Rapid Nano-gram scale screening method of micro-arrays to evaluate drug-polymer blends using high-throughput printing technology

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Table 1. Number of A and C values for each drug/polymer blend at all the w/w% ratios after 7 days.

Drug	Drug/PVPVA w/w%					AI%-7D
	5%	10%	15%	25%	50%	
Flutamide	AAAA	AAAA	AAAA	AAAA	AAAA	100
Carbamazepine	AAAA	AAAA	AAAA	AAAA	AAAC	95
Flufenamic	AAAA	AAAA	AAAA	AAAA	AAAC	95
Mefenamic	AAAA	AAAA	AAAA	AAAA	AACC	90
Finasteride	AAAA	AAAA	AAAC	AACC	CCCC	60
Caffeine	AAAC	AACC	AACC	CCCC	CCCC	35

As depicted from the table, it is possible to evaluate the extent of amorphicity for each drug/polymer spot and easily calculate the AI% -7D average to determine differences of stable amorphous miscibility. The table was produced considering only spots formed for a volume between 60-70 nl.

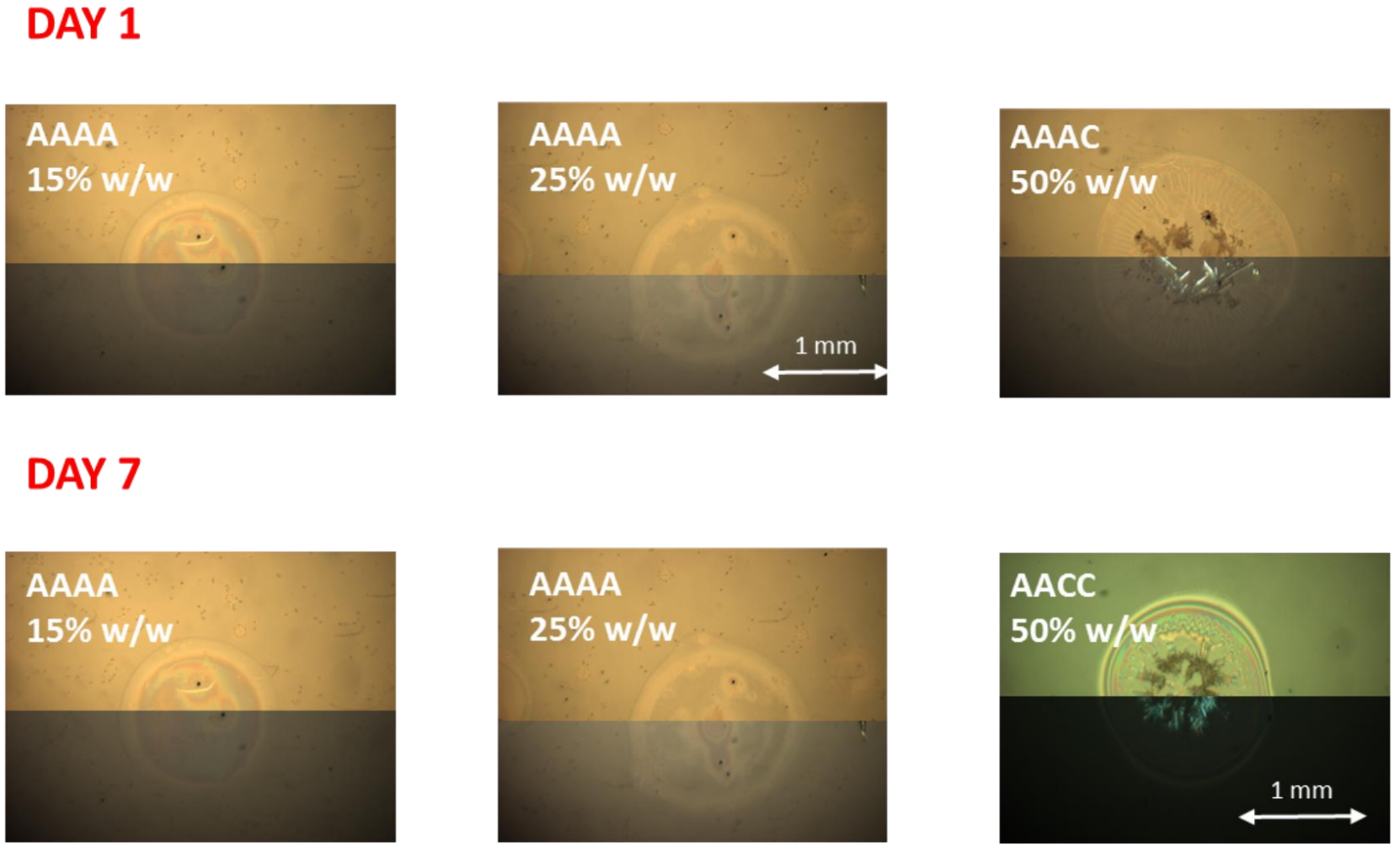


Figure 1SI. PVPVA/MEF blends at 15, 25 and 50% w/w ratios after 1day (top row) and 7 days (bottom row) were selected to show both an example of "A" degree due to polymer/drug ratios and the variation of AI% with time. Printed volume ranged from 62.5 to 70 nl (625-700 ng of final materials present on the slide).

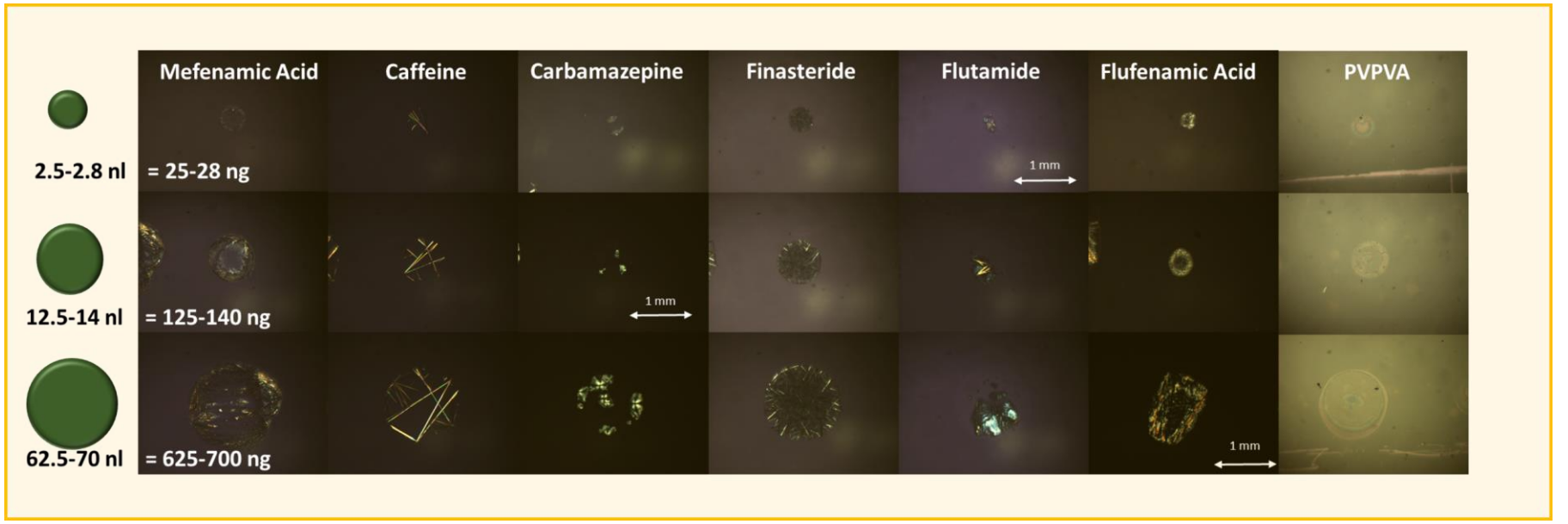


Figure 2SI. Pure drugs and PVPVA microarray depicted by POM with the polarizing filters on. From the top line: spots produced by depositing a volume solution between 2.5-2.8 nl (25-28 ng). Middle line: spots printed using 12.5-14 nl (125-140 ng). Bottom line: spots printed with a volume ranging 62.5-70 nl (625-700 ng). All the drugs but not the amorphous polymer show a characteristic birefringent pattern. In fact, PVPVA is barely visible with the polarizing filters on.

