Use of SDI to assess

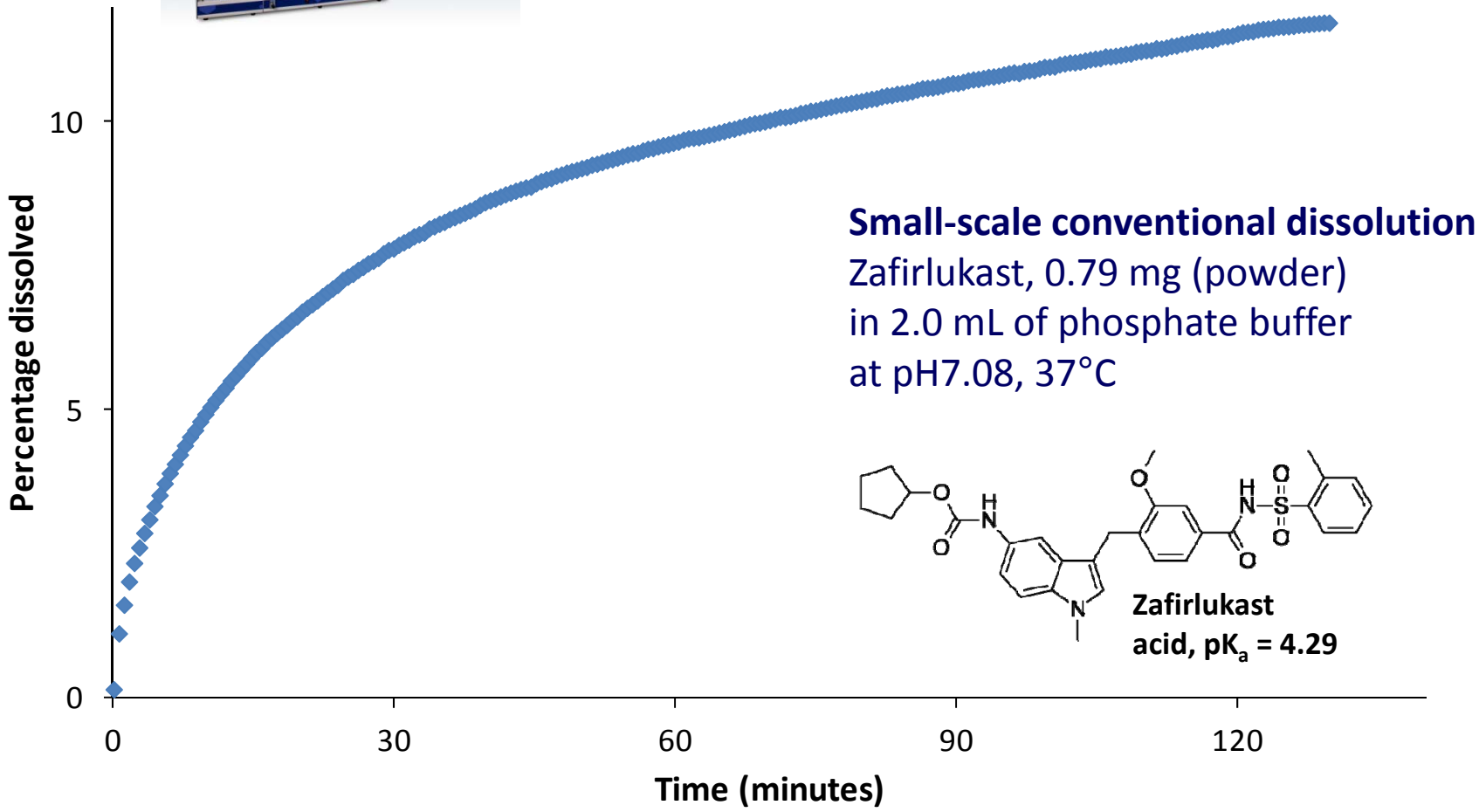
dissolution characteristics of
OTC pharmaceuticals with
controlled release rate

formulations

John Comer, CSO

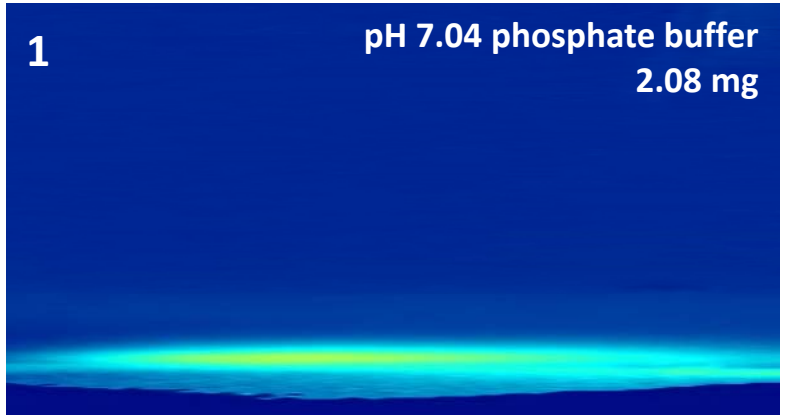
Sirius Analytical Ltd.

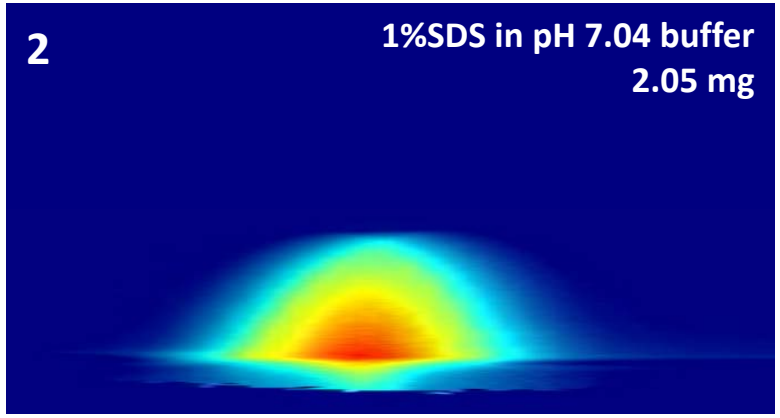

DELL
Insight
Insight Accessories

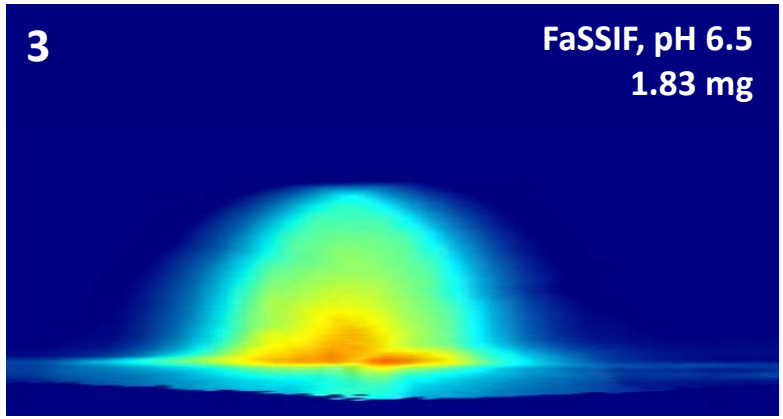


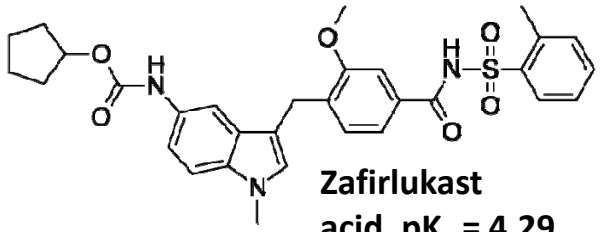
Small-scale conventional dissolution
Zafirlukast, 0.79 mg (powder)
in 2.0 mL of phosphate buffer
at pH7.08, 37°C

