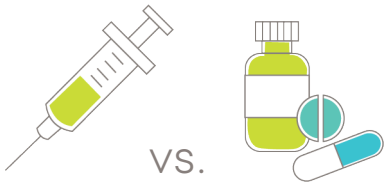
many drugs present

- toxicity, fast metabolism and excretion
- low uptake / PK variability after oral administration
- low drug concentrations in desired location



advantages of injectable sustained release drug delivery

- tuneable release profiles (days to months)
- decreased overall drug dosage / local delivery = reduced side effects
- consistent release within therapeutic window
- simplified drug stability by avoiding digestive system
- case dependent advantages (carriers, molecule types, other)



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history of LG polymers in medical products

1930s-60s	early patents and publications
1971	Dexon: first synthetic bioabsorbable suture
1973	DuPont: first lactide / glycolide drug delivery patent
1986	Decapeptyl*: first injectable extended-release microparticle product
1989	Zoladex*: first implantable extended-release implant product
2001	Atridox*: first local delivery product
2002	Eligard*: first injectable extended-release lactide/glycolide in-situ forming product
2004	Sculptra*: micronized PLLA dermal filler
2006	SmartShotB12: first injectable microparticle for animals
2007	Genexol* PM: first nanoparticle
2009	Ozurdex*: first product for ocular delivery
2009	Ellanse*: PCL microspheres dermal fillers
2011	Propel*: first drug-eluting device
2011	Revalor*: XS first implantable for animals
2016	Reseligo: first generic implantable
2016	Absorb GT1*: first bioabsorbable drug-eluting cardiovascular stent
2017	Zilretta*: first micro-particle product for intra-articular delivery (knee)

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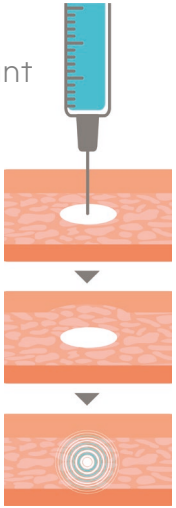
LG-based drug delivery systems

in situ forming depots (API + LG polymer + solvent)

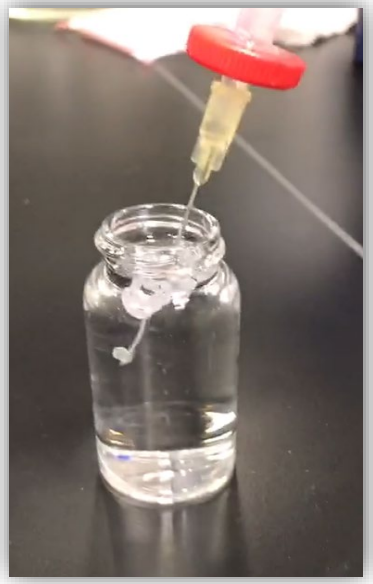
- formed in vivo, simplified formulation process
- cost effective
- administered through injection, larger initial burst effect, implant shape variance



In-situ forming system solution combined with drug injected SC

water causes system to solidify forming a depot to trap API

API releases as the polymer degrades over time



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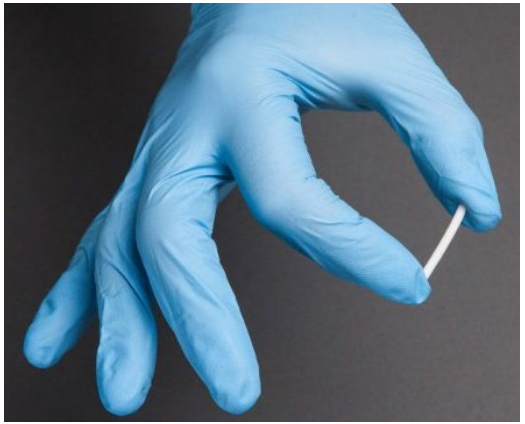
solid implants (API + LG polymer)

- no organic solvents, good stability, lower burst effect
- extrusion (thermal deg.), administered through surgery or injection



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LG-based drug delivery systems

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solid implants (API + LG polymer)

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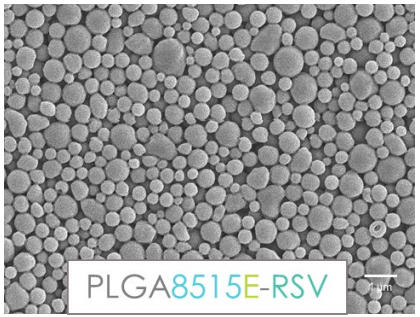
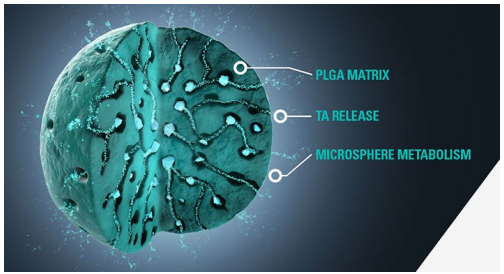
- extrusion (thermal deg.), administered through surgery or injection

particle technologies (API + LG polymer + diluent)