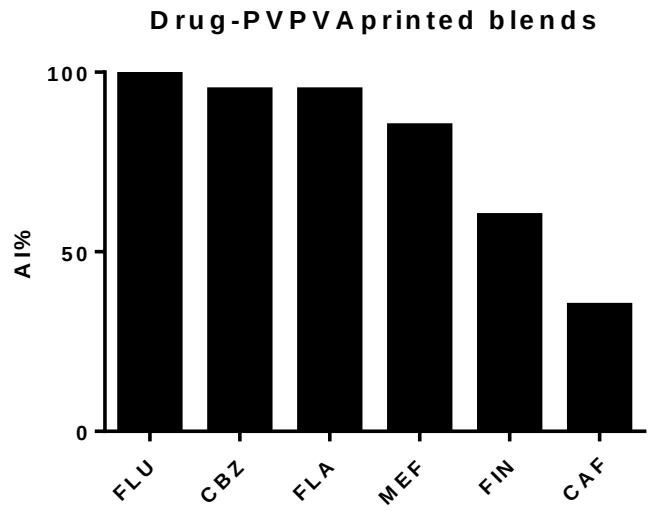
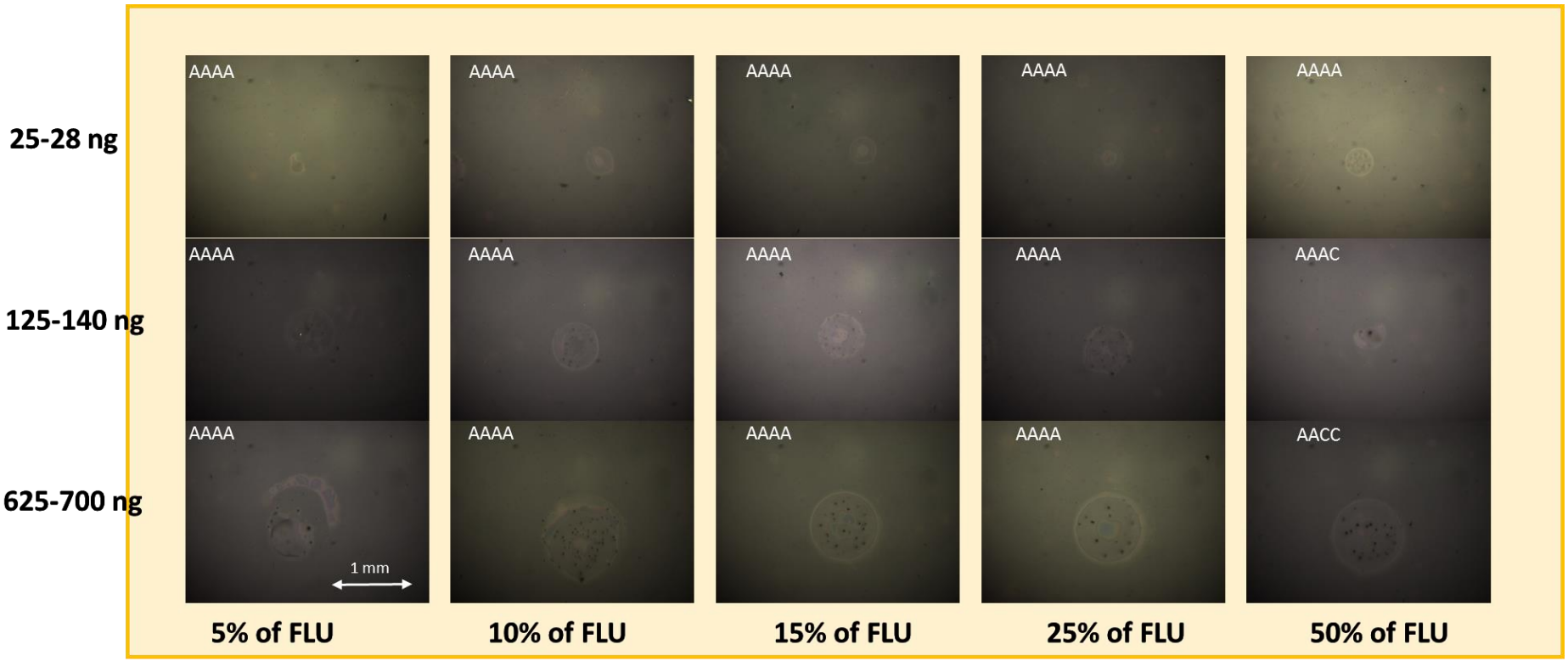
