Risperidone-loaded PLGA sustained release implants

from benchtop to commercial scale

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CRS 2024 Annual Meeting

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collaborators and case study

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viatel™ polymers for implants - case study

#	Polymer type/family	Product Code	Batch	L : G (mol%)	Molecular Weight Mn, Mw (kDa)	IV (dl/g)	End-group
1	Poly D,L-lactide-co-glycolide (PLGA)	DLG 5002 E	2591607	49.4 : 50.6	9.0, 18.3	0.20	Ester
2	Poly D,L-lactide-co-glycolide (PLGA)	DLG 5002 A	2588968	49.4 : 50.6	8.8, 19.2	0.20	Acid
3	Poly D,L-lactide-co-glycolide (PLGA)	DLG 5005 A	2567373	49.7 : 50.3	29.8, 54.3	0.49	Acid
4	Poly D,L-lactide-co-glycolide (PLGA)	DLG 7502 A	2597443	73.9 : 26.1	7.8, 16.2	0.20	Acid
5	Poly D,L-lactide-co-glycolide (PLGA)	DLG 7509 E	2573112	74.5 : 25.5	61.9, 104.2	0.82	Ester
6	Poly D,L-lactide-co-glycolide (PLGA)	DLG 8507 E	2588392	84.5 : 15.5	49.9, 90.7	0.70	Ester
7	Poly D,L-lactide (PDLLA)	DL 03 A	2550133	100 : 0	28.5, 50.8	0.39	Acid
8	Poly D,L-lactide (PDLLA)	DL 09 E	2596557	100 : 0	57.6, 89.6	0.72	Ester

8 distinct grades of amorphous polyesters utilised for screening varying: L:G ratios, Mw / IV, end-group

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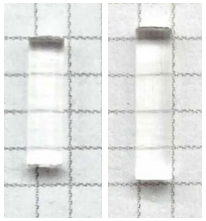
screening using VCM tool – no drug

checking the influence of melt processing on various viatel™ polymers

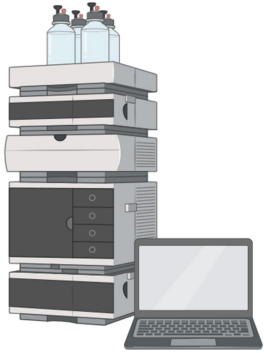
8 viatel™ polymers (PLGA + PDLLA)

4 Process Parameter

VCM



GPC



temperature	time
min process temp.	6 min
	15 min
min temp. + 20-25°C	6 min
	15 min

150 mg needed per measurement
4.8 g overall material
~6 h total time for 32 samples

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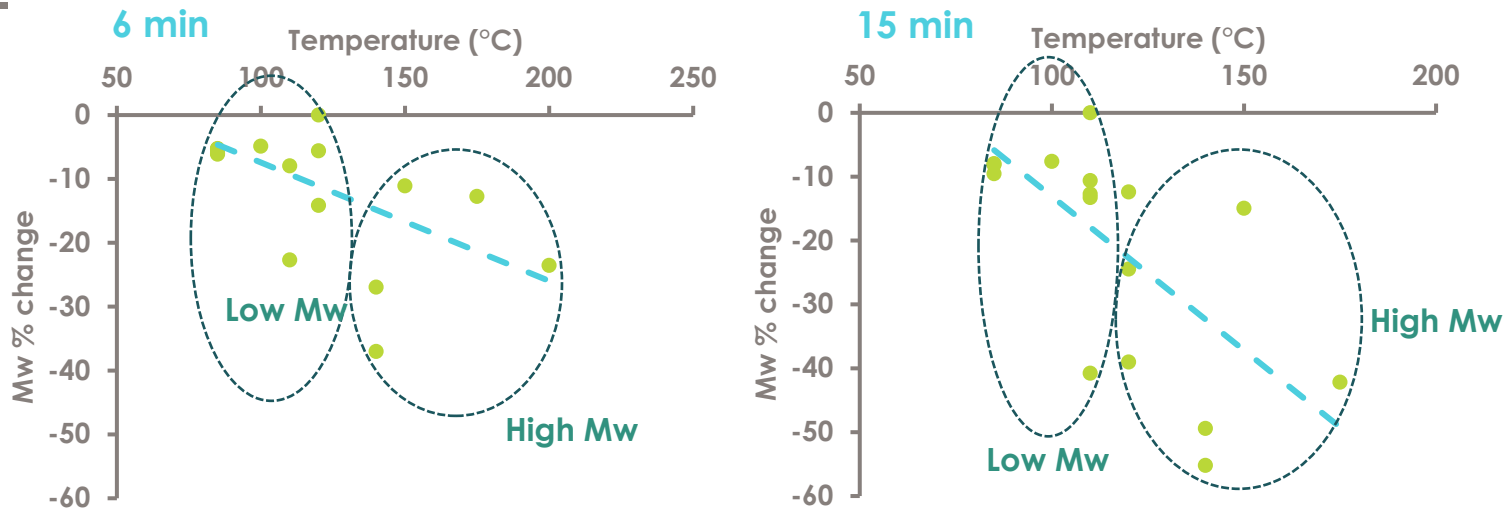
process influence on viatel™ polymers



melt processing should be done at mildest conditions possible to minimize Mw decay