Zafirlukast
acid, pK_a = 4.29

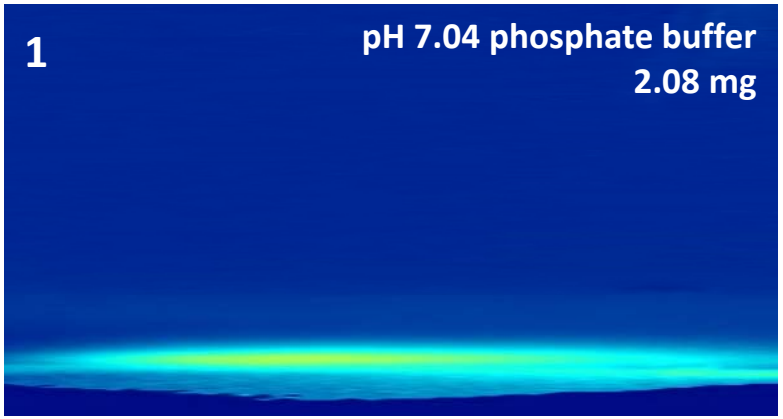


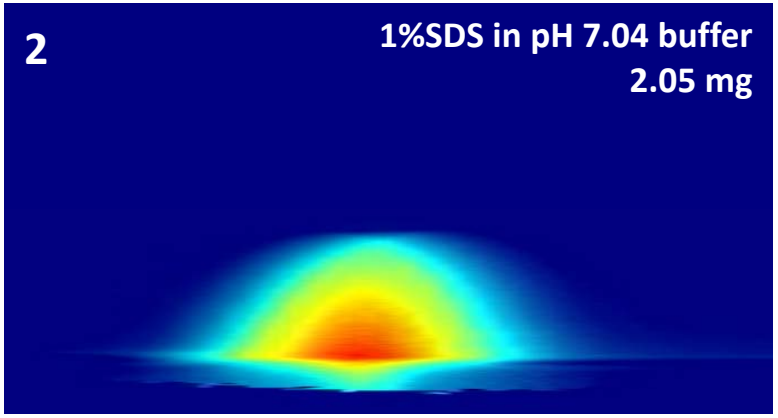


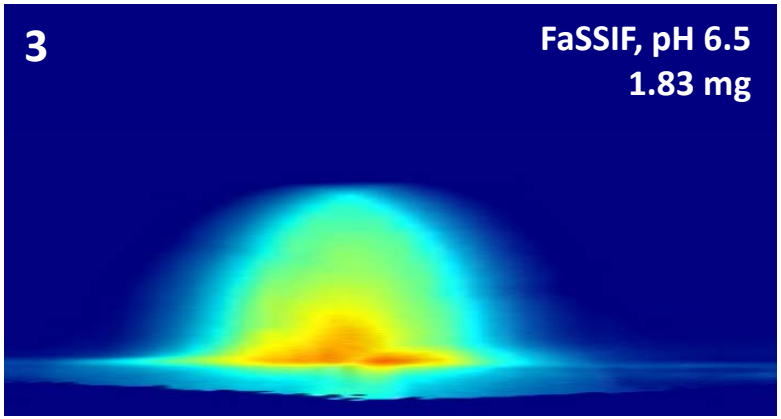


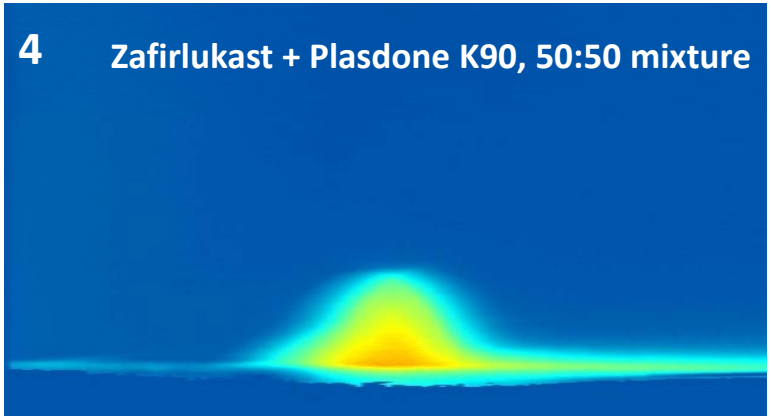


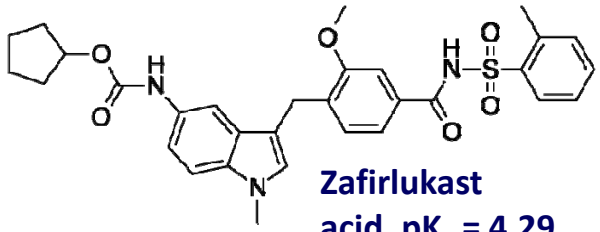
Zafirlukast
acid, pK_a = 4.29
Dissolution at 37°C



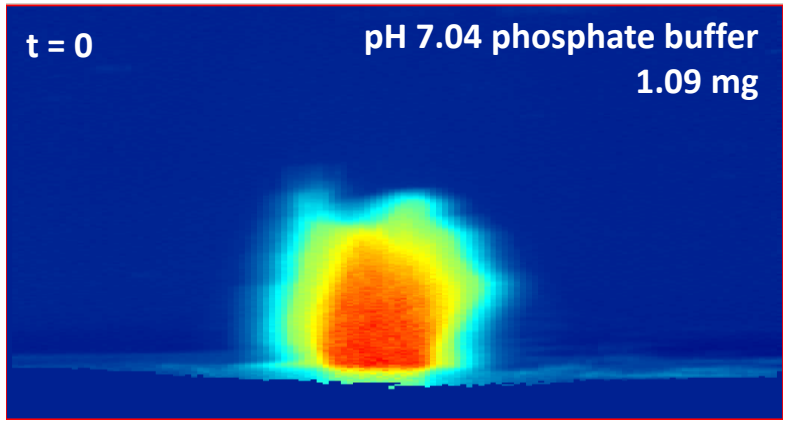


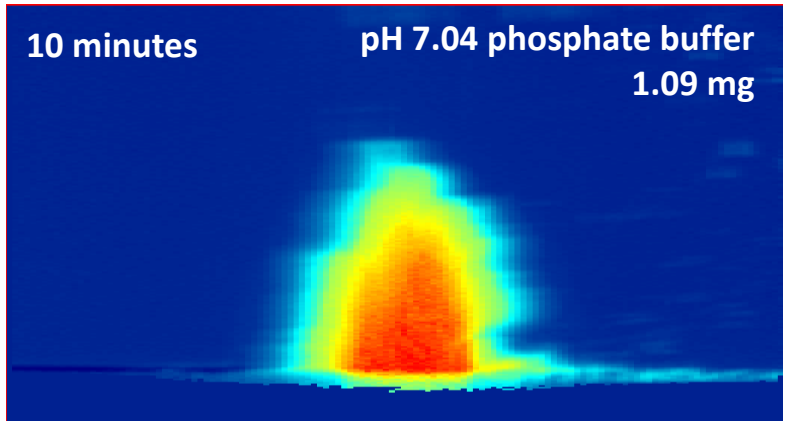


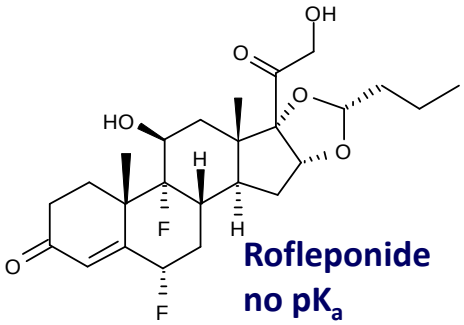




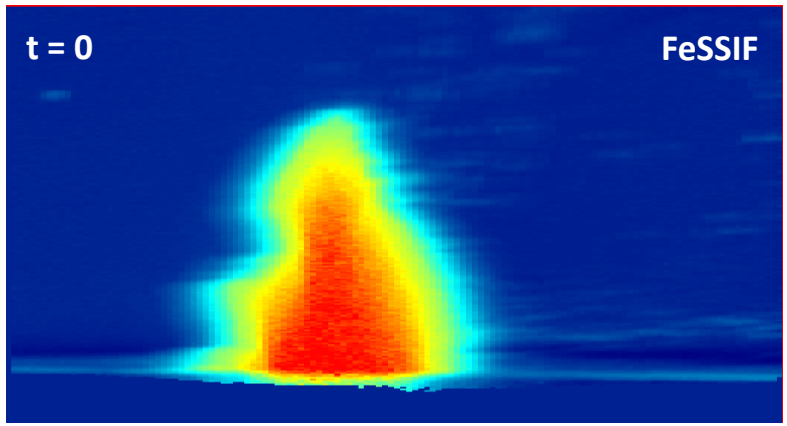
Zafirlukast
acid, pK_a = 4.29
Dissolution at 37°C

