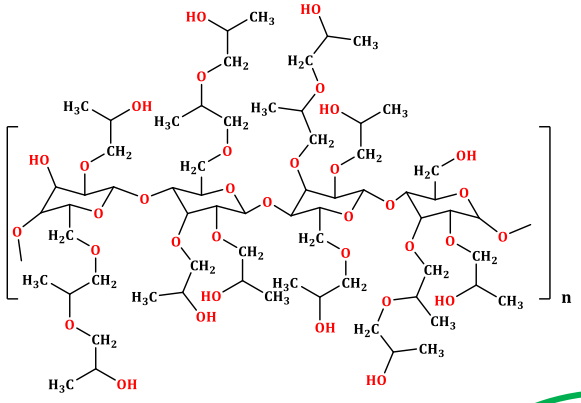
Excipients
NISSO HPC
HYDROXYPROPYL CELLULOSE
USP/NF, EP, JP • Silica/additive-free

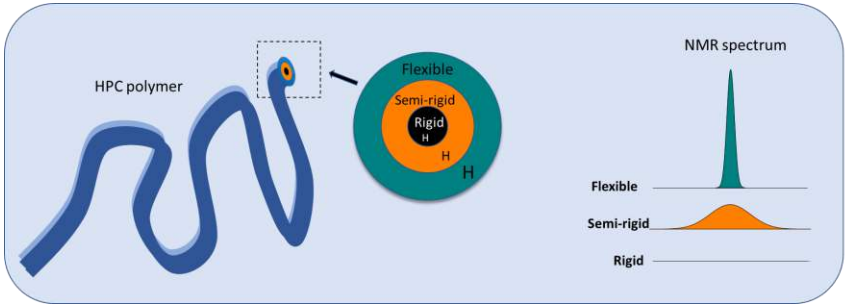
Novel Grade Hydroxypropyl cellulose (HPC-SLC) for Film Coating Application

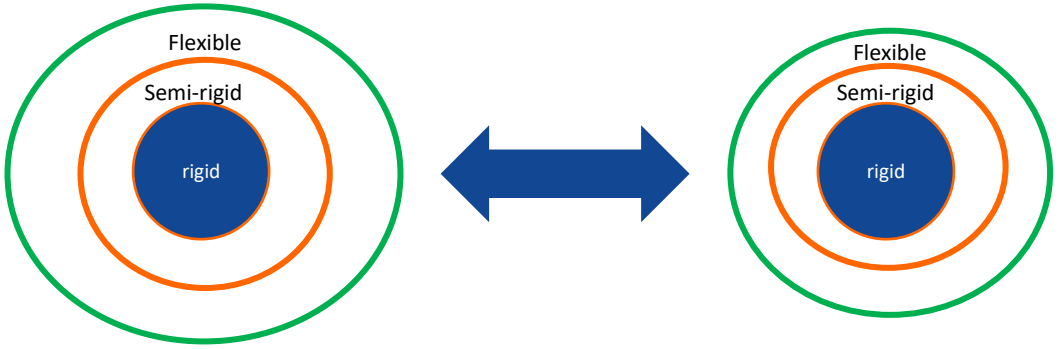
Edmont Stoyanov, PhD

HPC-SLC, a Novel Grade HPC for Film Coating



Hydroxypropylcellulose (HPC)





Regular Grade HPC, HP ~74 %

New Grade HPC, HP ~72 %

- Higher film tensile strength
- Good film plasticity without plasticizer
- Higher gel point for better coating processing – working at higher temperatures

Grade	M_w (kDa)	**Viscosity** (at 2 %)	**MS** (by NMR)	**DS** (by NMR)	**HPO (%)**	T_g (°C, by DSC)	**Gel Point** (°C)
HPC-SL	**100**	**3.0-5.9**	**4.4**	**2.2**	**74.0**	**86**	**44** (at 10 % in H_2O)
HPC-SLC	**100**	**3.0-5.9**	**3.7**	**2.0**	**72.0**	**n.a.**	**46** (at 10 % in H_2O)

Adhesion Properties of HPC-SLC

Case Study:
HPMC E5 vs. NISSO HPC-SL and SLC

Used Polymers:

Name	Parameter
Hydroxypropyl Methylcellulose 2910, HPMC E5	Molecular weight n.a.
	HPO content 10%; MeO content 29%
Hydroxypropyl cellulose, HPC-SL	Molecular Weight ~ 100,000 Da
	HPO content 75%*
Hydroxypropyl cellulose, HPC-SLC	Molecular Weight ~ 100,000 Da
	HPO content 70%*