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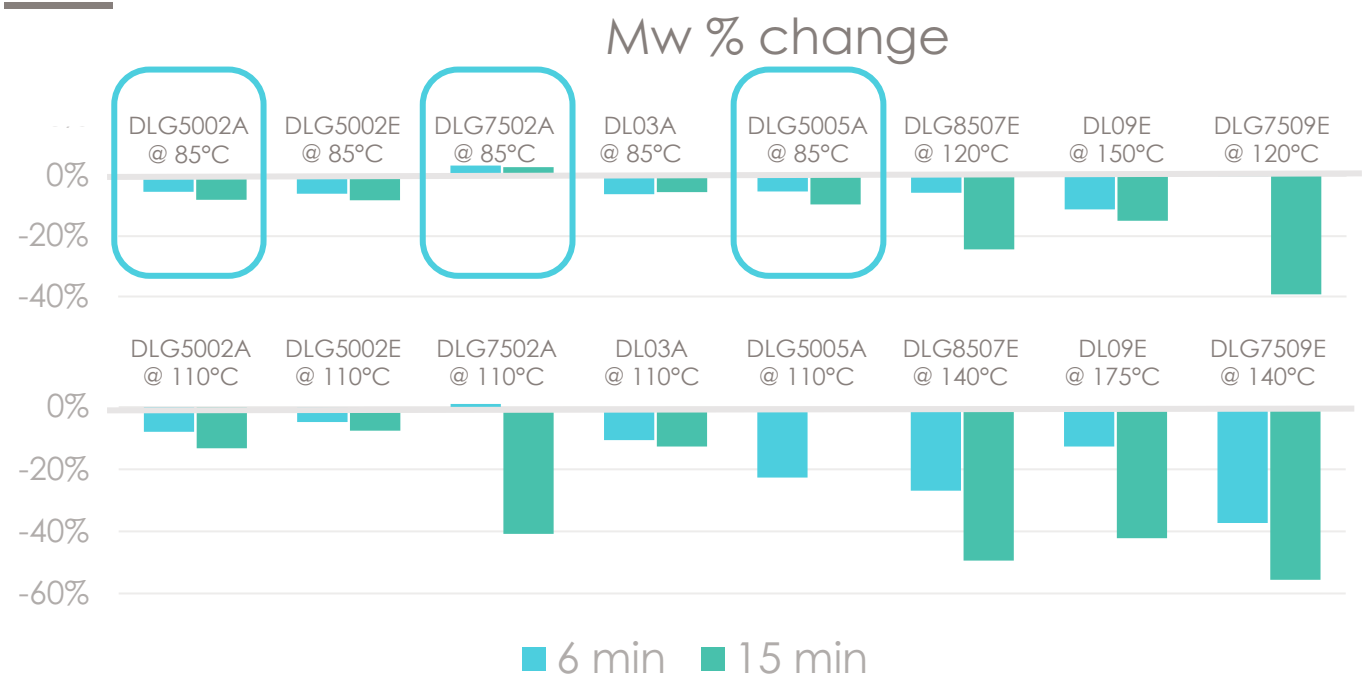

increased processing temperature

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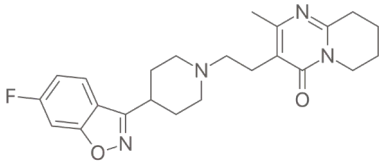
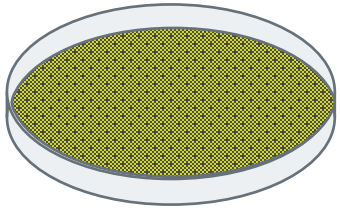
implant fabrication using VCM tool