- microspheres, nanoparticles
- smaller needles, tuneable profiles
- organic solvents, particle stability, complexity





https://zilrettapro.com/how-zilretta-works/extended-release-microspheres/

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commercial product examples

brand name	indication	company	drug substance	API Size (Da)	dose (mg)	months	needle	
Eligard*	Prostate cancer	Sanofi-Aventis	Leuprolide acetate	1260 (peptide)	7.5 – 45	1, 3, 6	18 – 20 G	in-situ
Sublocade*	Opioid dependency	Indivior	Buprenorphine	467.64 (SMD)	100, 300	1	19 G	in-situ
Longrange*	Parasite treatment	Merial Limited	Eprinomectin	914 (SMD)	50	5	16 / 18 G	in-situ
Lupron Depot*	**Prostate cancer, endometriosis**	**AbbVie**	**Leuprolide acetate**	**1209 (peptide)**	**3.75–30**	**1, 6**	**22–25 G**	microspheres
Bydureon*	**Diabetes (II)**	**AstraZeneca**	**Exenatide**	**4187 (peptide)**	**2**	**0.25**	**23 G**	microspheres
Sandostatin* LAR	**Acromegaly / flushing / cancer-induced diarrhea**	**Novartis**	**Octreotide acetate**	**1079 (peptide)**	**10 – 30**	**1**	**19 G**	microspheres
Vivitrol*	**Opioid/alcohol dependence**	**Alkermes**	**Naltrexone**	**341 (SMD)**	**380**	**1**	**20–22 G**	microspheres
Decapeptyl* SR	**Prostate cancer**	**Ipsen / Ferring**	**Triptorelin pamoate**	**1700 (peptide)**	**4 – 28**	**1, 3, 6**	**20 G**	microspheres
Risperdal Consta*	**Schizophrenia, bipolar disorder**	**Janssen**	**Risperidone**	**410 (SMD)**	**25–50**	**0.5, 1**	**21–23 G**	microspheres
Scenesse*	Erythropoietic protoporphyria (light intolerance)	Clinuvel	Afamelanotide	1707 (peptide)	16	2	14 G	implants
Zoladex* 1 / 3 month	Prostate / breast cancer	AstraZeneca	Goserelin Acetate	1269 (peptide)	3.6 – 10.8	1, 3	14 / 16 G	implants
Revalor*	Growth promotion (animal)	Intervet / Merck Animal Health	Trenbolone / estradiol	270 / 272 (SMD)	140 / 14	6	Implant tool	implants

https://www.merck-animal-health-usa.com/product/cattle/Revalor-XS/1
https://www.indiamart.com/proddetail/zoladex-10-8mg-21620634848.html
https://www.labonline.com.au/content/life-scientist/article/clinuvel-success-in-scenesse-trial-1347661844
https://www.mims.com/hongkong/drug/info/signifor%20lar
https://www.bi-vetmedica.com/species/cattle/products/longrange.html

https://ryortho.com/breaking/3-oa-studies-zilretta-superior-to-off-the-shelf-steroids/
https://www.americanpharmawholesale.com/store.php/AmericanPharmaWholesale/pd9359627/sandostatin_lar_depot_20mg_vial_by_novartis
https://www.mims.com/hongkong/drug/info/signifor%20lar
https://www.suprememed.com/eligard-kit-antineoplastic-agent-leuprolide-acetate-30-mg-4-month-subcutaneous-injection-prefilled-syringe-1-dose

controlling drug release via viatel™ polymer chemistry

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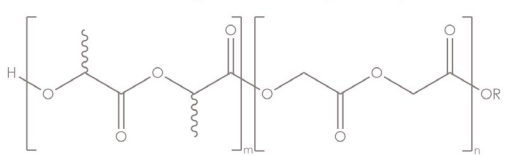
polymer chemistry controls release