*Analysis of HPO groups were done according to JP17

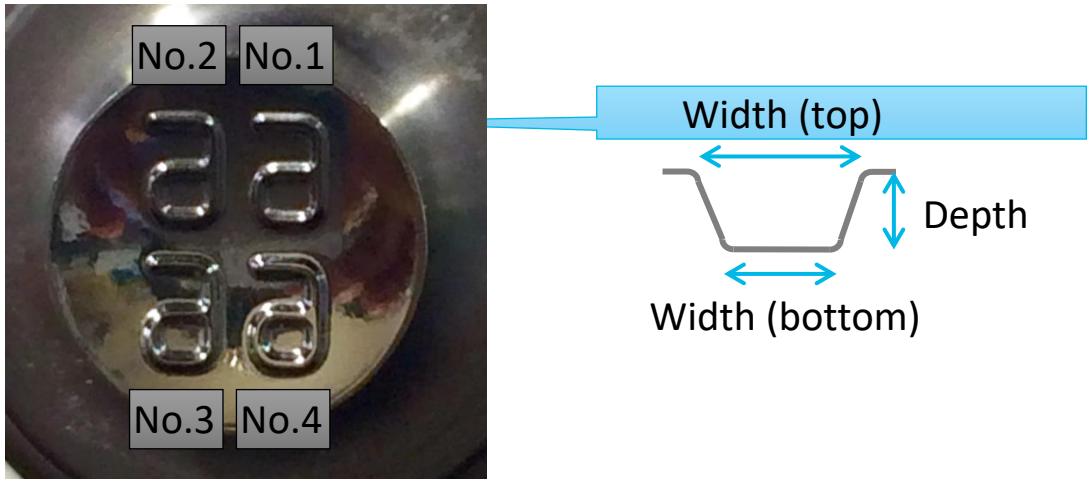
Formulation:

Polymer - 8.00%

Distilled water - 91.99%

Pigment Y-5 - 0.01%

Punch used for Carved Marking



	No. 1	No. 2	No. 3	No. 4
Width (top) (mm)	0.32	0.36	0.36	0.40
Width (bottom) (mm)	0.16	0.20	0.15	0.24
Depth (mm)	0.14	0.14	0.18	0.14

Preparation and Evaluation of the Tablets

Tablet Preparation Methods	Formulation: Lactose/Corn Starch/Mg-St=70/30/0.5 Compression Force: 7 kN Tablet Size: 8 mm - 200 mg
Film Coating Methods	Inlet temperature: 65-80°C Inlet airflow rate: 1.0 m^3/min Spray fluid rate: 2.6 g/min Pan rotation speed: 20 rpm Static pressure: -50 Pa
Breaking Force	Portable checker PC-30 (Okada Seiko CO., Ltd.)
Light Microscope Pictures	SKM-S30A-PC (Saitoh Kougaku Co.)

Evaluation on Coating Conditions: Adhesion

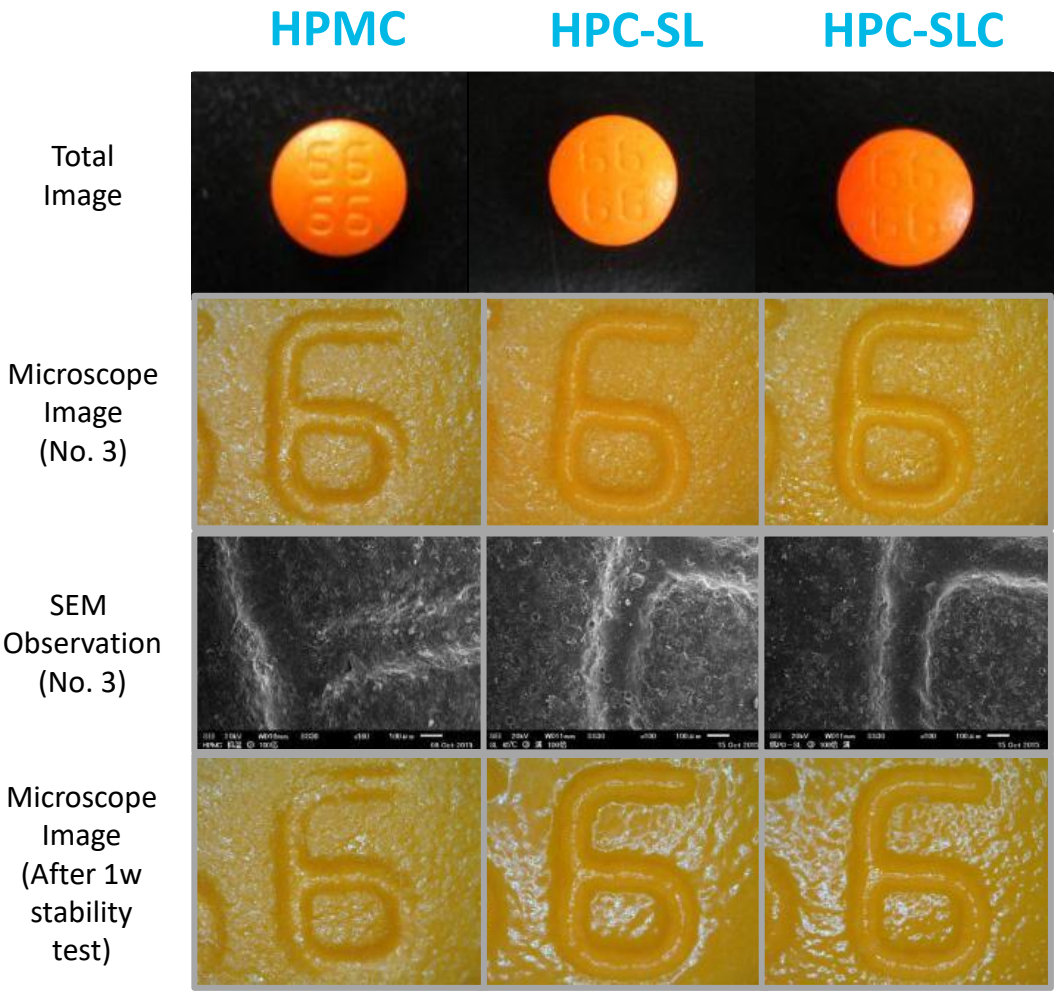
Inlet temp.: 75°C

Inlet temp.: 70°C

Inlet temp.: 65°C

- In the case of film coating by HPC-SLC, less clogging, clear appearance on the marking was observed when inlet temperature was lower.
- The most suitable inlet temperature for HPC-SLC was found to be 65˚C and 70˚C, respectively.