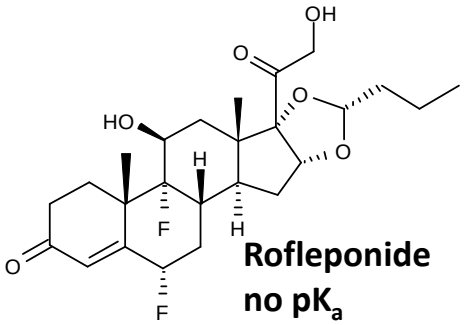




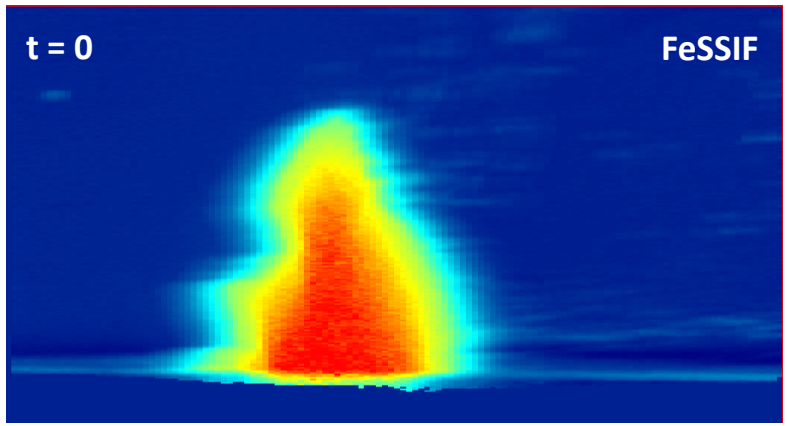


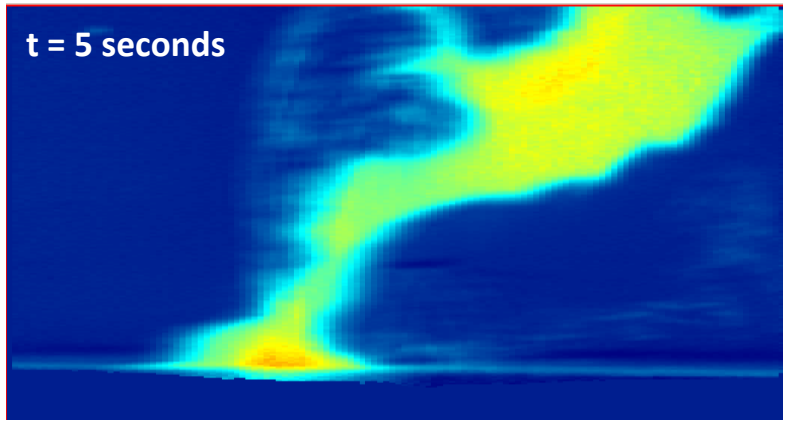
Rofleponide
no pK_a
Dissolution at 37°C

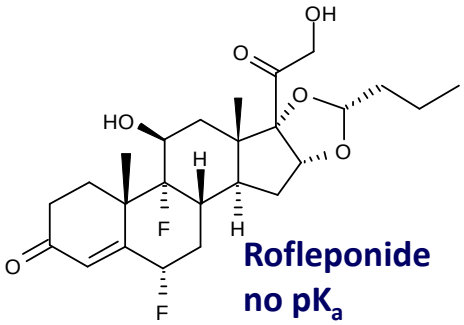




Rofleponide
no pK_a
Dissolution at 37°C







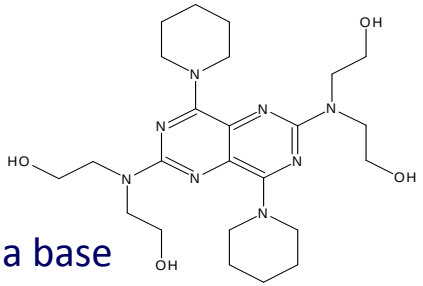
Rofleponide
no pK_a
Dissolution at 37°C

Dissolution studies with dipyridamole

Phosphate buffer, pH 6.8

Amorphous solid dispersions with HPMC-AS* to enhance solubility

Comparison of data from SiriusT3 and SDI

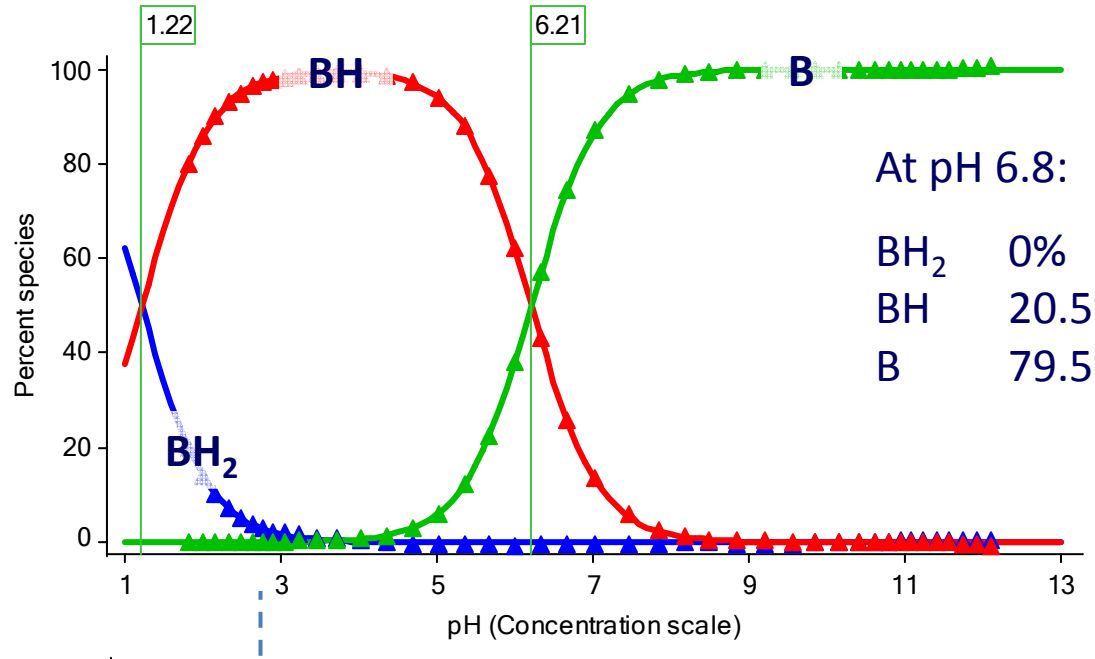


Dipyridamole is a base

It has two pK_as: 0.85 and 6.24

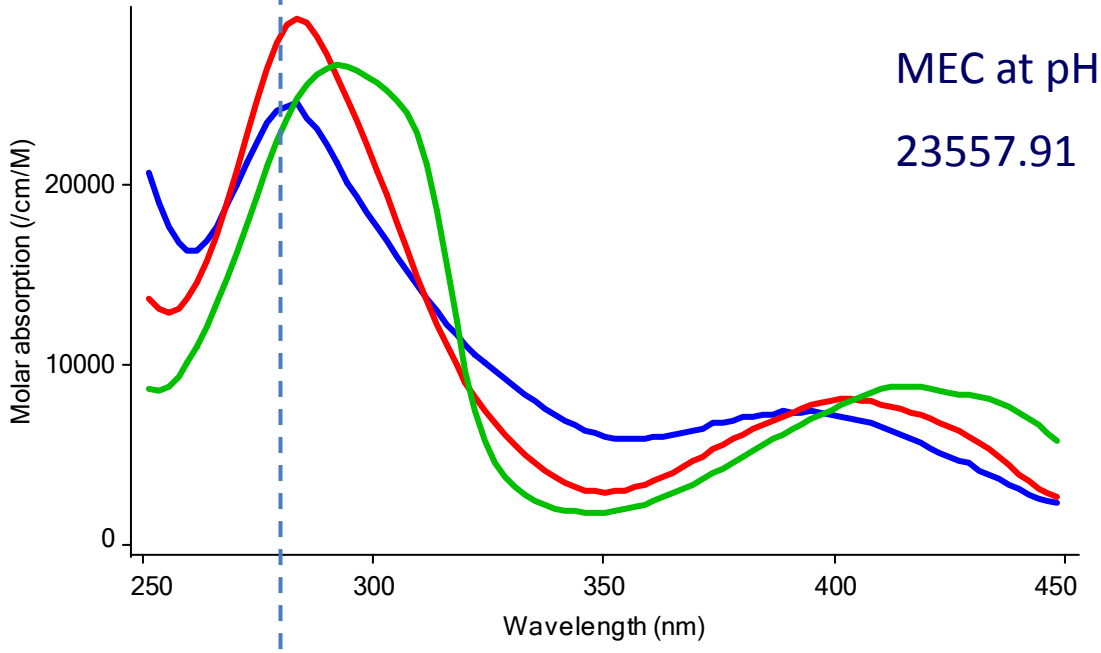
Sample introduced in neutral form

*** Hydroxypropyl Methylcellulose Acetate Succinate, Shin-Etsu Chemical Company Ltd.**



At pH 6.8:

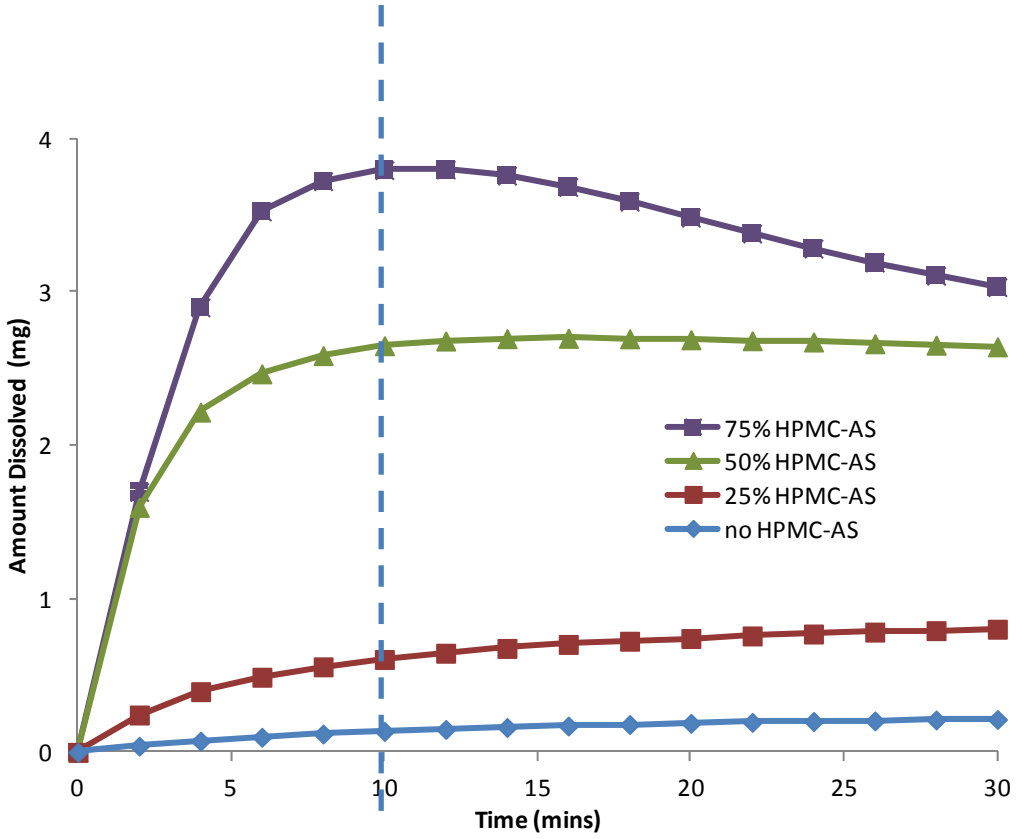
BH_2	0%
BH	20.5%
B	79.5%



MEC at pH 6.8, 280 nm:

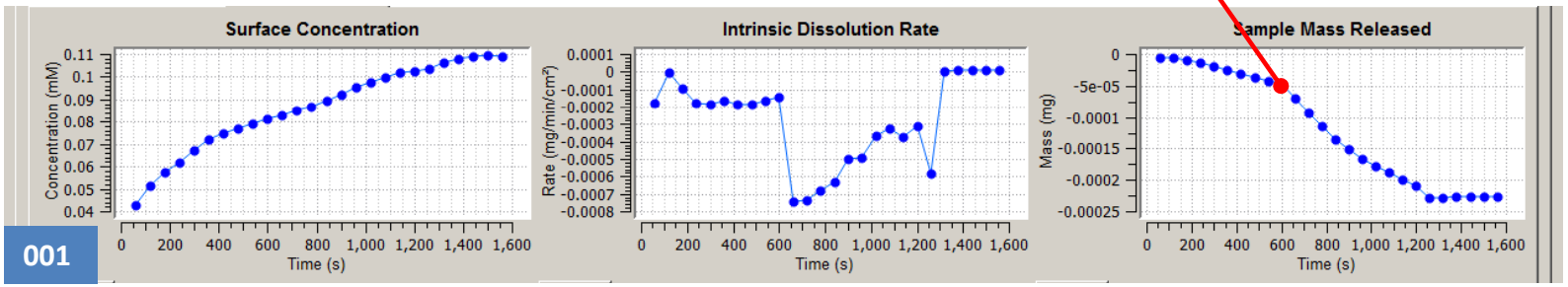
23557.91


SiriusT3


Amount Dissolved (mg)
Time (mins)
0
1
2
3
4
0
5
10
15
20
25
30
75% HPMC-AS
50% HPMC-AS
25% HPMC-AS
no HPMC-AS

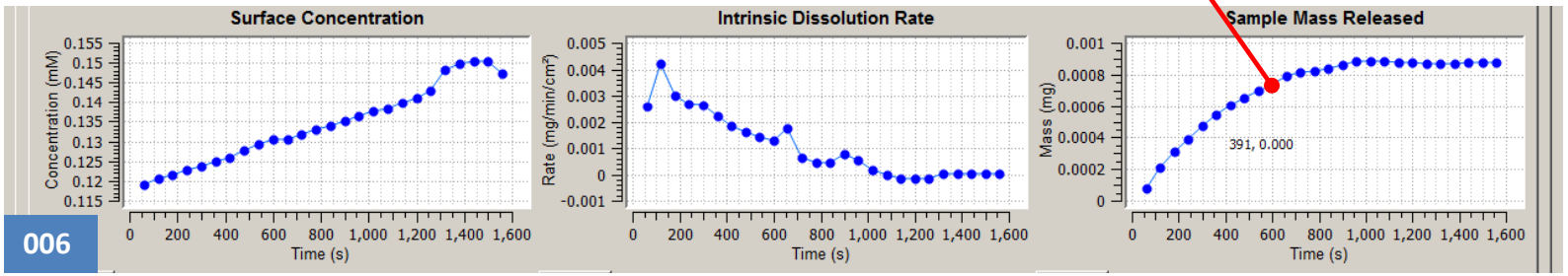
	Weights (mg) released after 600 sec.		
	T3	SDI	SDI x 1000
no HPMC-AS	0.136	0	0
25% HPMC-AS	0.606	0.0007	0.7
50% HPMC-AS	2.652	0.0026	2.6
75% HPMC-AS	3.796	0.0037	3.7