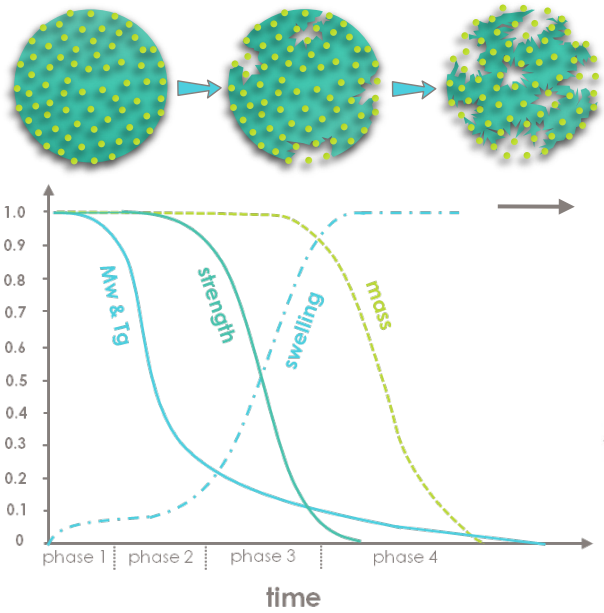
L:G ratio and distribution

molecular weight / IV

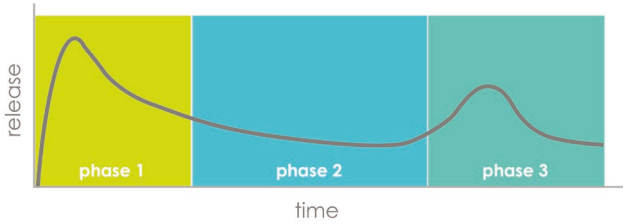
end-group and structure



viatel™ bioresorbable polymers



performance & release profile



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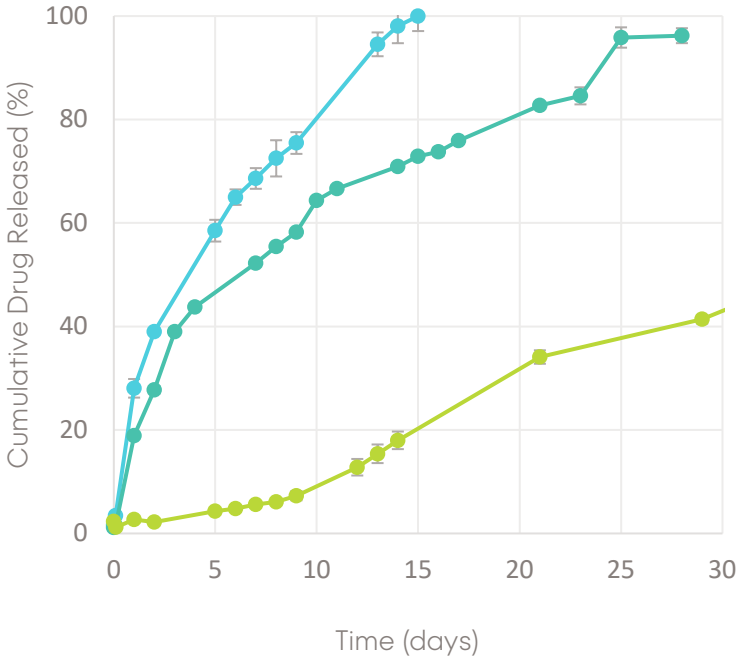
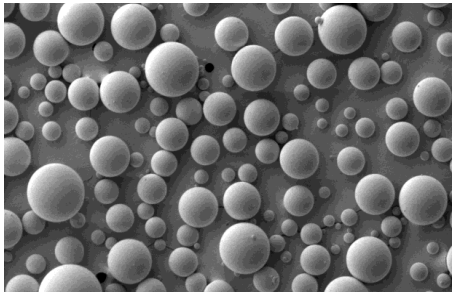
L:G ratio

Symbol			
Polymer [viatel™]	DLG 7503 A	DLG 8503 A	DL 03 A
L:G ratio (mol%)	75:25	85:15	100:0
Polymer IV (dL/g)	0.26	0.24	0.32

*All other microsphere parameters held constant

LG polymers with higher lactide contents provide slower rates of drug release





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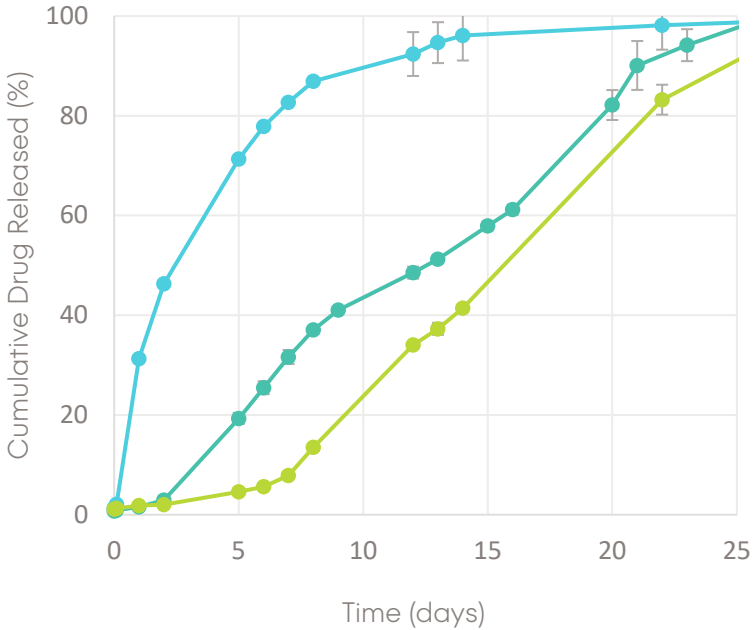
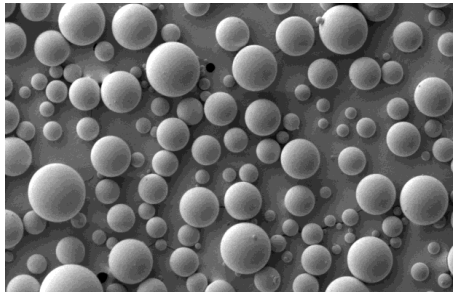
molecular weight / IV

Symbol			
Polymer [viatel™]	DLG 7503 A	DLG 7505 A	DLG 7505 A
L:G ratio (mol%)	75:25		
IV (dL/g)	0.26	0.41	0.56
Mw (kDa)	23.0	44.3	64.7

*All other microsphere parameters held constant

Increasing LG polymer molecular weight increases release duration





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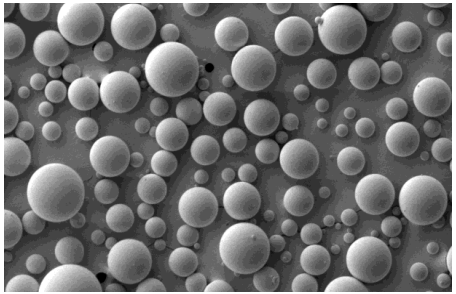
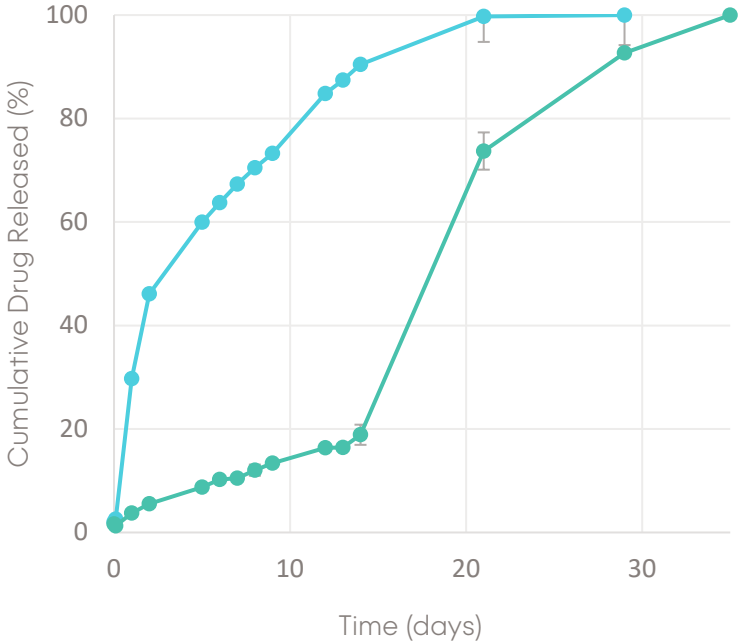
end-group