viatel™ PLGA

risperidone

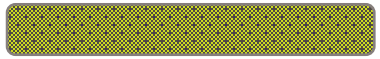




viatel™ PLGA + risperidone film

mild conditions
100°C / 5 min

⌀ 3 mm



viatel™ PLGA / risperidone implants

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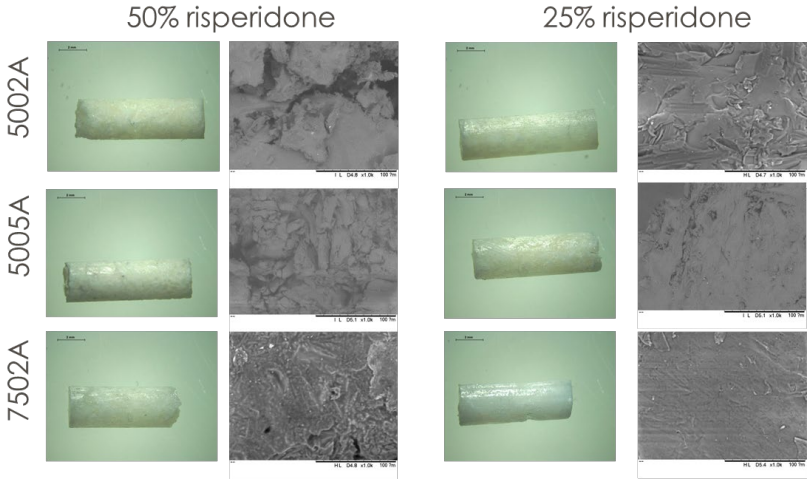
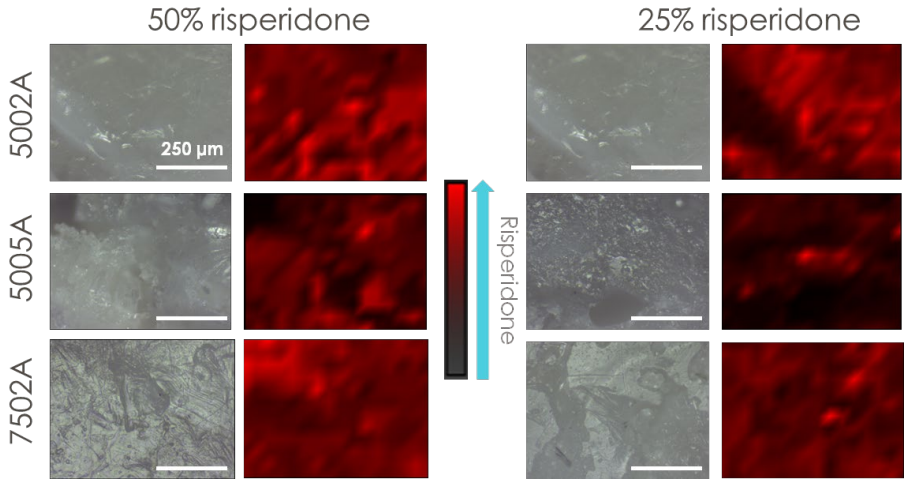
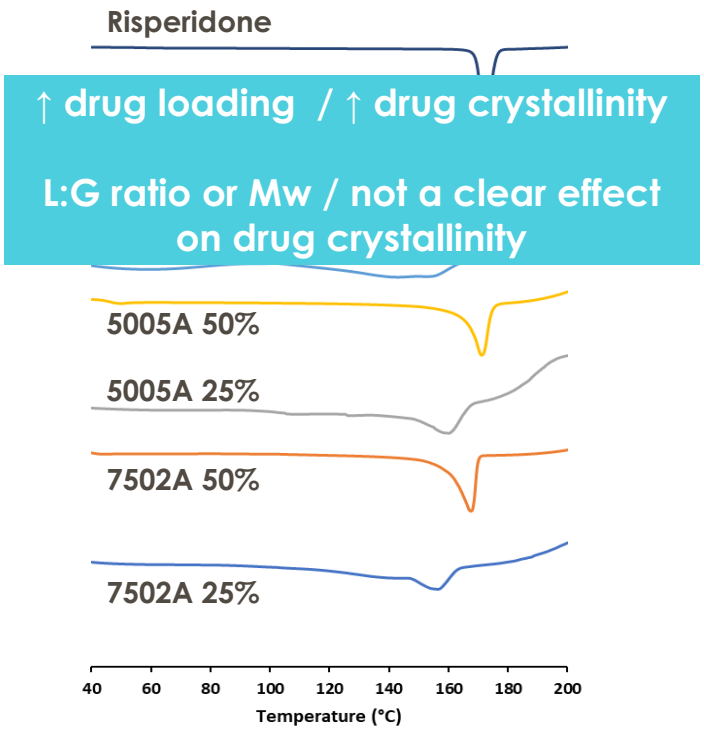
implant characterisation – SEM & Raman