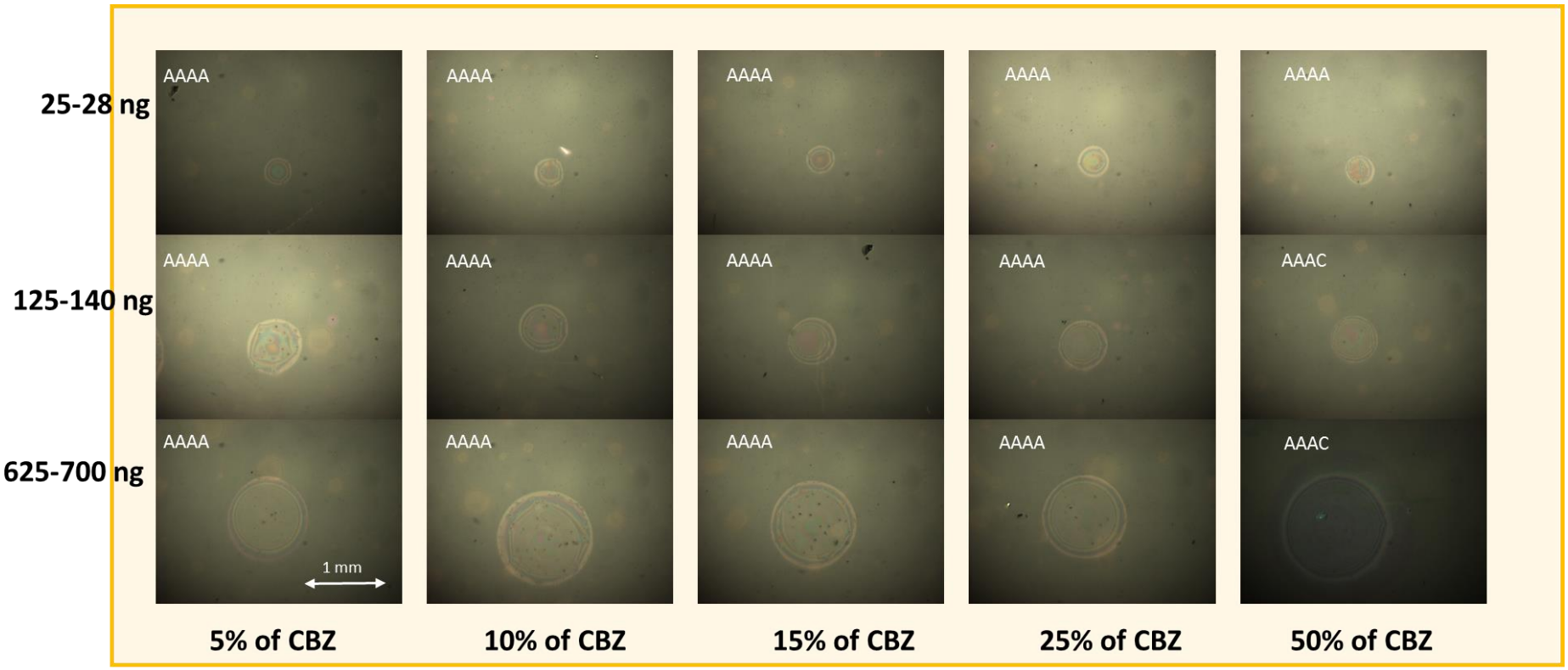


