

Effect of Ice fog-controlled ice nucleation on solution weight

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- Ice fog method provides control of ice nucleation temperature, improving uniformity in cake resistance across a vial batch, higher sublimation rates and elegant cake.
- Question: does ice fog add any weight to the product in vials?

<Purpose>

Investigate the weight changes for solution in glass vials with and without ice fog nucleation.

Material

Solution: UF Water

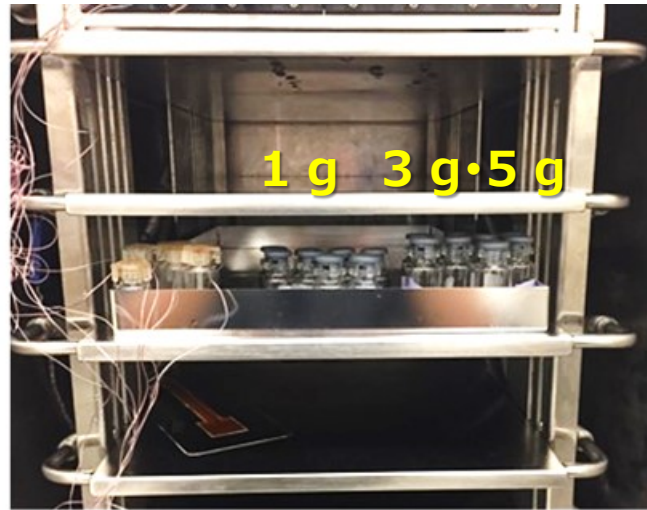
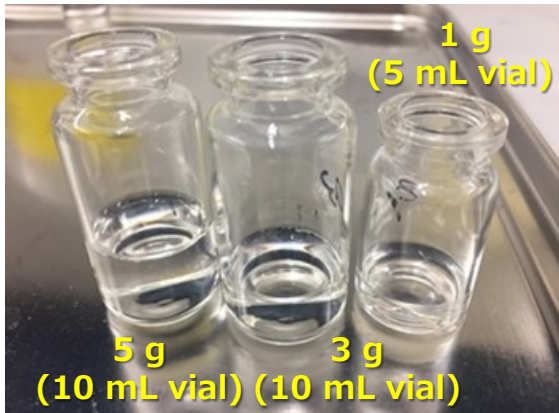
Containers: 5 mL glass vials (Type1 , SPG)

10 mL glass vials (Type 1, Wheaton)

Rubber stoppers (20 mm diameter outer, Wheaton)

Fill volume: 1, 3, or 5 g in a glass vial

Analytical balance: Denver Instrument, minimum Four decimal places



Equipment

Millrock Technology, Inc.

Revo[®]