- SEM shows uniform, well-formed implants
- Raman shows good drug distribution throughout



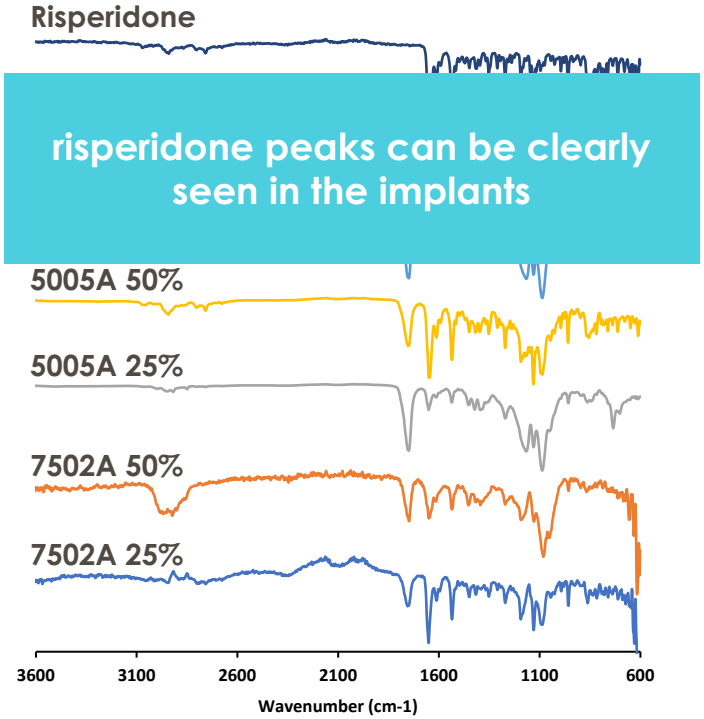


implant characterisation – DSC + FTIR



↑ drug loading / ↑ drug crystallinity

L:G ratio or Mw / not a clear effect on drug crystallinity



risperidone peaks can be clearly seen in the implants

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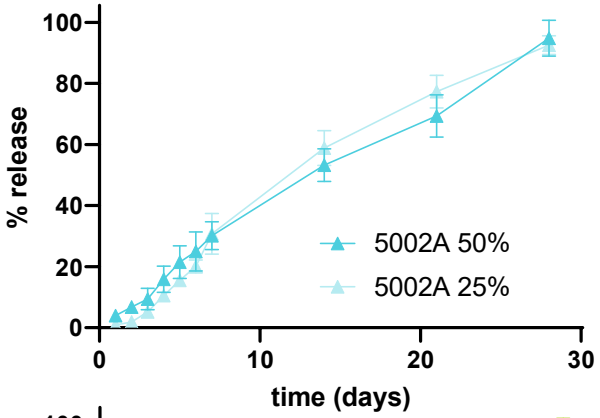
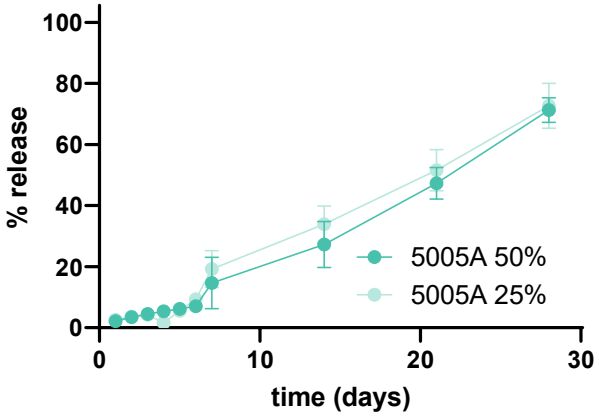
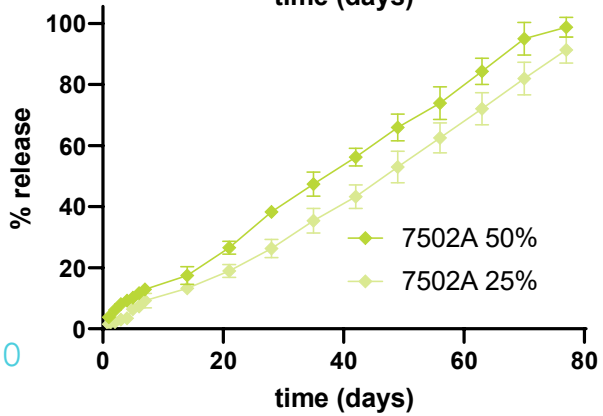
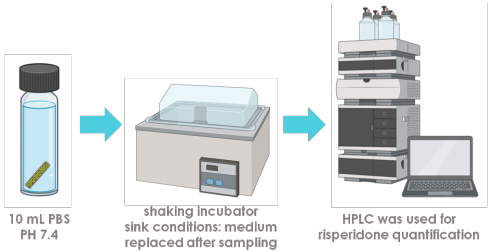
implant performance testing (VCM)