Comparison of Film Coating: Adhesion



All coating were done in inlet temperature of 65°C.

- Clearest edges of the carved marking was observed when HPC-SLC was used as a base material.
- In the case of HPC-SLC, no changing in the debossing was observed after 1 week stability test (40°C, 75%RH).

Case study:
HPC-SL vs. HPC-SLC (40 kg scale)

Materials and Methods

Film Coating Tablet Preparation Conditions

Film Coating Machine: DRC-900DS (POWREX)

Tablet Formulation: Lactose/Corn Starch/MgSt = 84/15/1

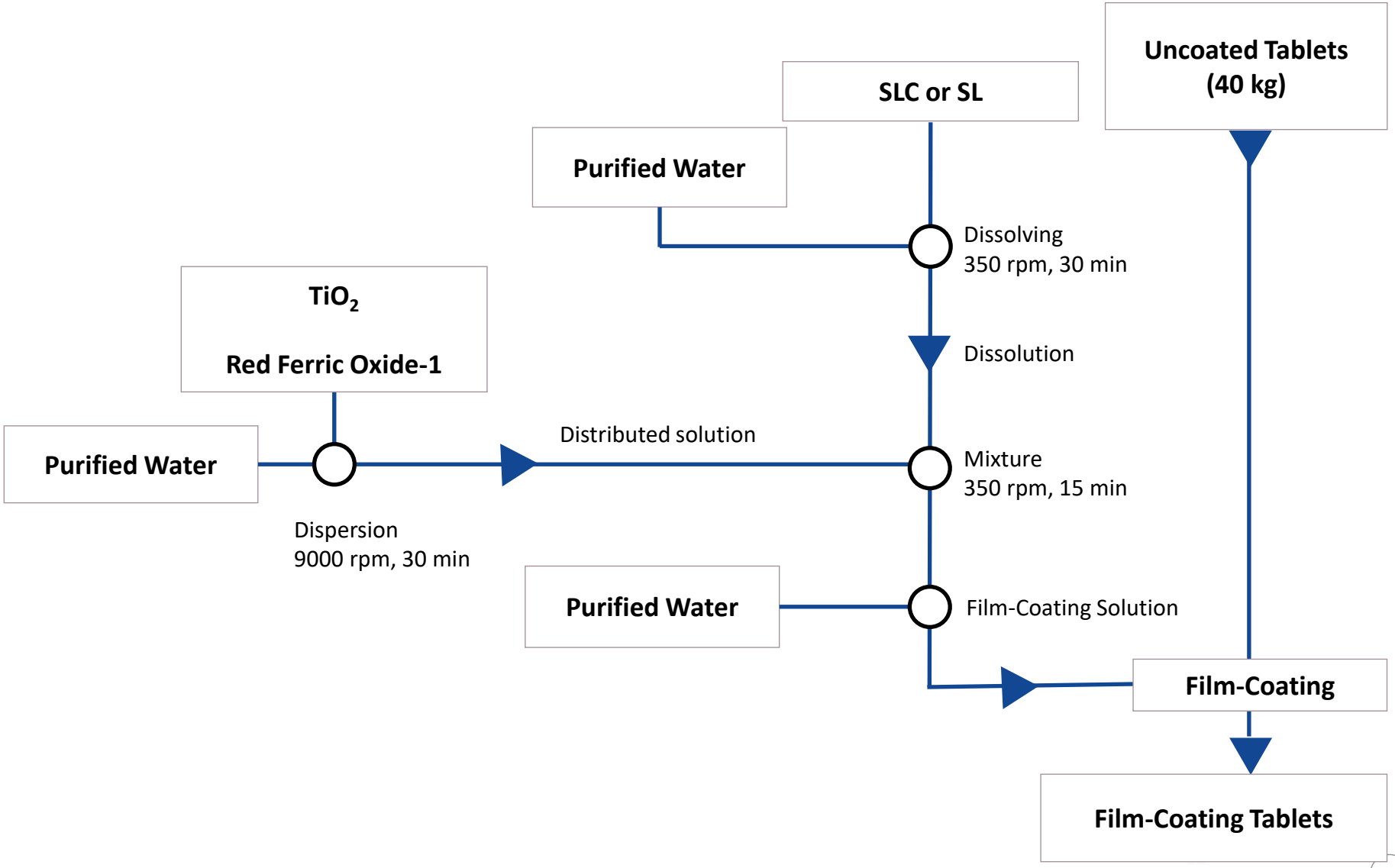
Tablet Size: 8 mmΦ-200 mg (uncoated tablets)