100% dipyridamole – no HPMC-AS



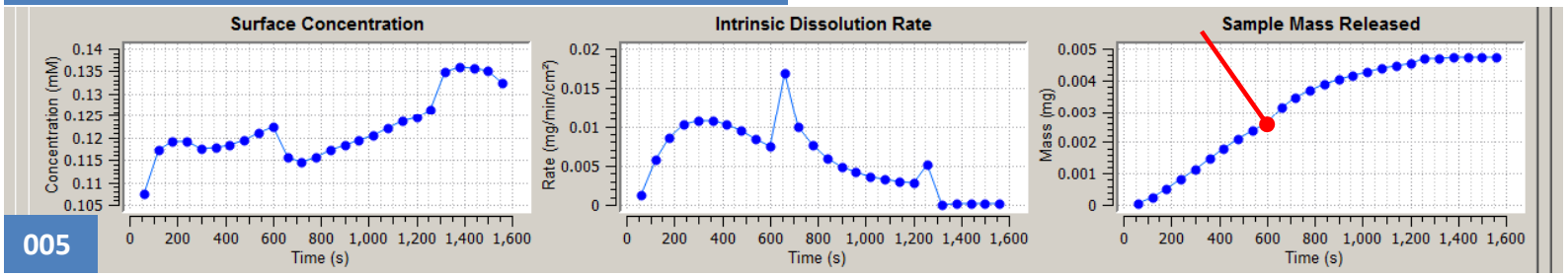
001

75% dipyridamole – 25% HPMC-AS



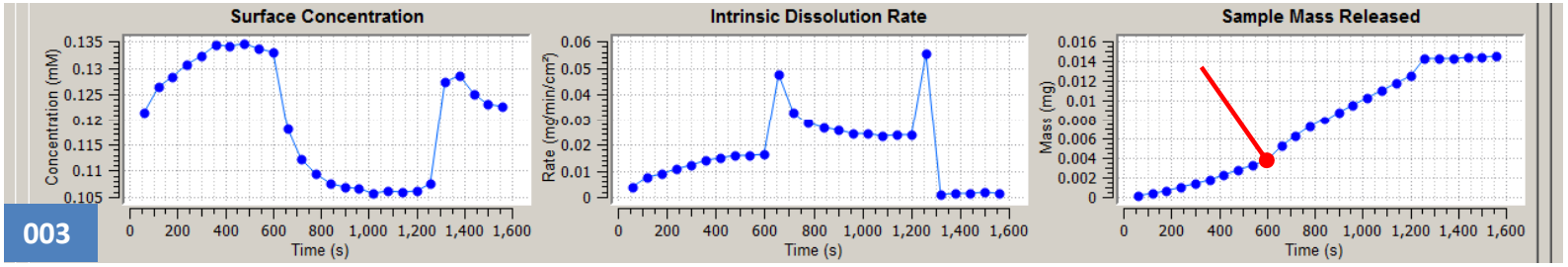
006

50% dipyridamole – 50% HPMC-AS



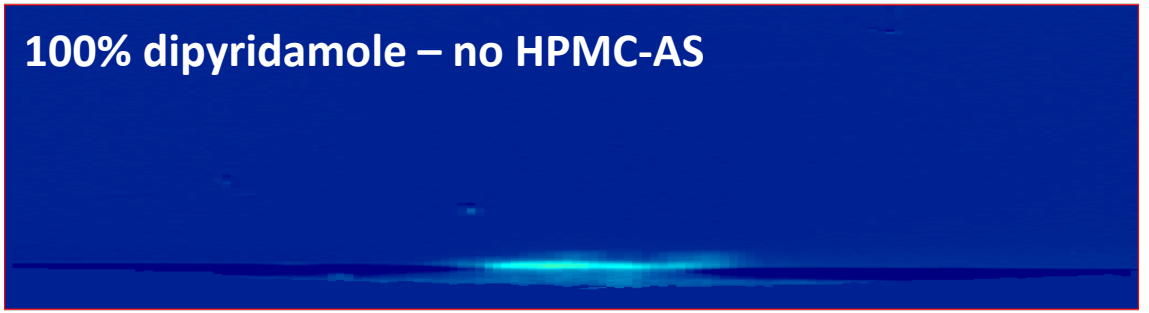
005

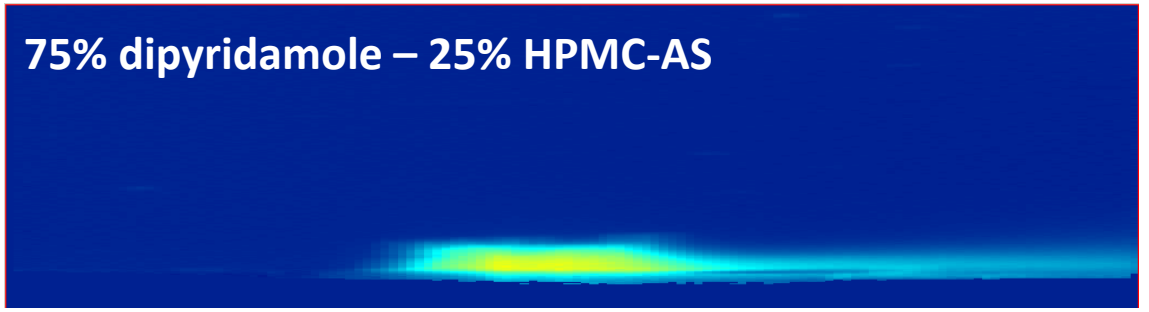
25% dipyridamole – 75% HPMC-AS

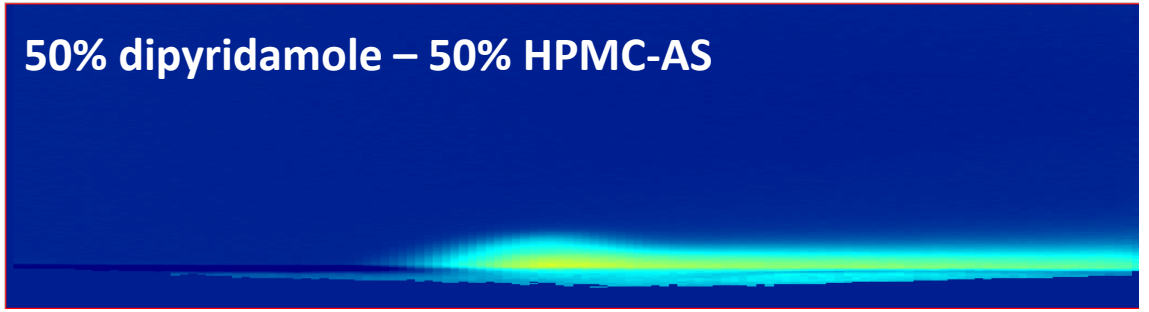


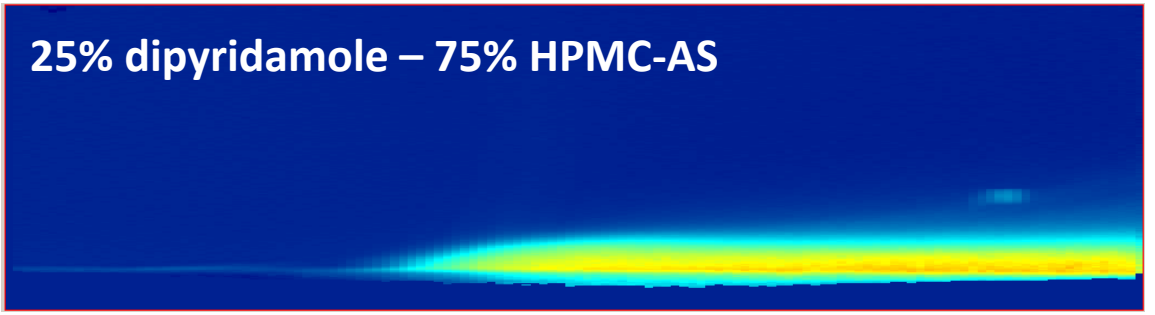
003

Snapshots at 10 minutes

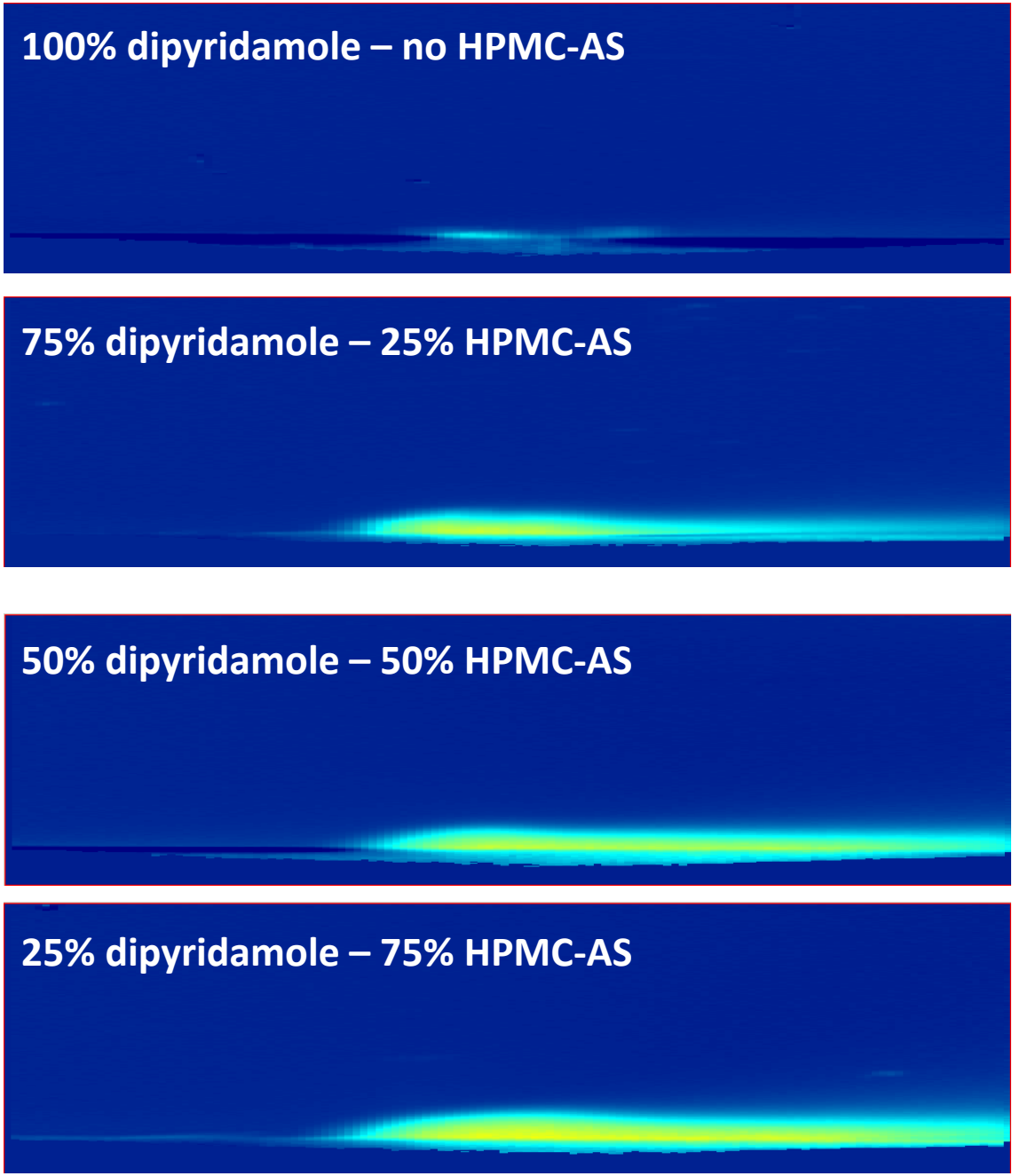








Snapshots at 2 minutes



SDI in solubility enhancement studies

- Easy to set up
- Easy to run at 37°C
- Learn enough in 2 minutes to see where experiment is going
  - A great feature if you're testing lots of trial formulations