drug loading had limited effect on % release rate
↑ drug loading / ↑ daily dose

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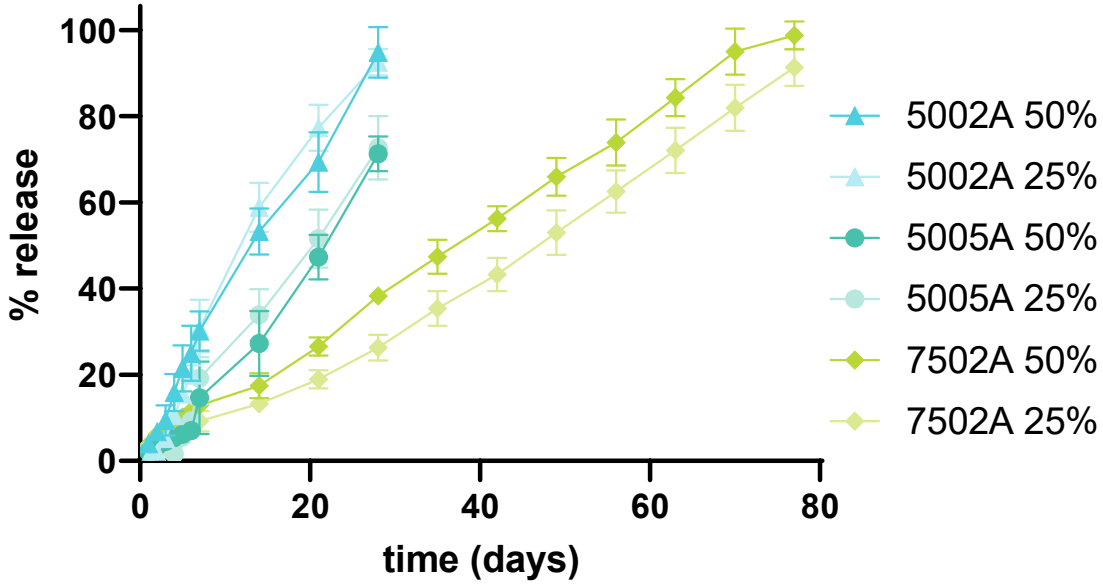

↑ Mw = ↑ release time
(5005A slower than 5002 A)

↑ L:G ratio = ↑ release time
(7502A slower than 5002/5A)

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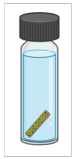
scale-up via hot melt extrusion (HME)

formulations
DLG 5002 A + 50% API
DLG 5005 A + 50% API
DLG 7502 A + 50% API

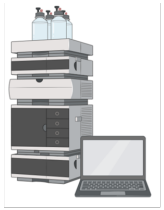
HME

analysis

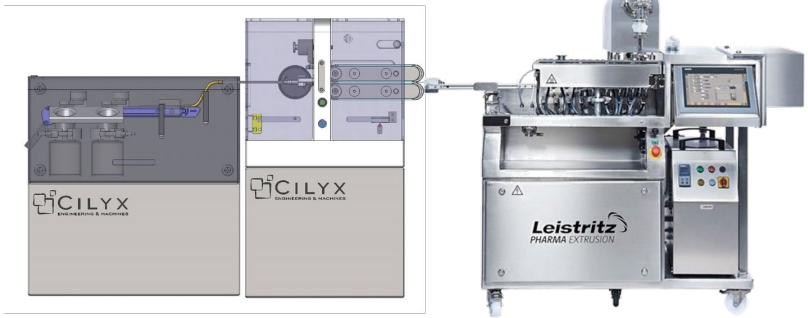


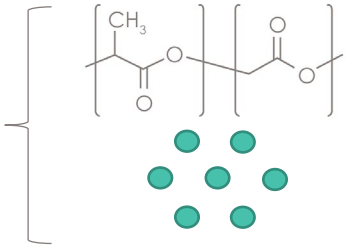
10 mL PBS
PH 7.4

shaking incubator
sink conditions: medium
replaced after sampling



HPLC was used for
risperidone quantification





polymer

API

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implant fabrication using extruder