Coating Solution: HPC-SLC, HPC-SL

Formulations

Ingredient	mg/tab	
Coating Solution	HPC-SLC	HPC-SL
HPC-SLC	8.9	—
HPC-SL	—	8.9
TiO_2	1	1
Red Ferric Oxide	0.1	0.1
Purified Water 1	75	75
Purified Water 2	10	10
Purified Water 3	5	5
Total	100	100

Method of Preparation



Coating Condition

Parameter		
Coating Solution	HPC-SLC	HPC-SL
Inlet temperature (°C)	75.0	75.0
Inlet Volume (Nm^3/min)	9.0	9.0
Drum Rotation Speed (rpm)	10.0	8.0
Atomized Air Flow Rate (NL/min)	180	180
Pattern Air Flow Rate (NL/min)	130	130
Liquid Velocity (g/min)	55.0	50.0
Distance (cm)	25.0	25.0

Results of Coating Test

Condition		
Coating Solution	HPC-SLC	HPC-SL
Adhesion for Pan	no	slight
Nozzle Clogging	no	slight
Scratch (n)	1	8
Black point (n)	0	1
Peeling (n)	0	17
Defect rate (%)	0.13	0.29
Coating Time (min)	290	381
Liquid yield (%)	76.9	65.1

- ✓ **HPC-SLC has high liquid yield.**
- ✓ **HPC-SLC can coating in a short time.**

Tablet Properties

Coating Solution		HPC-SLC	HPC-SL
Weight (mg)	Uncoated	200.6	199.3
	Coating tablets	209.3	209.9
Thickness (mm)	Uncoated	4.07	4.05
	Coating tablets	4.19	4.20
Diameter (mm)	Uncoated	8.05	8.05
	Coating tablets	8.16	8.18
Breaking Force (N)	Uncoated	87.5	79.0
	Coating tablets	100.2	95.1
Disintegration time (min)	Uncoated	1:16	1:18
	Coating tablets	3:37	3:37

✓ **Better tablet breaking forces for HPC-SLC.**

Case study:
HPC-SLC vs. HPMC E5 (40 kg scale)

Film Coating Tablet Condition

Film Coating Tablet Preparation Conditions

Film Coating Machine: DRC-900DS (POWREX)

Tablet Formulation: Lactose/Corn Starch/MgSt = 84/15/1

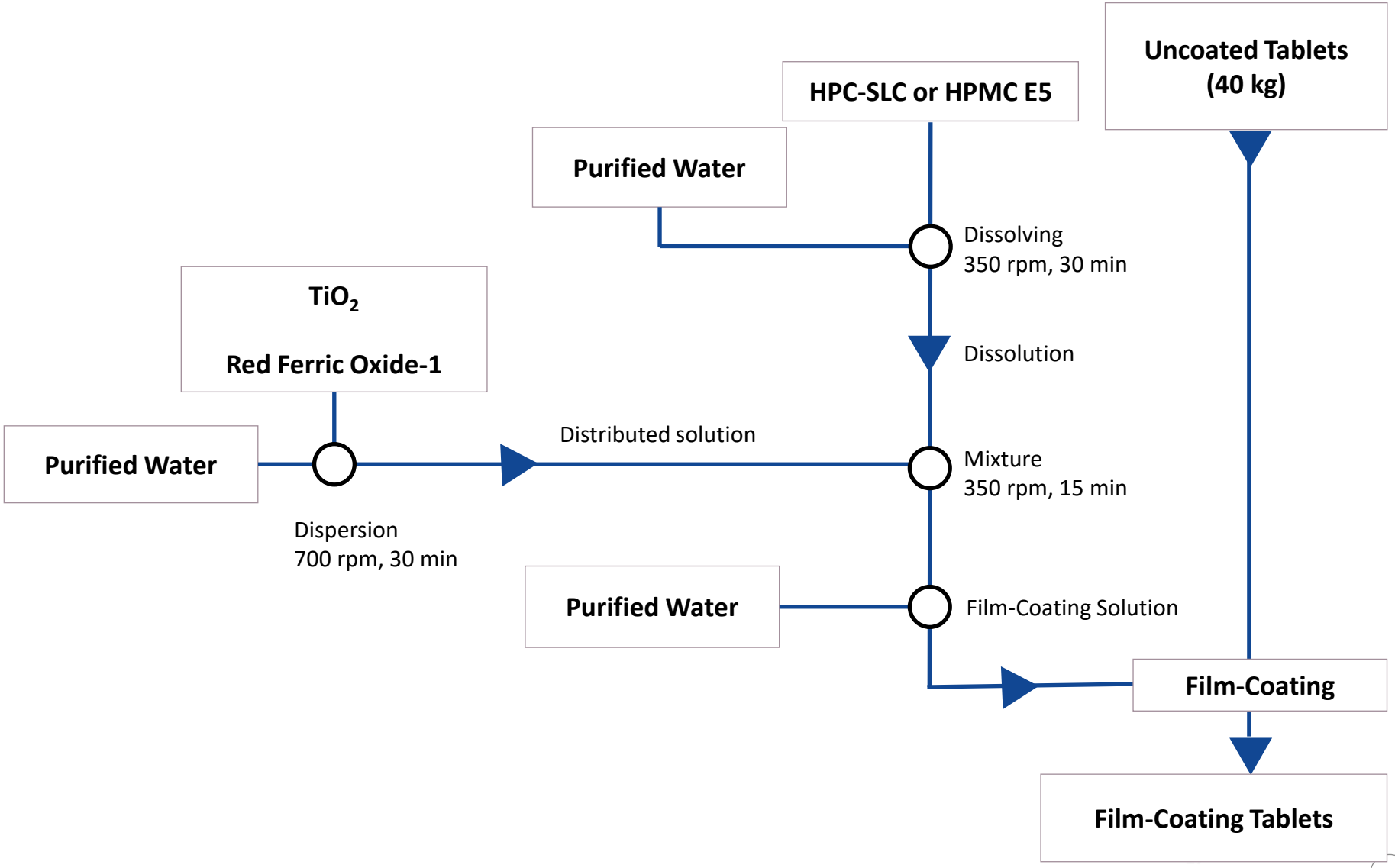
Tablet Size: 8 mmΦ-200 mg (uncoated tablets)