Figure 3SI. All the drugs showed an AI%-7D above 50% apart from CAF that re-crystallized easily at all the ratios with a final AI% of 35%.

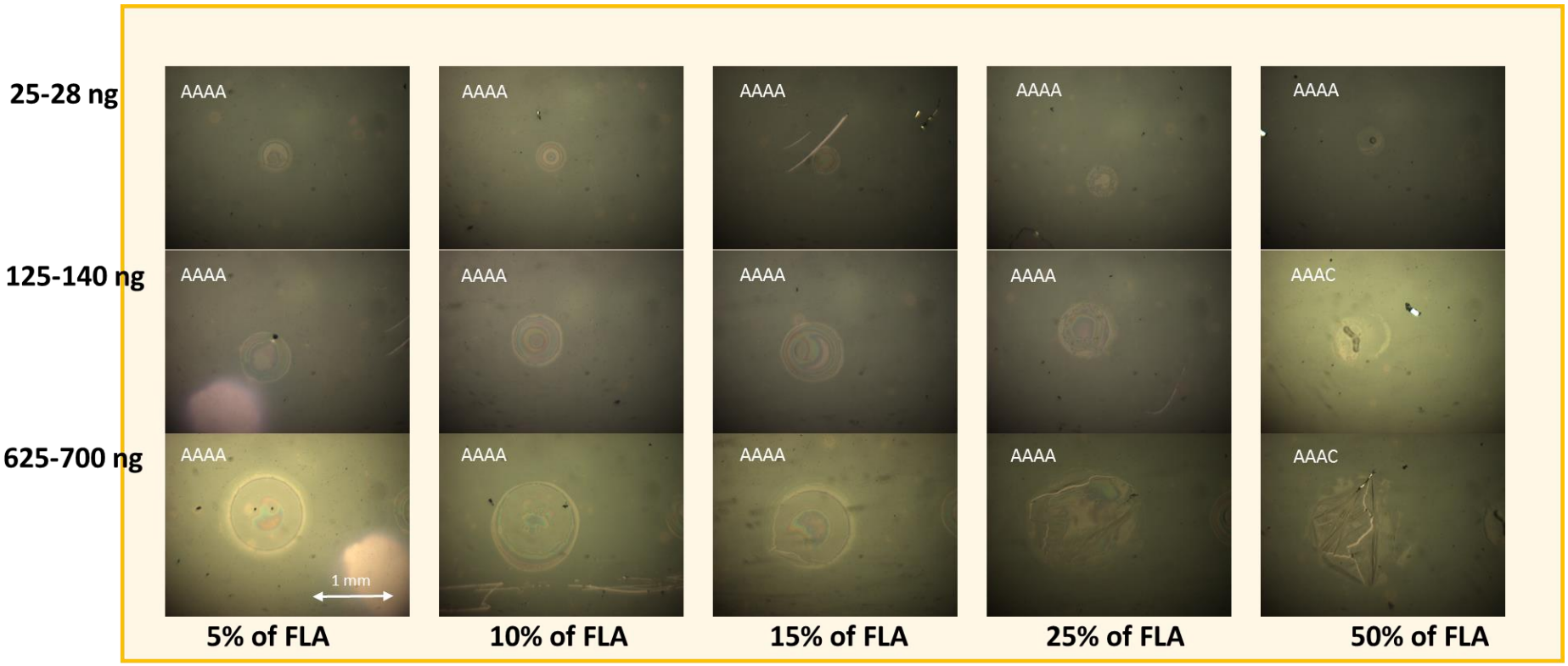
FLU-PVPVA


25-28 ng
125-140 ng
625-700 ng
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAC
AAAA
AAAA
AAAA
AAAA
AACC
1 mm
5% of FLU
10% of FLU
15% of FLU
25% of FLU
50% of FLU