Weighing
- NewClassic MS (Mettler Toledo)
- 30g polymer
- 30g API

Mixing
- Mixomat Mini (Fuchs)
- 30min at stage 5

Extruding
- ZSE12HPPH (Leistritz Extrusionstechnik GmbH)
- 100 g/h (gravimetric)
- 30 rpm
- 105°C at the nozzle

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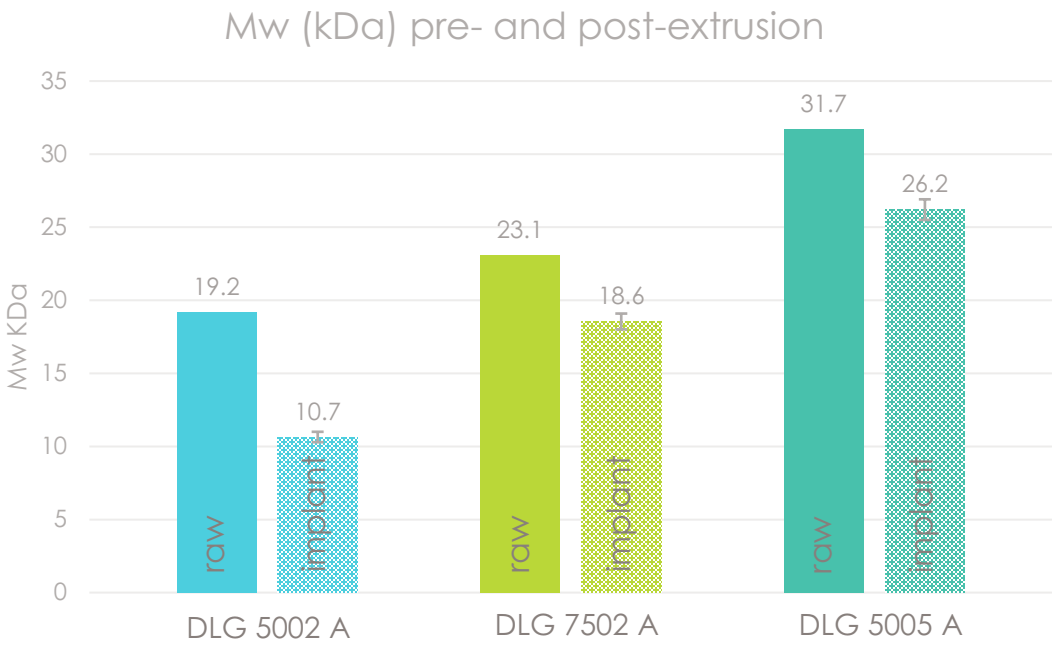
implant characterisation - GPC

Sample ID	Mn (kDa)	Mw (kDa)
DLG 5002 A raw	8	19.2
DLG 5002 A + 50% risperidone start 1	4.7	10.7
DLG 5002 A + 50% risperidone start 2	4.9	10.9
DLG 5002 A + 50% risperidone mid 1	4.3	9.5
DLG 5002 A + 50% risperidone mid 2	4.9	10.8
DLG 5002 A + 50% risperidone end 1	5.1	11
DLG 5002 A + 50% risperidone end 2	5.2	11
DLG 7502 A raw	10.4	23.1
DLG 7502 A + 50% risperidone start 1	8	19.3
DLG 7502 A + 50% risperidone start 2	7.7	19.1
DLG 7502 A + 50% risperidone mid 1	7.2	18.5
DLG 7502 A + 50% risperidone mid 2	7.7	18.8
DLG 7502 A + 50% risperidone end 1	7.5	16.9
DLG 7502 A + 50% risperidone end 2	7.6	18.7
DLG 5005 A raw	17.7	31.7
DLG 5005 A + 50% risperidone start 1	13.1	26.0
DLG 5005 A + 50% risperidone start 2	12.4	23.5
DLG 5005 A + 50% risperidone mid 1	13.2	27.00
DLG 5005 A + 50% risperidone mid 2	13.3	26.8
DLG 5005 A + 50% risperidone end 1	13.7	27.1
DLG 5005 A + 50% risperidone end 2	13.2	26.8