Symbol		
Polymer [Viatel™]	DLG 8503 A	DLG 8503 E
Polymer End Group	Acid	Ester
Polymer IV (dL/g)	0.24	0.25

*All other microsphere parameters held constant

LG polymer endcap affects release:
Acid endcap = more hydrophilic = faster release
Ester endcap = more hydrophobic = slower release





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viatel™ ultrapure

what is it? highly purified lactide/glycolide polymers

key features

- lowered residual monomer : ≤ 0.5% total
- pre-filtered polymer during additional purification process to ensure exceptional quality

benefits

- reduced acidity
  - improved API stability
  - improved shelf-life stability
- improved release consistency across all applications due to fewer variables
- extended release in hot melt extrusion and in situ forming depot applications

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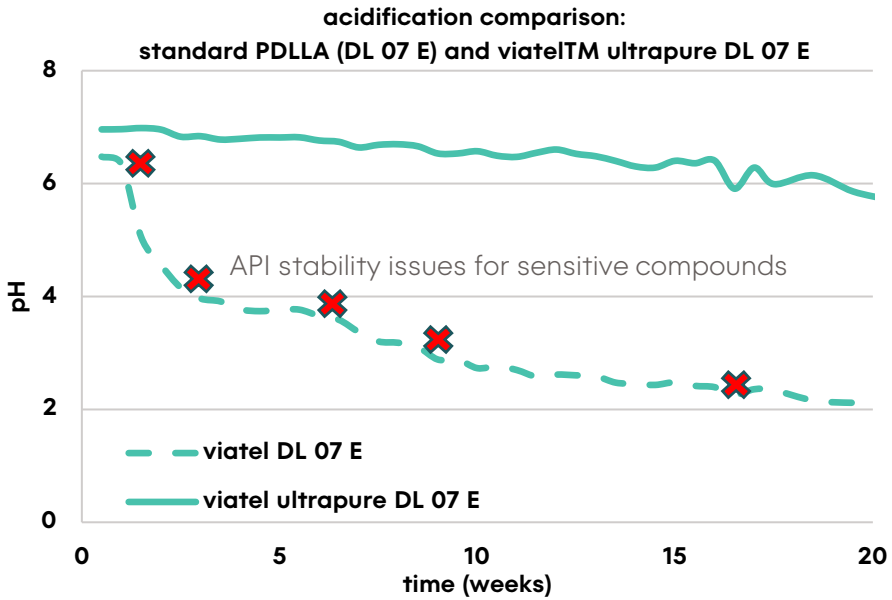
viatel™ ultrapure = less acidic



Grade	DL 07 E	DL 07 E ultrapure
Polymer	PDLLA - ester	PDLLA - ester
Batch	2595893	2595893-UP
Residual monomer (wt.%)	**2 %**	**0.07%**
Mn	39.5 kDa	39.8 kDa
Mw	92.6 kDa	91.7 kDa
IV	0.72 dl/g	0.71 dl/g

DL 07 E = Poly D,L-Lactide (PDLLA), Ester terminated, IV 0.7 dl/g,

viatel™ ultrapure polymers exhibit decreased acidity

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theoretical polymer influence on release

characteristic	option & effect
L:G ratio	○ ++ lactide content = ++ hydrophobicity = slower release
molecular weight / IV	○ ++ Mw = ++ degradation time = slower release
end-group	○ acid = more hydrophilic = faster release ○ ester = more hydrophobic = slower release
structure / architecture	○ PEGylated di-/tri-blocks = amphiphillic/hydrophilic polymer ○ branching = ++ functionality, degradation, release
microstructure (blockiness)	○ more random distribution results in less G blocks = ++ solubility & more steady and consistent degradation + release
residual monomer	○ residual monomer catalyzes degradation process = faster and more inconsistent release

there can be exceptions!

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API can alter LG polymer performance

API type

- organic small molecule
- peptide
- protein

solubility

- hydrophobic vs. hydrophilic
- amphiphilic molecules
- water solubility

dosage requirements and duration

- therapeutic level
- possibility for increased bioavailability vs. current dosing

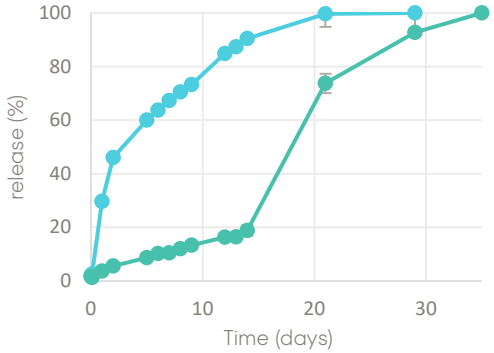
small molecule (300 - 500 Da)