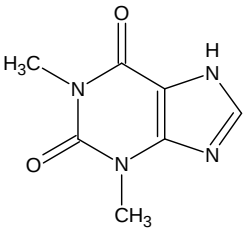
Dissolution studies with theophylline

Phosphate buffer, pH 6.8

Controlled release formulations with Metolose® SR* to delay dissolution

Comparison of data from SiriusT3 and SDI

Theophylline is an acid

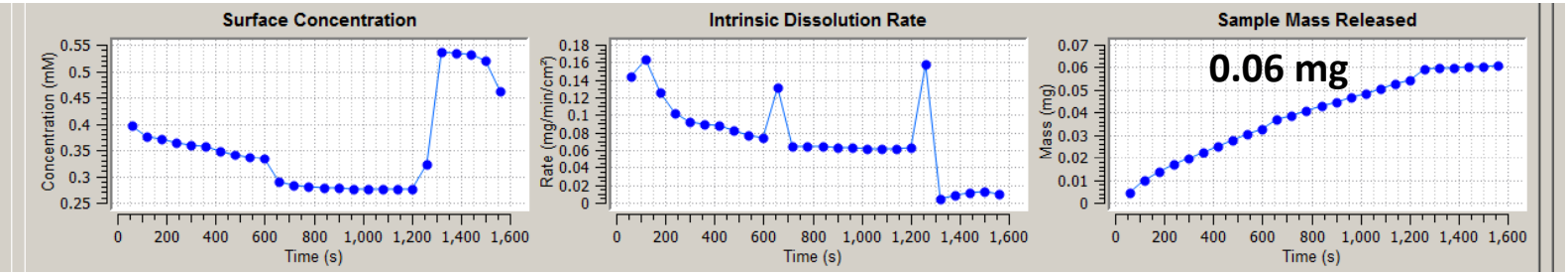


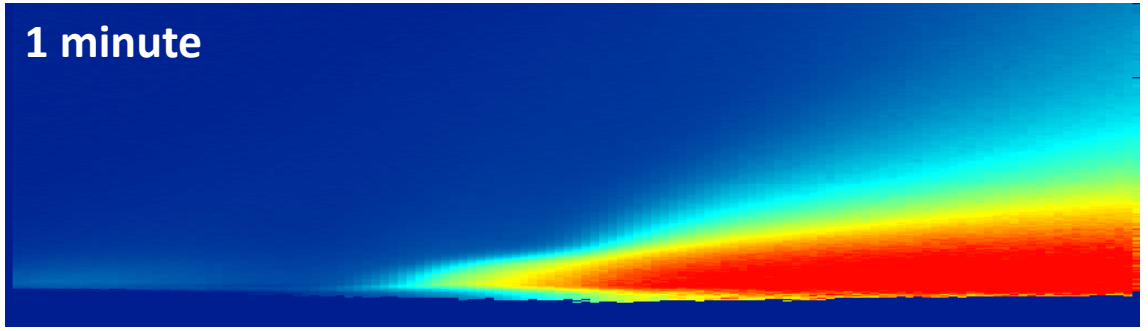
It has one pK_a: 8.61

Sample introduced in neutral form

*** Hydroxypropyl Methylcellulose, Shin-Etsu Chemical Company Ltd.**

100% Theophylline – no Metolose SR

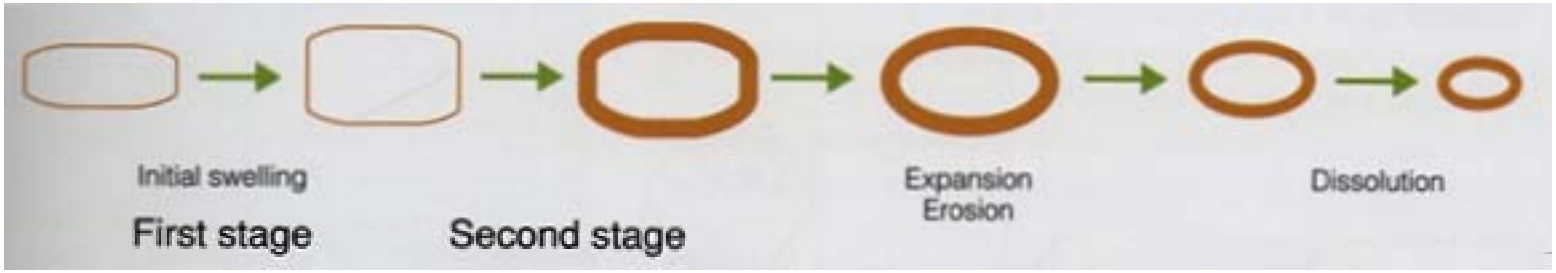


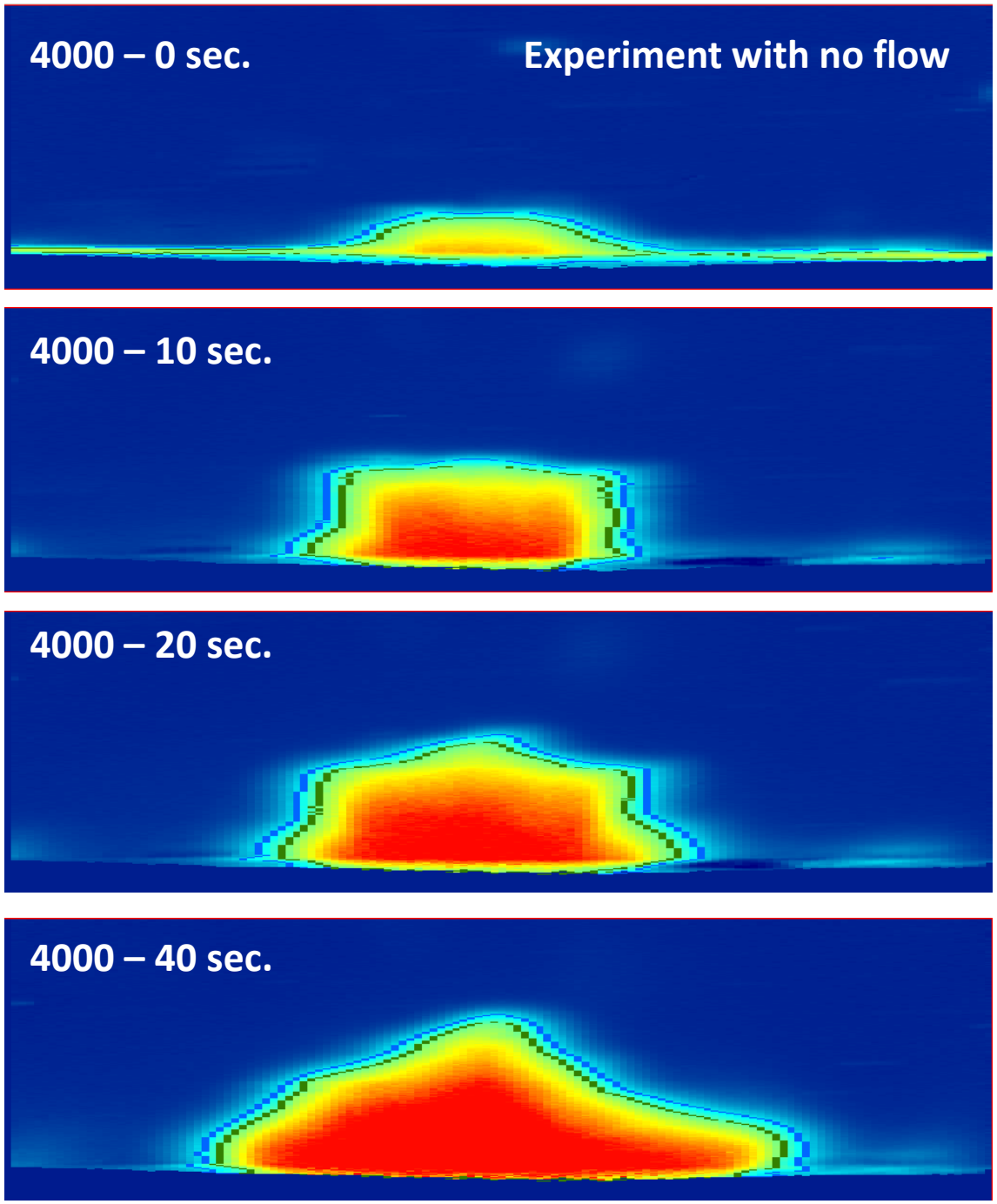


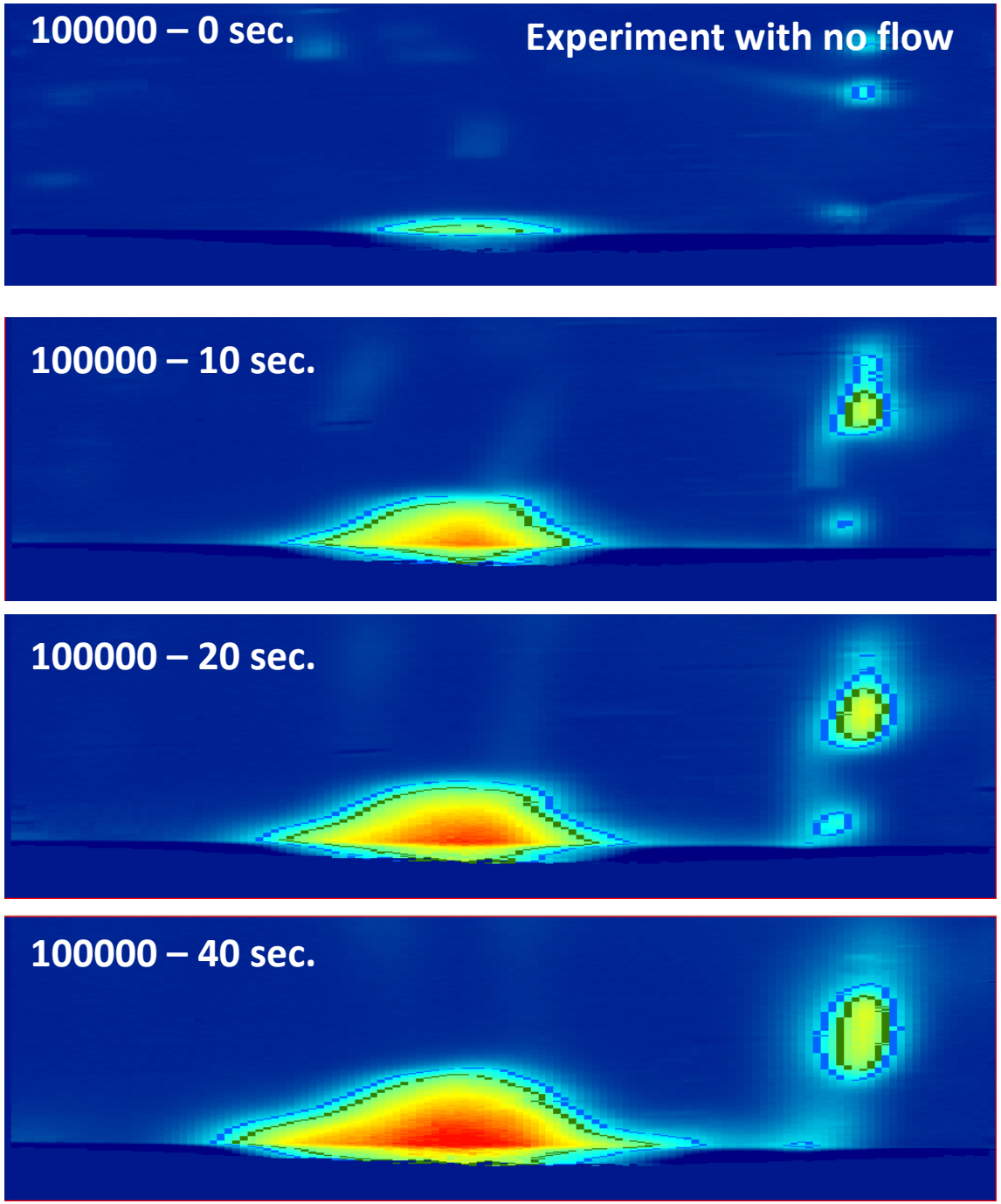
Slow release formulations with Metolose SR

- Mix together the two powders (theophylline + Metolose SR)
- Two grades used: 90SH-4000SR; 90SH-100000SR
- Make pellet and place in instrument

- Expected behaviour during dissolution:

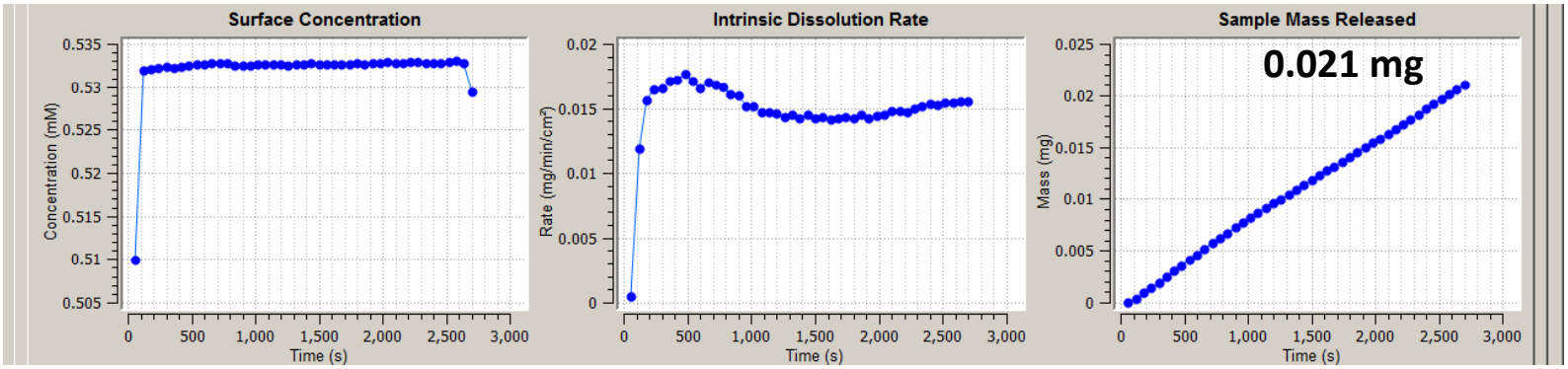


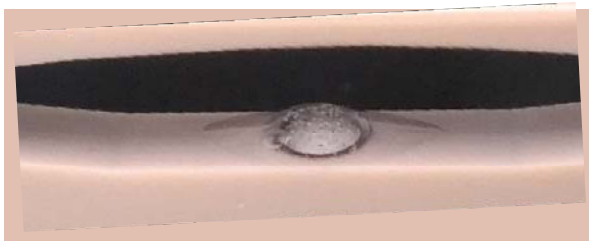

4000 – 0 sec.
Experiment with no flow
4000 – 10 sec.
4000 – 20 sec.
4000 – 40 sec.


100000 – 0 sec.
Experiment with no flow
100000 – 10 sec.
100000 – 20 sec.
100000 – 40 sec.