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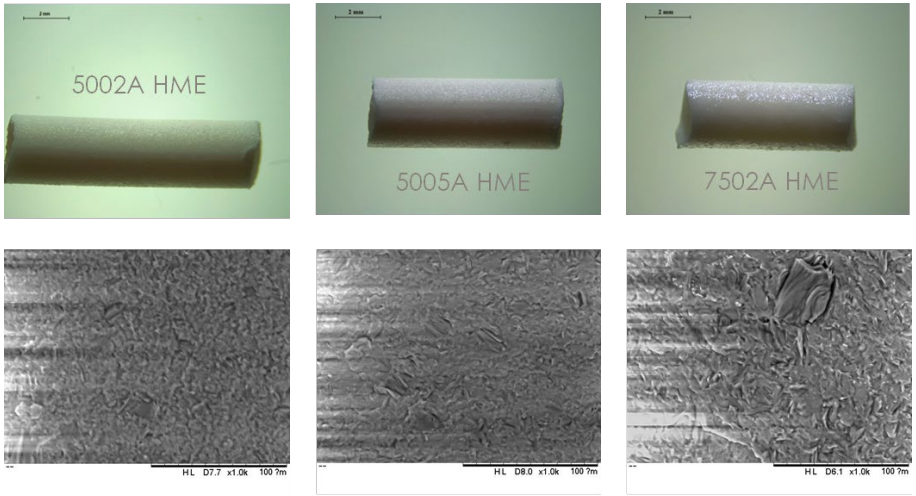
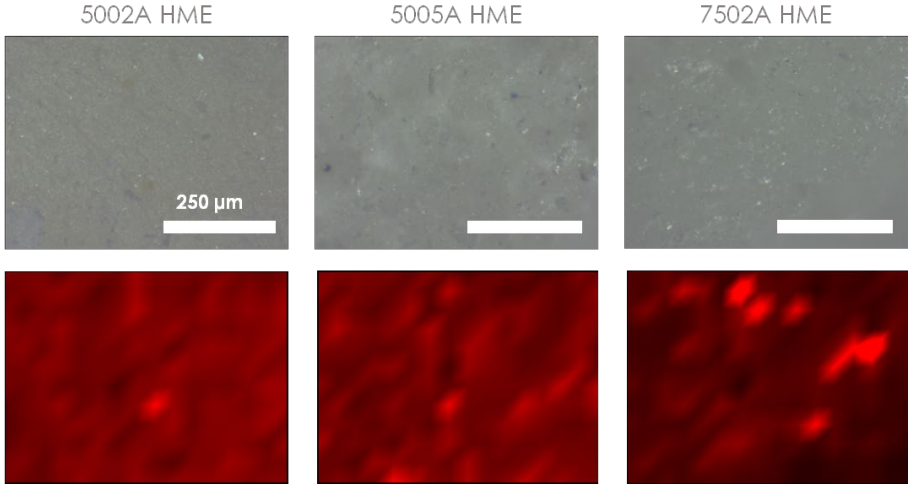
implant characterisation – SEM & Raman

- SEM showed X
- Raman showed Y





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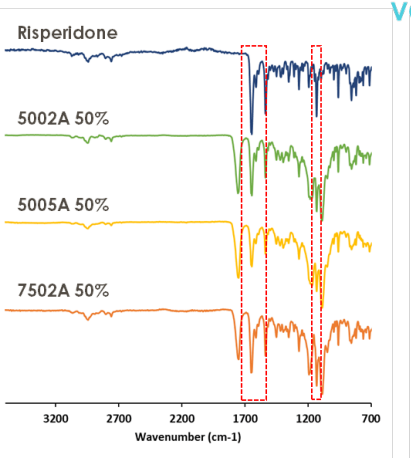
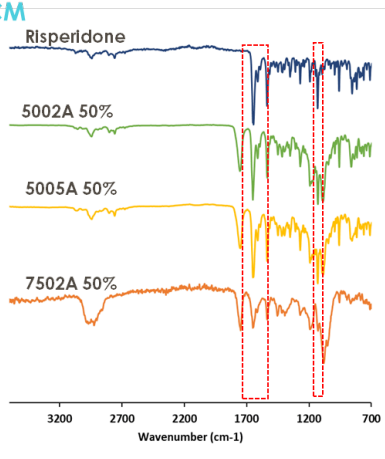
implant comparison – FTIR & DSC