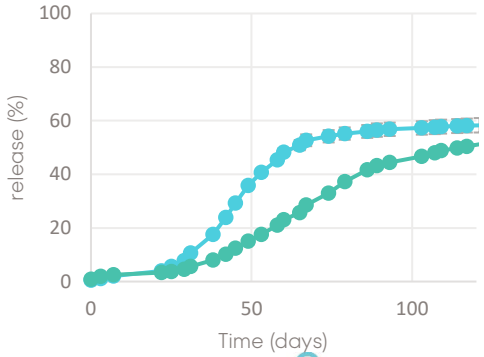
< 0.1 mg/ml, 50 % DL

Symbol		
Polymer [Viatel™]	DLG 8503 A	DLG 8503 E
Polymer End Group	Acid	Ester
Polymer IV (dL/g)	0.24	0.25

peptide (750 - 1250 Da)

> 100 mg/ml, 10 % DL





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solving the “sustained release” puzzle

molar mass

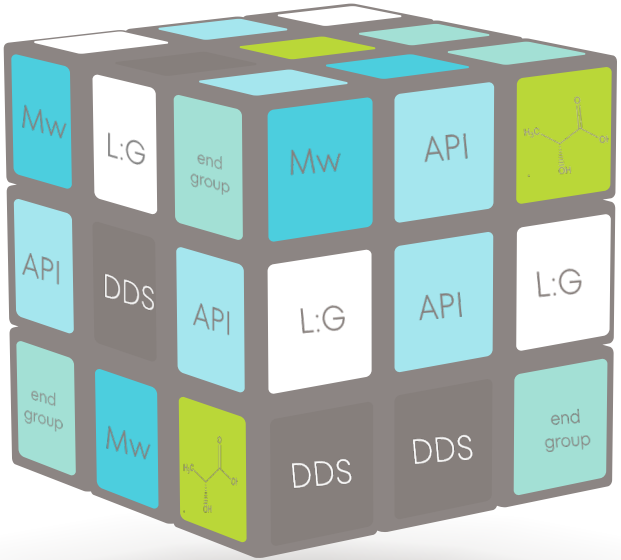
- IV, MW, PDi.
- increased = +hydrophobic
- degradation & release implications
- viscosity implications

L : G ratio

- increased L = more hydrophobic
- slowed degradation& release,
- EE%, processing solvents, compatibility

end group

- hydrophobicity : Ester > Acid > PEG
- swelling, release, degradation
- EE%, compatibility, other



depot format & processing (dds)

- category: particle, ISI depot, implant
- particle type/size, surface area
- solvent type, processing conditions

polymer structure + archtecture

- linear, diblock, triblock, branched

API related

- loading, encapsulation efficiency
- drug form, molecule size & solubility
- drug dispersion

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Ashland's offerings

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Ashland's viatel™ portfolio

- comprehensive platform of bioresorbable polyesters produced from lactide, glycolide, ε-caprolactone, and PEGylated chemistries

for drug delivery

- poly D,L-lactide-co-glycolide (PDLGA)
- poly D,L-lactide (PDLLA)
- poly D,L-lactide-b-methoxy polyethylene glycol (PDLLA-mPEG)

for medical devices

- poly L-lactide-co-glycolide (PLGA)
- poly ε-caprolactone (PCL)
- poly L-lactide (PLLA)
- poly D-lactide (PDLA)
- poly L-lactide-co- ε-caprolactone (PLCL)

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viatel™ product range – drug delivery

Product Family	L : G	IV (dl/g)	End Group	Product Code
PLGA	50:50	0.1 – 0.3	Acid / Ester	viatel™ DLG 5002 A/E
	50:50	0.2 – 0.4	Acid / Ester	viatel™ DLG 5003 A/E
	50:50	0.4 – 0.6	Acid / Ester	viatel™ DLG 5005 A/E
	50:50	0.6 – 0.8	Acid / Ester	viatel™ DLG 5007 A/E
	50:50	0.8 – 1.0	Ester	viatel™ DLG 5009 E
	55:45	0.2 – 0.4	Acid / Ester	viatel™ DLG 5503 A/E
	55:45	0.4 – 0.6	Acid / Ester	viatel™ DLG 5505 A/E
	65:35	0.2 – 0.4	Acid / Ester	viatel™ DLG 6503 A/E
	75:25	0.1 – 0.3	Acid / Ester	viatel™ DLG 7502 A/E
	75:25	0.2 – 0.4	Acid / Ester	viatel™ DLG 7503 A/E
	75:25	0.4 – 0.6	Acid / Ester	viatel™ DLG 7505 A/E
	75:25	0.6 – 0.8	Acid / Ester	viatel™ DLG 7507 A/E
	75:25	0.8 – 1.0	Acid / Ester	viatel™ DLG 7509 A/E
	75:25	1.0 – 1.2	Ester	viatel™ DLG 7511 E
	75:25	1.2 – 1.4	Ester	viatel™ DLG 7513 E
	80:20	0.1 – 0.3	Acid / Ester	viatel™ DLG 8002 A/E
	80:20	0.2 – 0.4	Acid / Ester	viatel™ DLG 8003 A/E
	85:15	0.1 – 0.3	Acid / Ester	viatel™ DLG 8502 A/E
	85:15	0.2 – 0.4	Acid / Ester	viatel™ DLG 8503 A/E
	85:15	0.4 – 0.6	Acid / Ester	viatel™ DLG 8505 A/E
	85:15	0.6 – 0.8	Acid / Ester	viatel™ DLG 8507 A/E
	85:15	0.8 – 1.0	Acid / Ester	viatel™ DLG 8509 A/E
	85:15	1.0 – 1.2	Acid / Ester	viatel™ DLG 8511 A/E
	85:15	1.2 – 1.4	Acid / Ester	viatel™ DLG 8513 A/E

Product Family	IV (dl/g)	End Group	Product Code
PDLLA	0.1 – 0.3	Acid / Ester	viatel™ DL 02 A/E
	0.2 – 0.4	Acid / Ester	viatel™ DL 03 A/E
	0.4 – 0.6	Acid / Ester	viatel™ DL 05 A/E
	0.6 – 0.8	Acid / Ester	viatel™ DL 07 A/E
	0.8 – 1.0	Acid / Ester	viatel™ DL 09 E
	0.33 – 0.38	mPEG	viatel™ DL 03 PEG5K

> 50 distinct GMP grades

ultrapure grades available for all drug delivery polymers!