Coating Solution: HPC-SLC, HPMC E5

Formulations

Ingredient	mg/tab	
Coating Solution	HPC-SLC	HPMC E5
HPC-SLC	8.9	—
HPMC E5	—	8.9
TiO_2	1	1
Red Ferric Oxide	0.1	0.1
Purified Water 1	75	75
Purified Water 2	10	10
Purified Water 3	5	5
Total	100	100

Method of Preparation



Coating Condition

Conditions		
Coating Solution	HPC-SLC	HPMC E5
Inlet temperature (℃)	75.0	75.0
Air Volume (Nm^3/min)	9.0	9.0
Drum Rotation Speed (rpm)	10.0	10.0
Atomize Air Flow Rate (NL/min)	180	180
Pattern Air Flow Rate (NL/min)	130	130
Liquid Velocity (g/min)	55.0	55.0
Distance (cm)	25.0	25.0

Results of Coating Test

Condition		
Coating Solution	HPC-SLC	HPMC E5
Adhesion for Pan	no	no
Nozzle Clogging	no	no
Scratch (n)	0	1
Black point (n)	0	2
Peeling (n)	0	1
Defect rate (%)	0.00	0.02
Liquid yield (%)	81.2	87.4

✓ **Slightly better tablet quality with less losses for HPC-SLC.**

Tablet Properties

Coating Solution		HPC-SLC	HPMC E5
Weight (mg)	Uncoated	199.9	200.1
	Coating tablets	208.1	209.5
Thickness (mm)	Uncoated	4.09	4.09
	Coating tablets	4.19	4.21
Diameter (mm)	Uncoated	8.05	8.05
	Coating tablets	8.17	8.17
Breaking Force (N)	Uncoated	93.0	90.7
	Coating tablets	100.3	147.2
Disintegration Time (min)	Uncoated	1:24	1:17
	Coating tablets	3:32	4:04

✓ **Better tablet disintegration with HPC-SLC vs. HPMC, at lower breaking forces.**

Tablet Properties Comparison: SL vs. SLC vs. HPMC

Breaking Force
HPMC > HPC-SLC > HPC-SL

Tablet Desintegration
HPC-SLC ≈ HPC-SL < HPMC

Case study:
HPC-SLC vs. PVA (40 kg scale)

Film Coating Condition

Film Coating Tablet Preparation Conditions

Film Coating Machine: DRC-900DS (POWREX)

Tablet Formulation: Lactose/Corn Starch/MgSt = 84/15/1

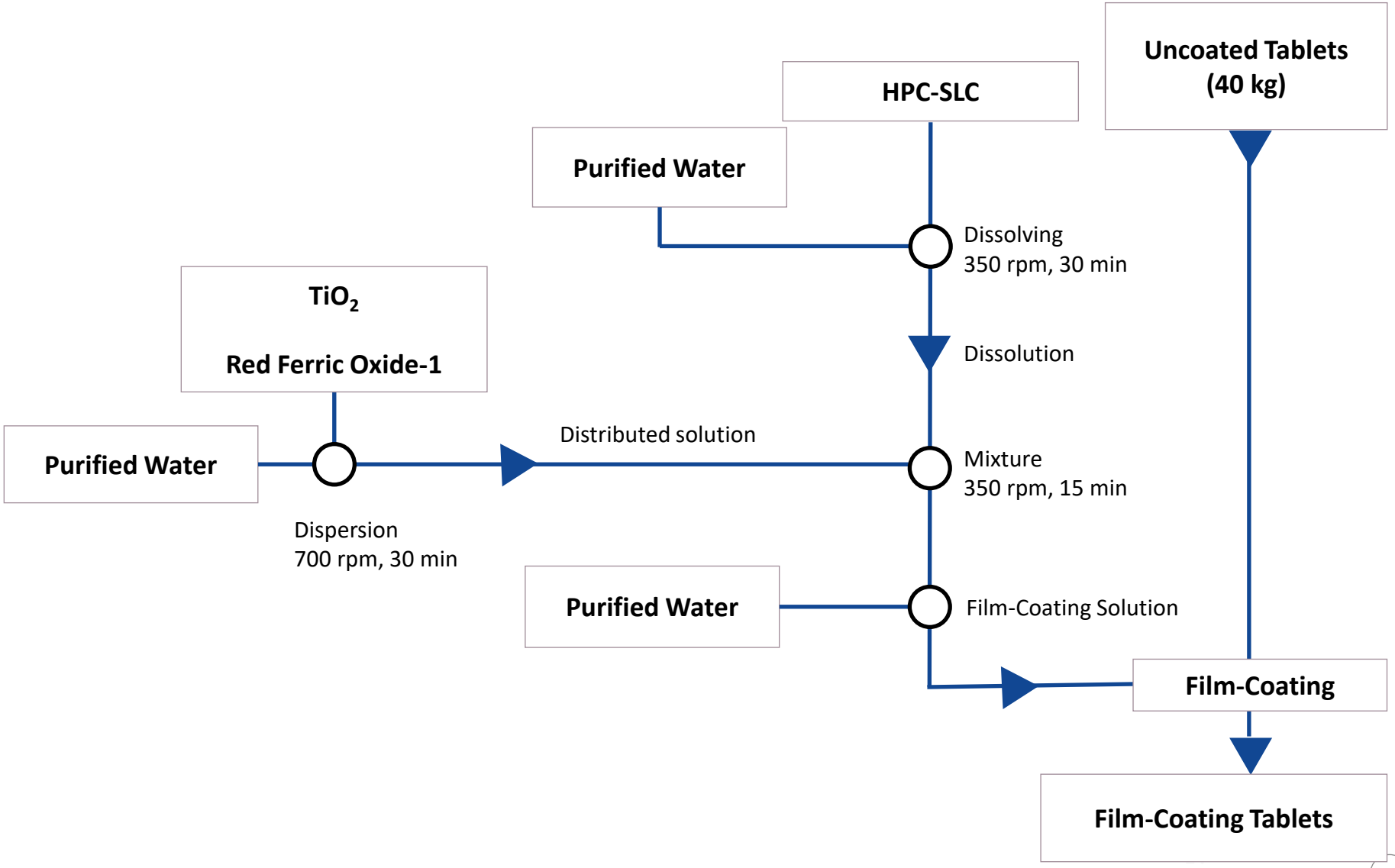
Tablet Size: 8 mmΦ-200 mg (uncoated tablets)