VCM and HME fabricated implants are very similar

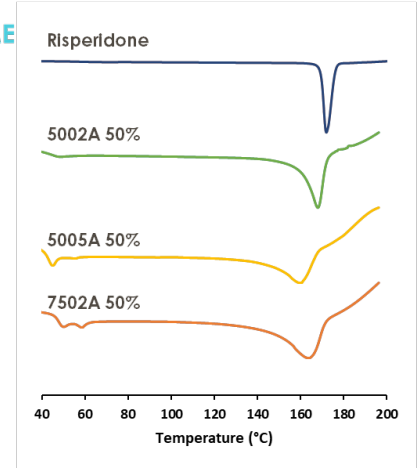
HME



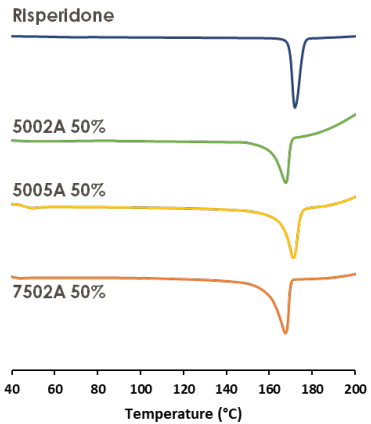
VCM



HME



VCM



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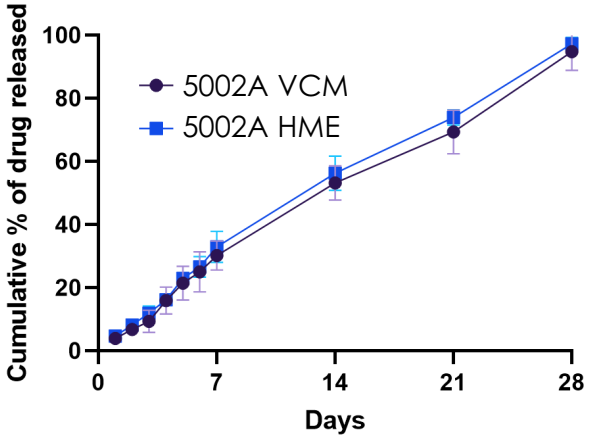
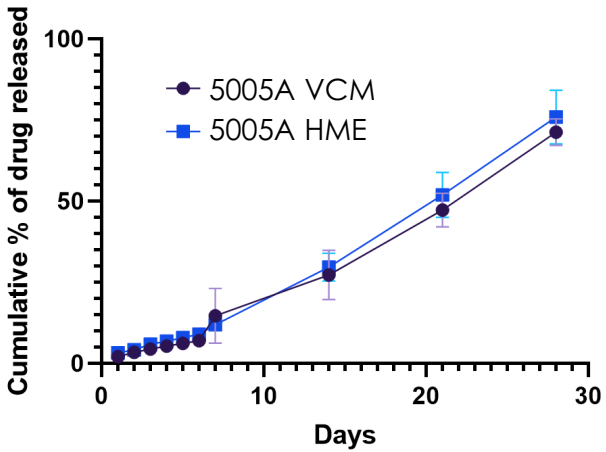
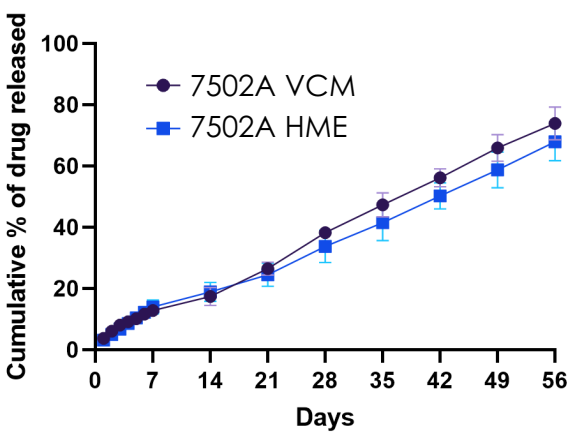
implant performance testing







release from VCM implants = release from HME implants

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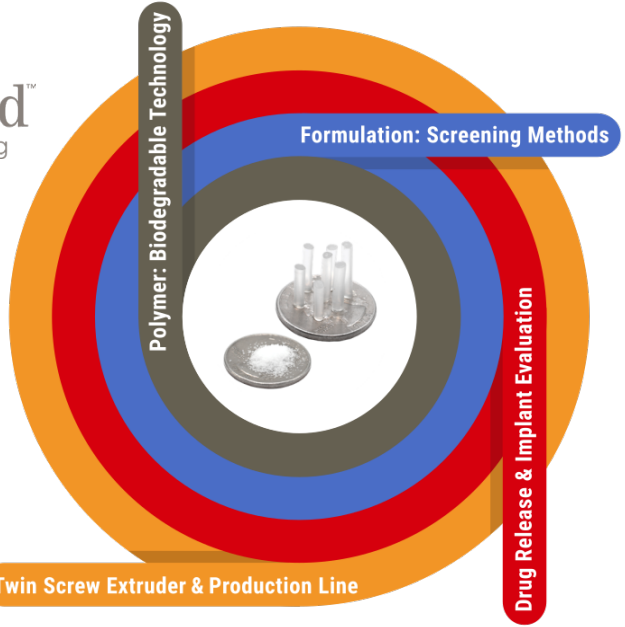

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