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*D,L-LA = D,L-lactide. GA = glycolide

quality and regulatory

good manufacturing process (GMP) compliance

- USP <1078> and Joint IPEC-PQG GMP Guide for Pharmaceutical Excipients (IPEC, 2017)
- manufactured in an ISO Class 8 clean room
- ISO 13485:2016 certified since 2013
  (Notified Body: LRQA Lloyds)

regulatory status

- type IV DMF filed with FDA 33847
- chemical registration (NMPA) completed in China
- **Note:** USP-NF monograph (right hand side)

lead times

- **3 weeks** for in-stock materials
- made-to-order : **5–8 weeks** for shipping
- up to 30Kg batch size
- customisable polymers
- **samples are available**

Ashland announces expansion of Viatel™ bioresorbable (globenewswire.com)

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Ashland announces expansion of Viatel™ bioresorbable polymers manufacturing and R&D capabilities in Mullingar, Ireland

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Ashland announces compliance of viatel™ lactide/glycolide polymers versus upcoming LG polymer USP-NF monographs.

February 5, 2025

WILMINGTON, Del., February 5, 2025, – Ashland, a premier specialty materials company, is pleased to announce compliance with the upcoming Lactide (or lactic acid) and Glycolide (or glycolic acid) (LG) polymer USP-NF monographs. The announcement came during a joint webinar with Ashland and Oakwood laboratories on scale-up of long-acting injectables. Ashland has been actively involved in the development of USP-NF monographs, general chapters and reference standards for LG Polymers. Patrick Duffy, PhD, R&D team leader, Ashland, serves as an expert advisor to USP's joint sub-committee working on LG polymer monographs.

The USP–NF combines the United States Pharmacopeia (USP) and the National Formulary (NF) and contains more than 5,000 public quality standards for chemical and biologic medicines, active pharmaceutical ingredients (APIs), dietary ingredients and dietary supplements, and excipients. It also maintains standards for various analytical testing methods, medicine storage and distribution, compounded medicines, prescription labeling and many other aspects of medical product development, manufacture and use.

Regulatory evaluation of LG polymer-containing drug products remains challenging due to the complexities of LG polymers, their characterization and testing, and use in formulations. The USP developed a suite of solutions to help formulators meet the regulatory expectations and characterization challenges associated with these polymers. Refer to www.usp.org/excipients/lg-polymers. This work included the development of a series of NF monographs – which are used to articulate the quality expectations for a medicine. Expectations are included for a drug's identity, strength, purity, and performance. Monographs also describe tests needed to validate the medicine and its ingredients meet expected criteria.

custom structures

tailored LG copolymers

- narrowed specifications : useful to standardise release (± 0.02 dl/g)
- DOE studies : varying L:G, Mw, end groups (incremental batches)
- test specification limits: batch provision at high, middle and low end of specification
- batch consistency testing : repeat lots within target range

adjusted polymer structures

- composition: lactide, glycolide, caprolactone, PEG, other
- linear, di-block, tri-block, branched/dendritic structures
- end groups for active targeted delivery (e.g. maleimide)

new chemistries

- new polymers for sustained release
- surface eroding polymers

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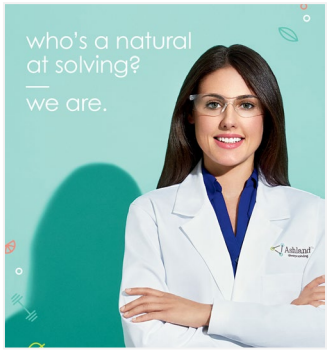
made-to-order (MTO) examples



- example 1 : DOE study example - increment at ± 0.02 dl/g
- example 2: lot-to-lot variability & spec setting - repeat batches within ± 0.01 dl/g
- MTO batch options: 0.1 kg, 0.5 kg, 1.5 kg, 3.5 kg, 10 kg, 20-30 kg
- typical MTO lead time : 5 - 8 weeks to ship

rational	grade	L:G ratio	IV request (dl/g)	batch #	IV result	Mw	quantities
DOE study	DLG 7505 A	75:25	0.38 – 0.42	2619314	0.38 dl/g	42.7 kDa	1 kg
			0.42 – 0.46	2619063	0.43 dl/g	45.8 kDa	1 kg
			0.46 – 0.50	2619881	0.46 dl/g	53.0 kDa	1 kg
			0.50 – 0.54	2567897 2601092 2594415	0.50 dl/g 0.50 dl/g 0.51 dl/g	60.8 kDa 59.5 kDa 61.7 kDa	3 x 1 kg
lot-to-lot variability & specification establishment (high, mid, low)	DL 02 A	100 : 0	0.15 – 0.17	2585007	0.17 dl/g	13.8 kDa	500 g
				2588391	0.16 dl/g	13.2 kDa	500 g
				2586589	0.15 dl/g	11.8 kDa	500 g