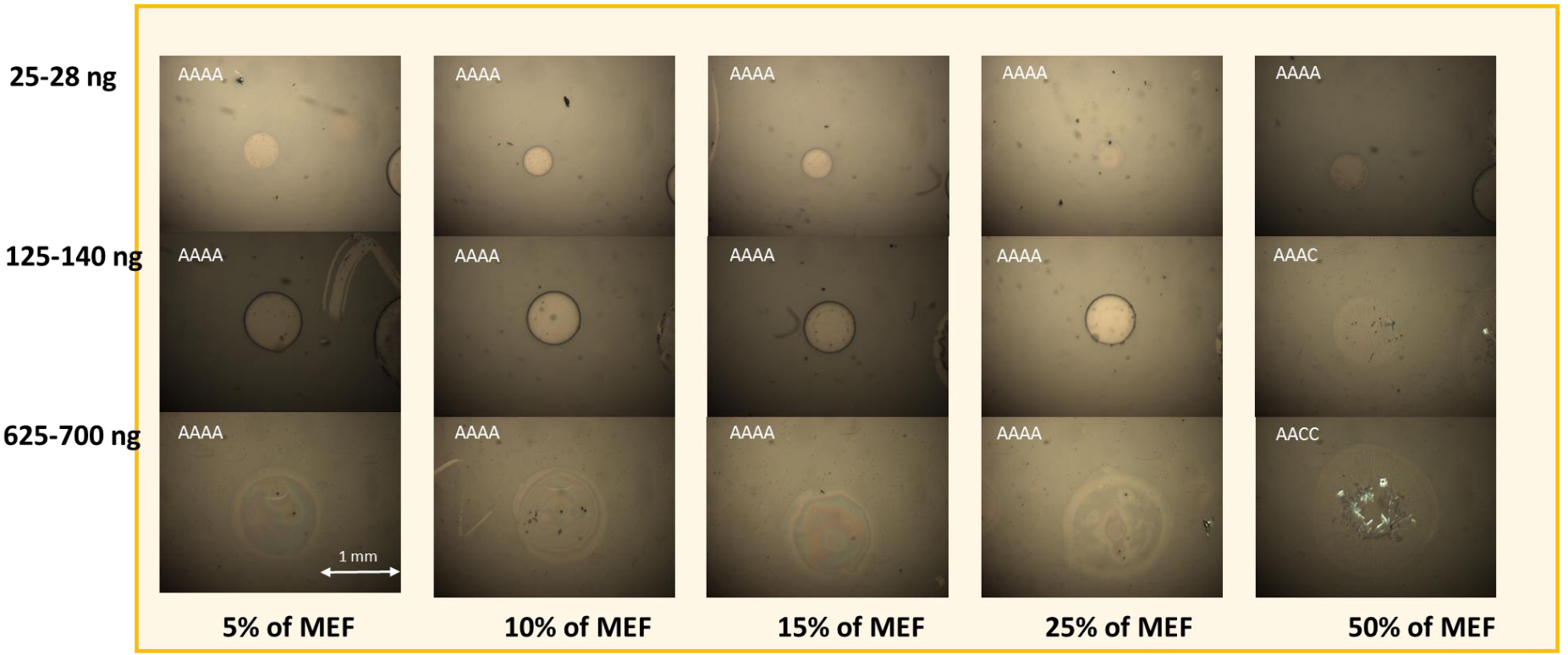
CBZ-PVPVA


25-28 ng
125-140 ng
625-700 ng
AAAA
AAAC
1 mm
5% of CBZ
10% of CBZ
15% of CBZ
25% of CBZ
50% of CBZ

FLA-PVPVA


25-28 ng
125-140 ng
625-700 ng
AAAA
AAAC
1 mm
5% of FLA
10% of FLA
15% of FLA
25% of FLA
50% of FLA

MEF-PVPVA


25-28 ng
125-140 ng
625-700 ng
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAA
AAAC
AAAA
AAAA
AACC
1 mm
5% of MEF
10% of MEF
15% of MEF
25% of MEF
50% of MEF