Freeze booster[®], 1



1) Ice fog type-controlled ice nucleation technique

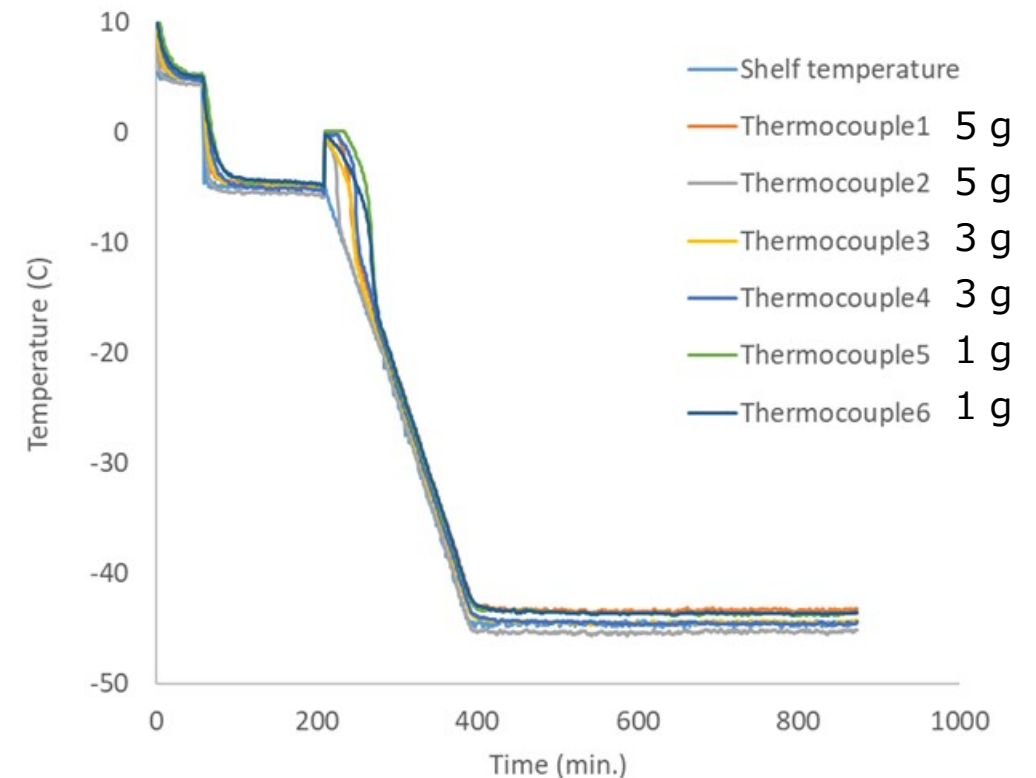
Lyophilization program

Segment	1	2	3	4	5	6
Shelf temperature (°C)	5	5	-5	-5	-45	-45
Time (min.)	0	60	0	120	180	Stop

Freeze booster

Water to be injected	30 mL
Rate of injection	1.5 mL/min

Typical product temperature profile during freezing process with controlled nucleation





Ice weight variation after injection of ice fog

Glass vial (Vial weight)	Number of vial per a sample	Ave. fill weight (g)	Δ Weight on fill weight (mg/1 vial)	Δ Weight on fill weight (%)	Average Δ Weight (mg/1 vial)	Average Δ Weight (%)
5 mL (9.1 g)	2	0.980 g	-8, -4, -1 mg	-0.82%, -0.41%, -0.05%	-6 mg	-0.61%
	2	0.989 g	-5, -5, -6 mg	-0.51%, -0.45%, -0.56%		
	5	0.986 g	-12, -8, -6 mg	-1.24%, -0.79%, -0.65%		
	2	0.972 g	-2, -3, -6 mg	-0.22%, -0.27%, -0.60%		
10 mL (11.8 g)	1	2.999 g	+2, +3, +2 mg	+0.07%, +0.10%, +0.07%	-2 mg	-0.07%
	1	2.969 g	-1, 0, -3 mg	-0.03%, 0.00%, -0.10%		
	2	2.981 g	-5, -6, -7 mg	-0.17%, 0.19%, -0.22%		
	1	2.940 g	-4, -5, -3 mg	-0.12%, 0.15%, -0.10%		
10 mL (11.8 g)	1	5.040 g	+3, +1, 0 mg	+0.06%, +0.02%, +0.03%	-3 mg	-0.05%
	1	4.970 g	-4, -3, -4 mg	-0.08%, -0.06%, -0.08%		
	2	4.950 g	-5, -9, -3 mg	-0.09%, -0.18%, -0.06%		
	1	4.928 g	-6, -4, -4 mg	-0.12%, -0.08%, -0.08%		



Ice weight variation without freeze booster

Glass vial	Number of vial per a sample	Target fill weight (g)	Δ Weight on fill weight (mg/1 vial)	Δ Weight on fill weight (%)	Average Δ Weight (mg/1 vial)	Average Δ Weight (%)
5 mL	2	1 g	-6, -9, -5 mg	-0.55%, -0.85%, -0.45%	-6 mg	-0.62%
10mL	2	3 g	-6, -4, -4 mg	-0.12%, -0.08%, -0.08%	-5 mg	-0.09%
10 mL	5	5 g	-5, -3, -4 mg	-0.17%, -0.10%, -0.13%	-4 mg	-0.13%

- **With ice fog:** No increase of ice weight in the samples after injection of ice fog was observed.
- **Without ice fog:** Slight decrease of ice weight (4-6 mg on average) was observed as same as it with ice fog (2-6 mg on average). It was thought that small amount of water evaporates from vials after filling during loading and cool down in the chamber at the reduced pressure, 500 torr.

No added water in the sample after injection of ice fog was detected.