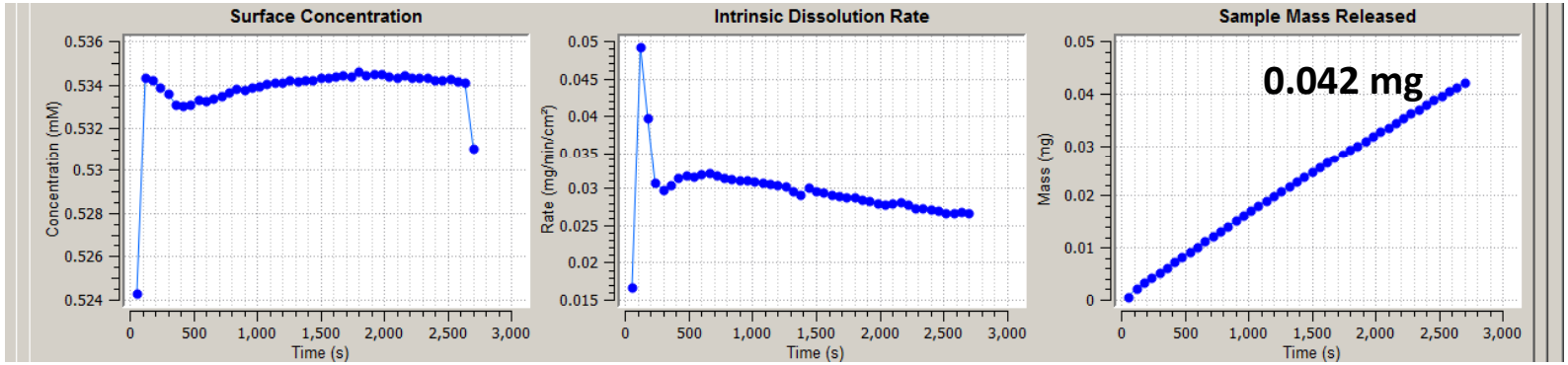
45 minutes at 0.2 mL/min

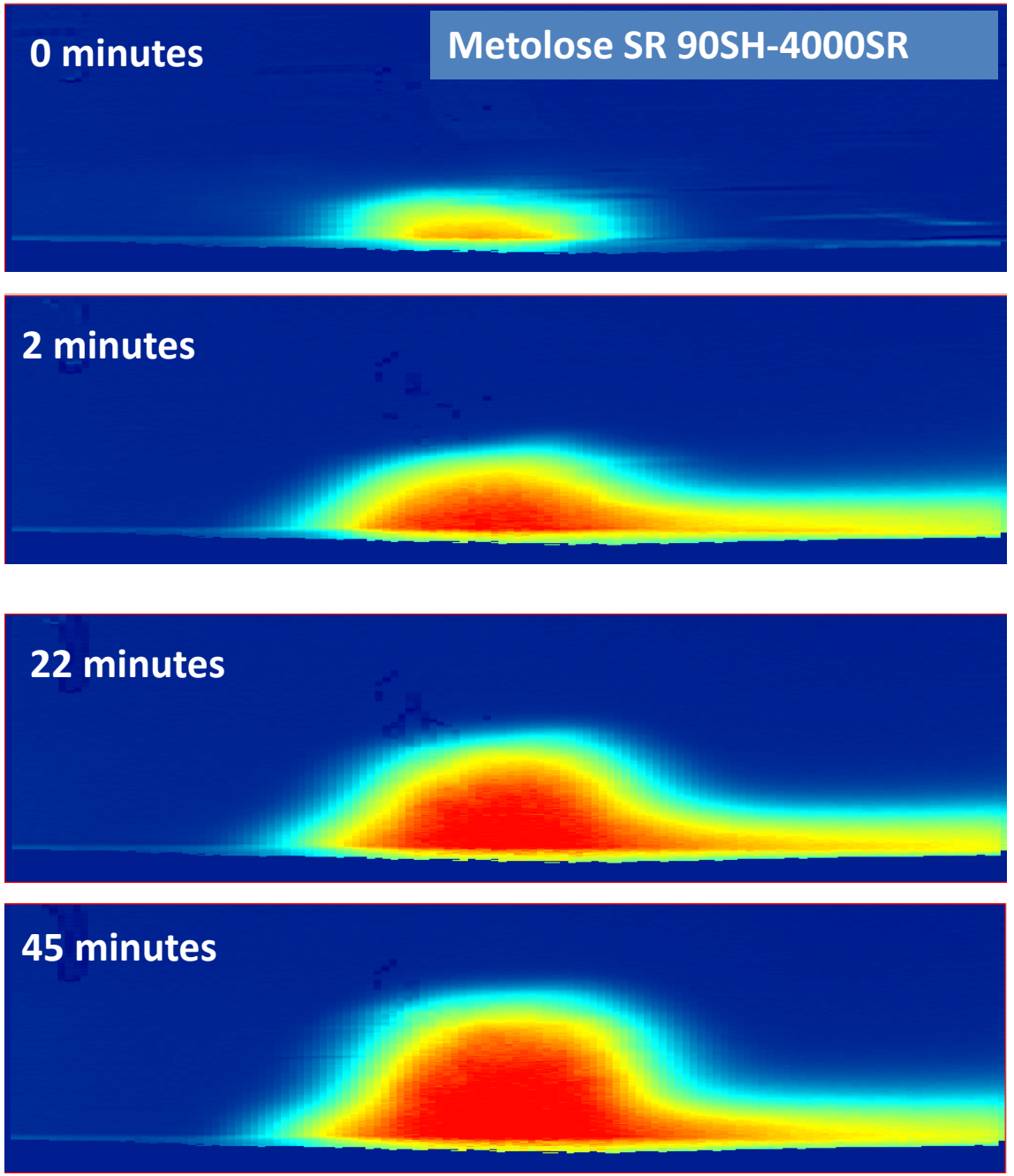
Metolose SR 90SH-4000SR

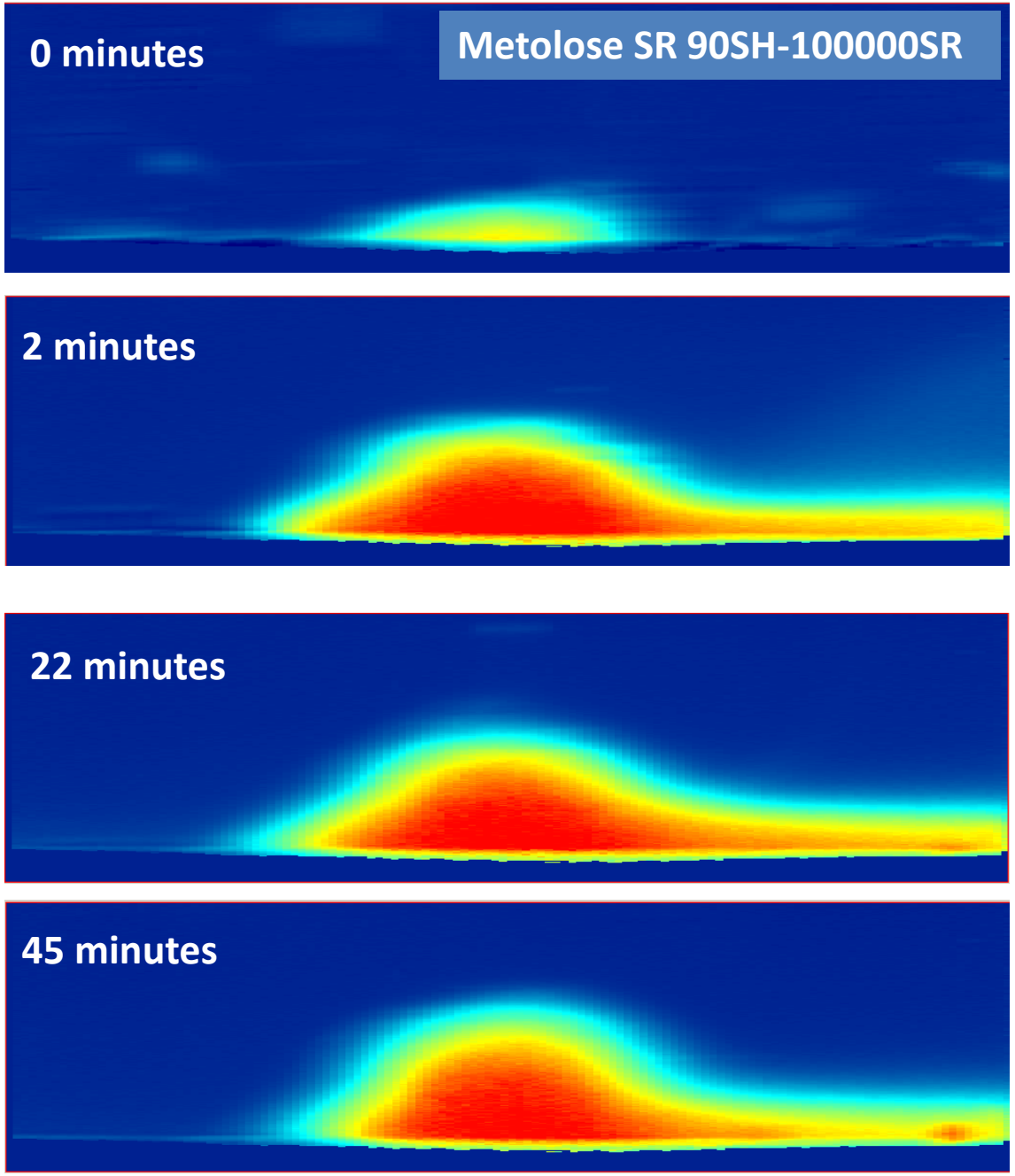




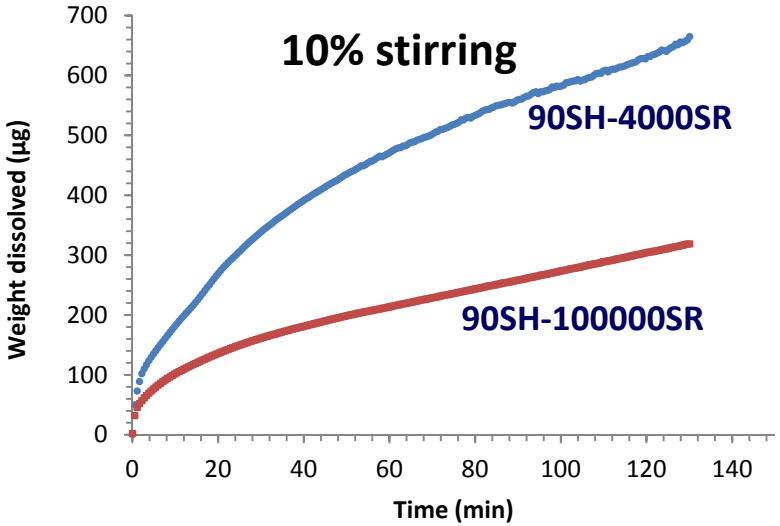
Metolose SR 90SH-10000SR

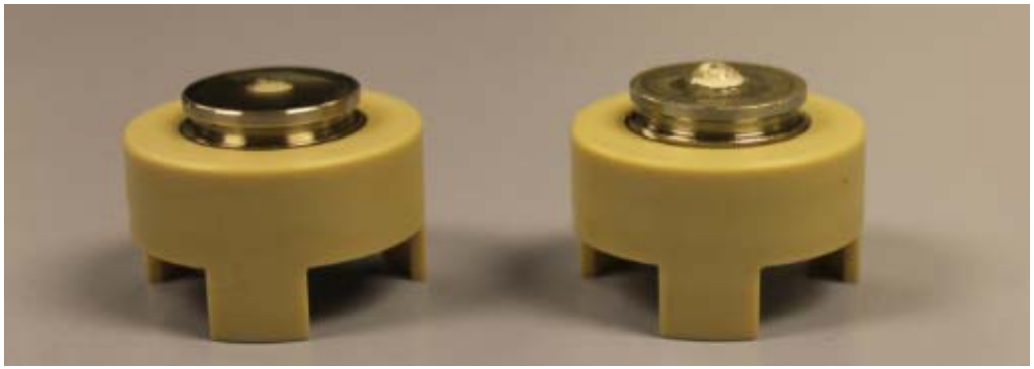



0 minutes
Metolose SR 90SH-4000SR
2 minutes
22 minutes
45 minutes

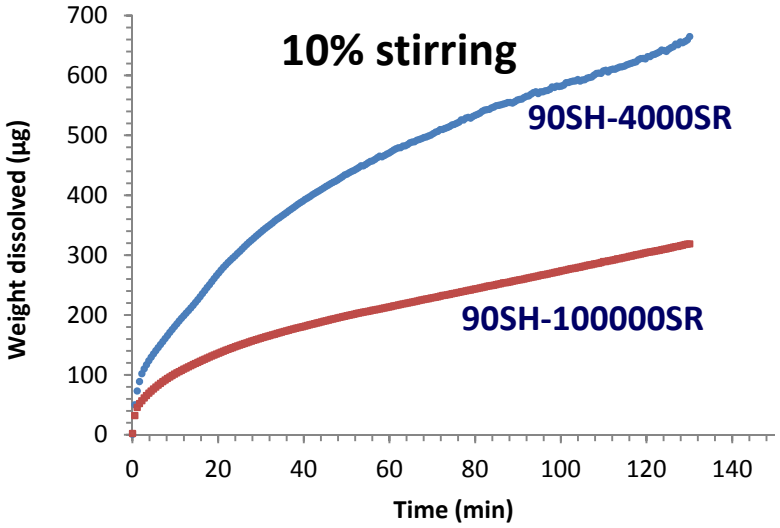

0 minutes
Metolose SR 90SH-100000SR
2 minutes
22 minutes
45 minutes

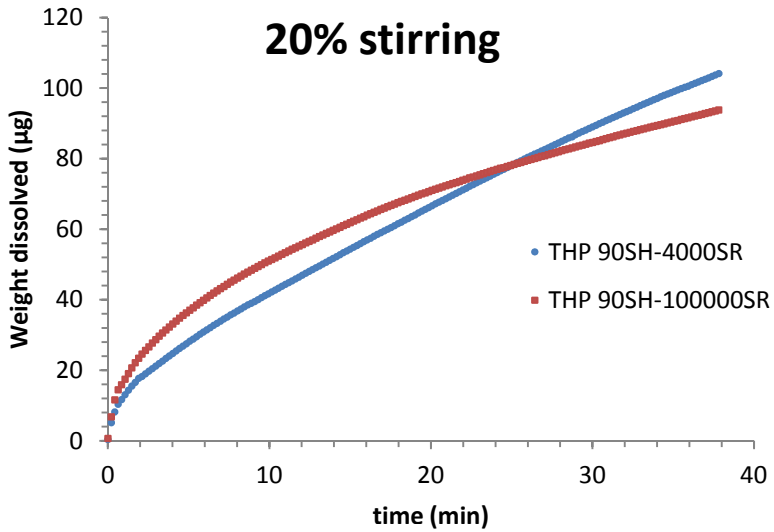

SiriusT3

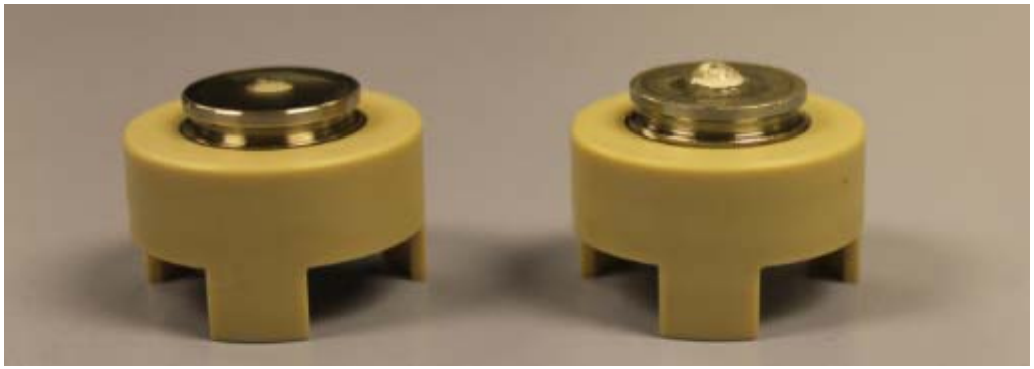

10% stirring
90SH-4000SR
90SH-100000SR
Weight dissolved (µg)
Time (min)
0
100
200
300
400
500
600
700
0
20
40
60
80
100
120
140




SiriusT3


10% stirring
90SH-4000SR
90SH-100000SR
Weight dissolved (µg)
Time (min)
0
100
200
300
400
500
600
700
0
20
40
60
80
100
120
140


20% stirring
THP 90SH-4000SR
THP 90SH-100000SR
Weight dissolved (µg)
time (min)
0
20
40
60
80
100
120
0
10
20
30
40



SDI in controlled release studies

- Easy to set up
- Easy to run at 37°C
- Learn a lot in a short time

- Some ideas why SiriusT3 and SDI disagree
- More research required

Thanks to …

- Rebeca Ruiz
- Darren Matthews
- Alex Chapman