CAF-PVPVA

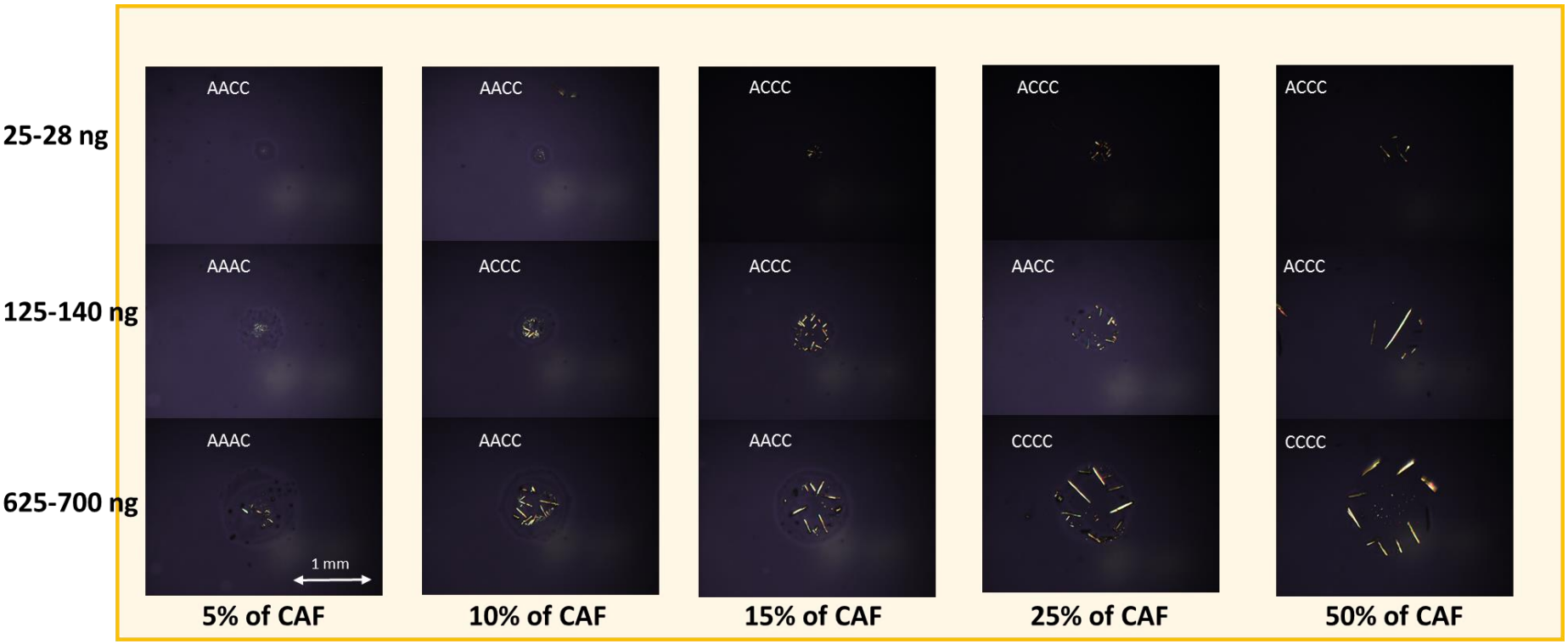


Figure 4SI. Drug-PVPVA spot array POM pictures, varying both printed amount (number of droplets) and drug polymer ratio.

Table 2SI. AI% of FLA against PAA, HPMC, PVPVA and PVP, at each w/w% ratio and as final average. The AI% for each drug\polymer formulation was calculated as an average between day 1 and 7.

	10/90 AI% 1-7days	25/75 AI% 1-7days	40/60 AI% 1-7days	50/50 AI% 1-7days	60/40 AI% 1-7days	75/25 AI% 1-7days	90/10 AI% 1-7days	Average AI%
FLA/PAA	25	25	0	0	0	0	0	7
	25	25	0	0	0	0	0	7
FLA/HPMC	100	100	100	50	25	0	0	54
	100	100	100	100	25	0	0	61
FLA/PVPVA	100	100	100	75	50	0	0	61
	100	100	100	100	100	63	0	80
FLA/PVP	100	100	100	100	75	25	0	71
	100	100	100	100	100	100	0	86

In the table both experimental (black) and literature (red) AI% values are reported. It is possible to exploit AI% to follow the presence of amorphicity stability trends amongst both polymers and between data generated by printing and literature results.