Coating Solution: HPC-SLC, PVA

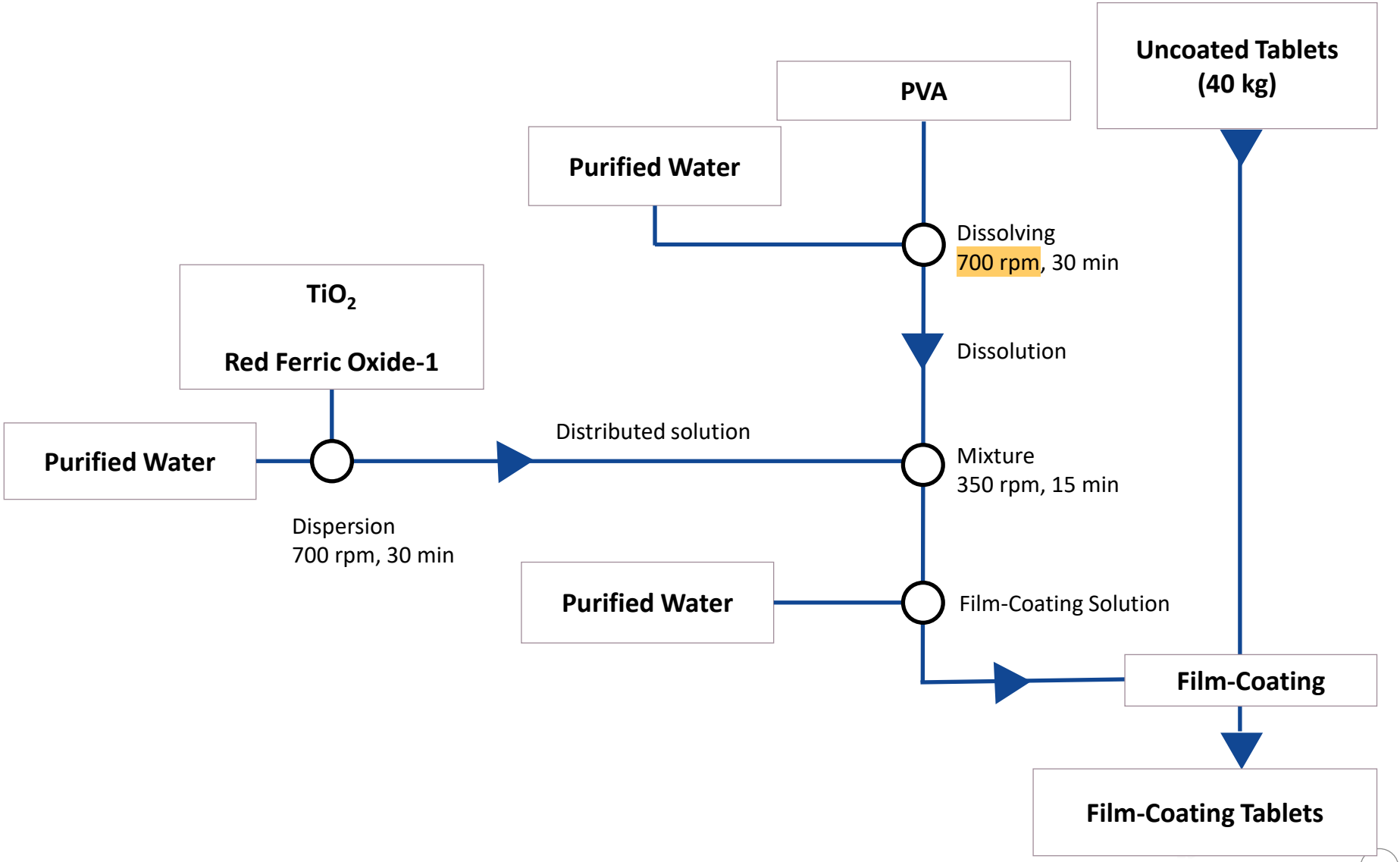
Formulations

Ingredient	mg/tab	
Coating Solution	HPC-SLC	PVA
HPC-SLC	8.9	—
PVA	—	8.9
TiO_2	1	1
Red Ferric Oxide	0.1	0.1
Purified Water 1	75	75
Purified Water 2	10	10
Purified Water 3	5	5
Total	100	100

Method of Preparation with HPC-SLC



Method of Preparation with PVA



Coating Condition

Conditions		
Coating Solution	HPC-SLC	PVA
Inlet temperature (℃)	75.0	75.0 → 80.0
Air Volume (Nm^3/min)	9.0	9.0
Drum Rotation Speed (rpm)	10.0	10.0
Atomize Air Flow Rate (NL/min)	180	180
Pattern Air Flow Rate (NL/min)	130	130
Liquid Velocity (g/min)	55.0	55.0 → 45.0
Distance (cm)	25.0	25.0

Results of Coating Test

Condition		
Coating Solution	HPC-SLC	PVA
Adhesion for Pan	no	no
Nozzle Clogging	no	no
Scratch (n)	0	0
Black point (n)	0	0
Peeling (n)	0	0
Defect rate (%)	0.00	0.01
Liquid yield (%)	81.2	91.3

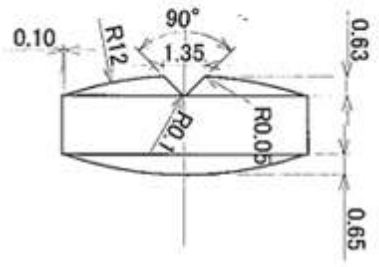
✓ **No significant difference is observed.**

HPC-SLC for Film Coating of ODTs

Materials and Methods Tableting

Formulation:

GLANFILLER D211* / Mg-St ＝99.0 / 1.0 (wt%)



*Multifunctional excipient for ODTs that contains mannitol, MCC, croscarmellose and crospovidone.

Mixing: V-type mixer for 3 min; batch size 6 kg

Compaction:

- Rotary Compaction（VIRGO, Kikusui, Japan）
- Compaction pressure ~11 kN at 25 rpm
- Tablet weight 200 mg; round shape Φ-R12

Tablet properties:

- Tablet breaking force 61 N
- Disintegration time 0.3 min (18 sec)
- Friability (cores) 0.27 %

Materials and Methods Film Coating

Equipment: HC-LABO (Freund-Vector, Japan)

Process parameters:

Spray rate:	3.0 g/min
Spray air pressure:	0.1 MPa
Inlet air temperature:	65℃
Outlet air temperature:	44～46℃
Intake air volume:	0.5 m^3/min
Pan Rotation:	20 rpm
Batch scale:	300 g

Film coating parameters:

Weight gain: 1.0,2.0 and 3.0 wt%
Coating polymer: HPC-SLC
Applied as 8.0 wt% aqueous solution