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disclaimer

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Appendix - supplementary

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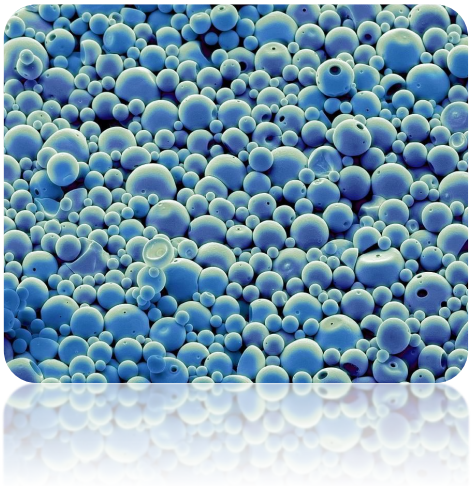
case microspheres: Bydureon*

Bydureon* (exenatide extended-release) – Diabetes type II

- Long-acting polymer
  - **30-50% poly D,L lactide-co-glycolide (PLGA) 50:50**
- active pharmaceutical ingredient
  - **5% exenatide (API)**
- Stabilizer
  - **2% Sucrose**
- Diluent components
  - 40-50% **Na-CMC**, polysorbate 20, Sodium phosphate (monobasic and dibasic, sterile water)



long-acting performance

- 1- week: drug release approximate for 5-10 days

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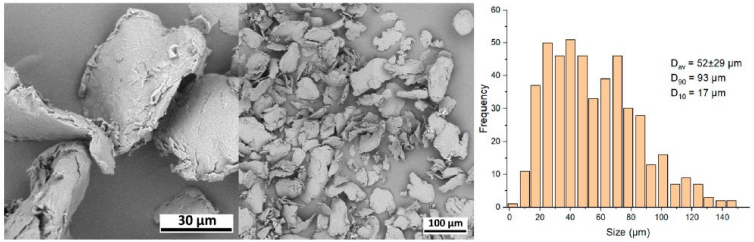
Bydureon® (exenatide extended-release) is manufactured by **Alkermes.**

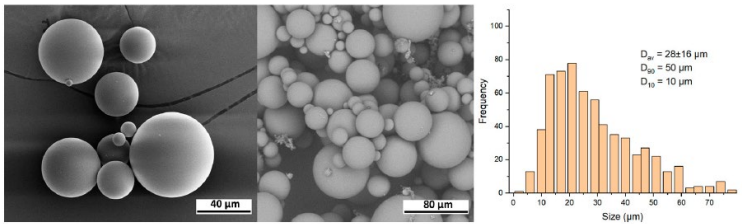
Case dermal fillers: Sculptra*

Filler	Composition			Degradation Period, Months
	Microparticles	Na-CMC	Mannitol	
AestheFill®	154 mg poly(*D,L*-lactic acid)	46	-	24
Gana V®	210 mg poly(*L*-lactic acid)	132	177	27.6
Repart PLA®	154 mg poly(*D,L*-lactic acid)	46	167.2	24
Sculptra®	150 mg poly(*L*-lactic acid)	90	127.5	24

SCULPTRA



REPART



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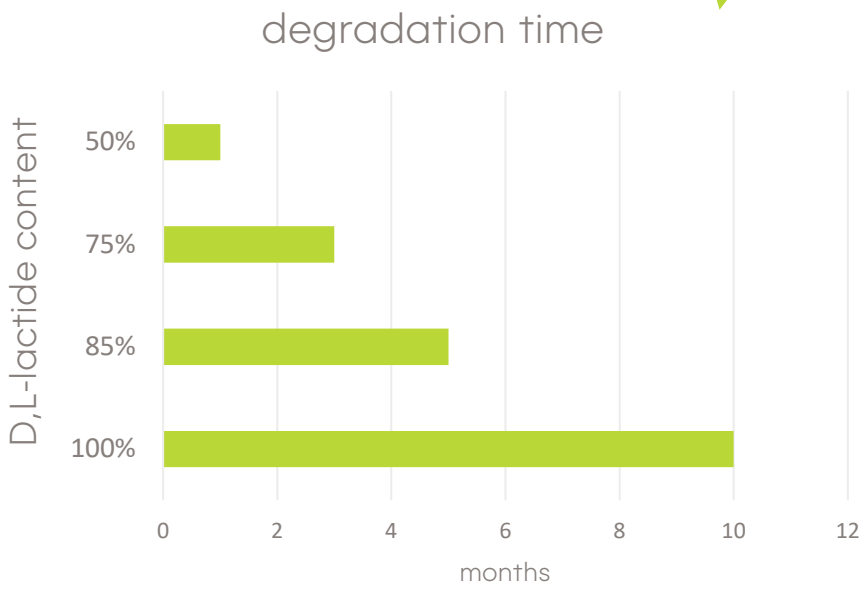
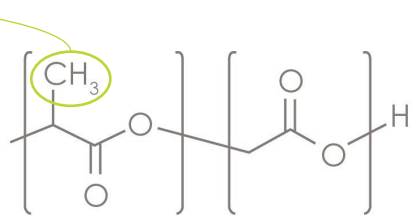
L:G ratio