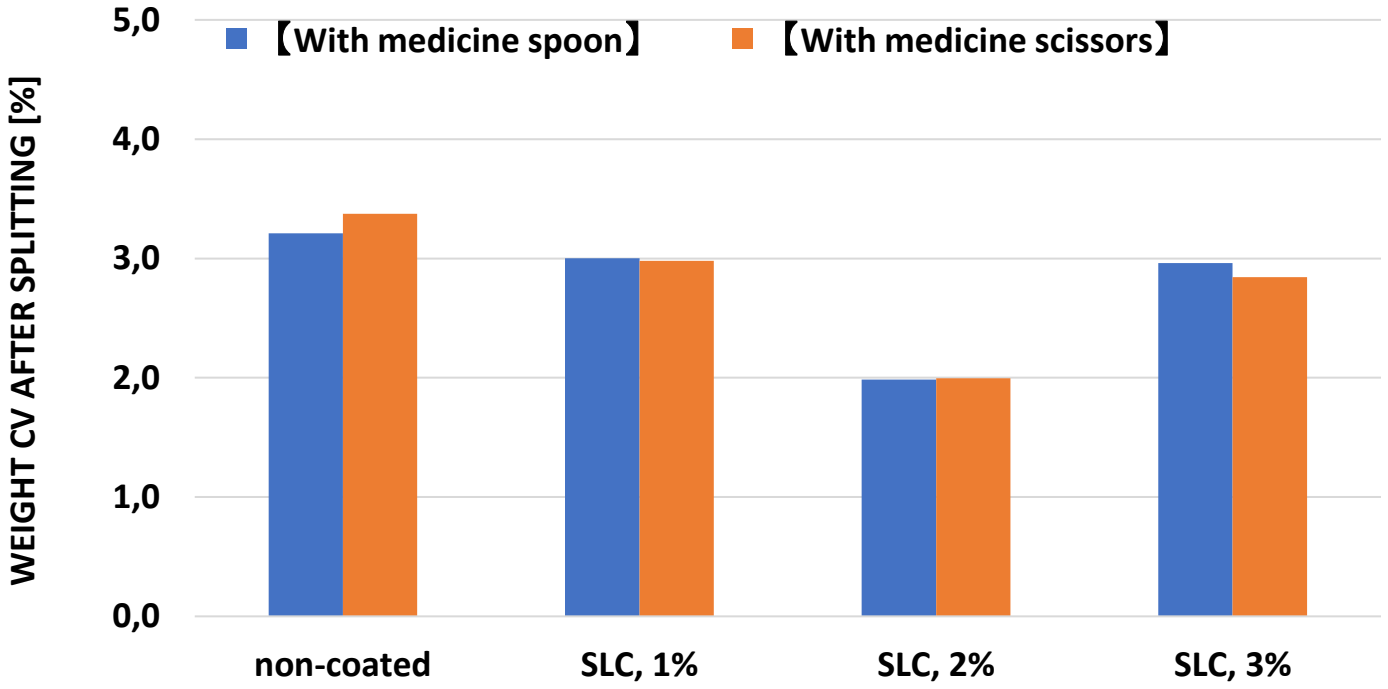
Materials and Methods Tablet Splitting

- Ten tablets were split into two pieces by using the two methods given below: with medicine spoon and scissors.
- The weight of each split piece was measured, and the coefficient of variation (CV) of the weight was calculated in percent.

TABLETS WERE SPLIT WITH MEDICINE SPOON

TABLETS WERE SPLIT WITH MEDICINE SCISSORS

Results Splitting Test



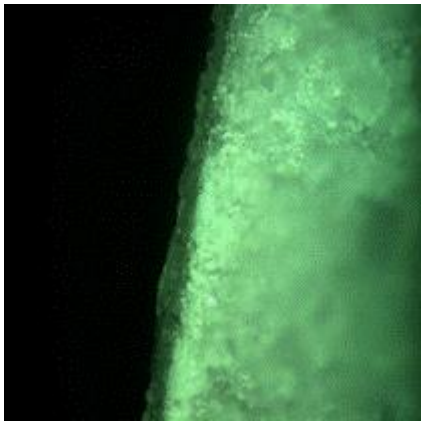