lactide glycolide

L:G ratio

L	0	10	20	30	40	50	60	70	80	90	100	L
G	100	90	80	70	60	50	40	30	20	10	0	G

insoluble in most solvents

solvent-dependent solubility

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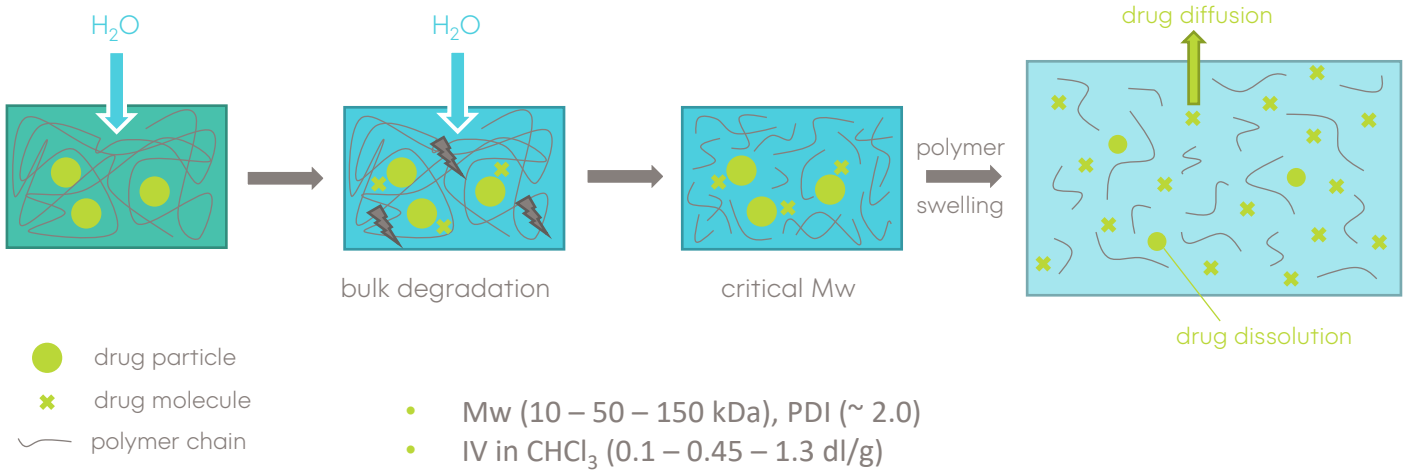
molecular weight / inherent viscosity

Mw / IV greatly affects matrix properties (Tg, crystallinity, strength) + water uptake and erosion/degradation rates



- Mw (10 – 50 – 150 kDa), PDI (~ 2.0)
- IV in $CHCl_3$ (0.1 – 0.45 – 1.3 dl/g)

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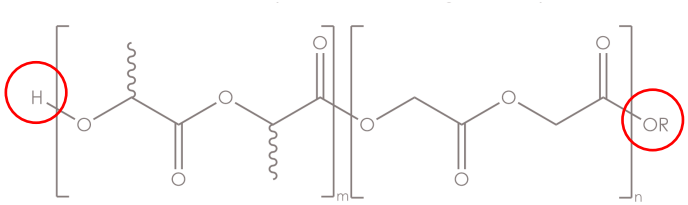
end group options



- hydrophilicity of end group
  - PEG > Acid > Ester
- API sensitivity / stability
- process related (e.g. EE%)

initiator	end groups	effect
monofunctional alcohol	ester and hydroxyl	hydrophobic ↕ hydrophillic
diol	hydroxyl and hydroxyl	
α-hydroxyl acid	carboxylic acid and hydroxyl	
polyethylene glycol methyl ether (mPEG)	PEG and hydroxyl	

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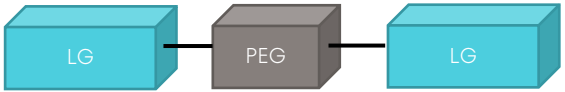
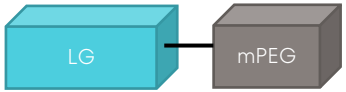
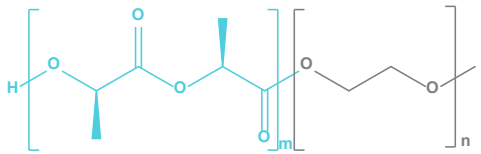
structure/architecture

PEGylated di-block and tri-block LG co-polymers

- amphiphilic block co-polymers (LG-PEG-LG or mPEG-LG)
- thermoresponsive, water-soluble hydrogels
- tune Mw + ratio of PEG/LG to modulate properties

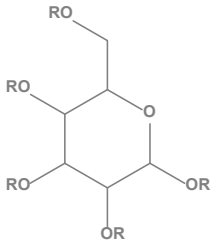


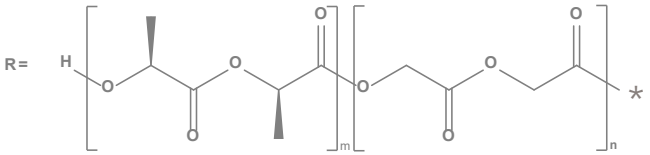




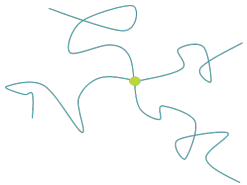
multi-arm / branched LG polymers

- glucose-star co-polymer & others
- higher degree of functionality
- reduced viscosity at high concentration





* = connection to oxygen



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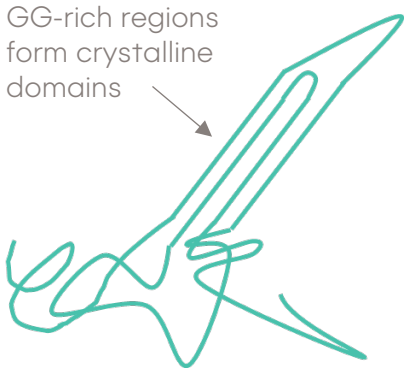
microstructure

^{13}C-NMR

monomer distribution

alternating (uniform)	L G L G L G L G L G L G
random	L L G L G G L G L G L G
increased blockiness (and block length)	L L L G G G G L L L G G



$$Rc = \frac{I_{GG}}{I_{GL}} \qquad L_G = \frac{I_{GG}}{I_{GL}} + 1$$

impact on performance

- decreased solubility
  - processing
- degradation rate – GG hydrolyzes faster than GL/LL
  - release profile

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