- Easy and excact tablet splitting with both instruments; very low CV
- No effect of the SLC coating on the tablet splitting properties even at 3 wt% weight gain

Results Film Thickness

The thickness of coated film was measured by using light microscope

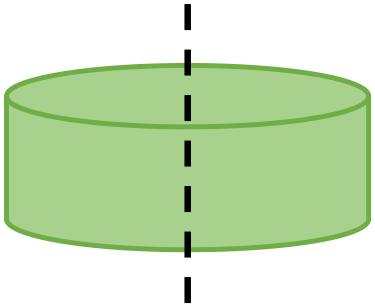
Tablet split in two pieces

Observation

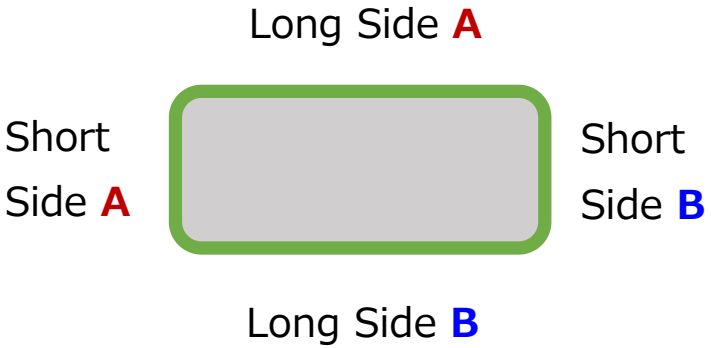


Measure the film thickness

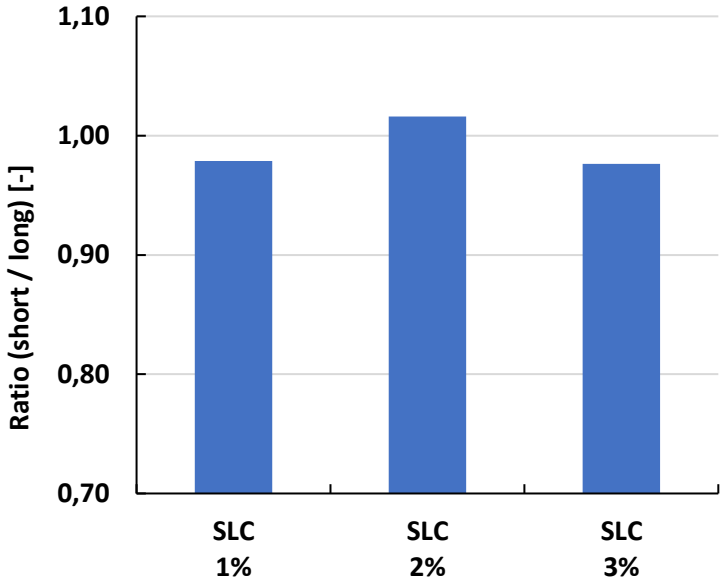
Cutting



[Film thickness : green line]

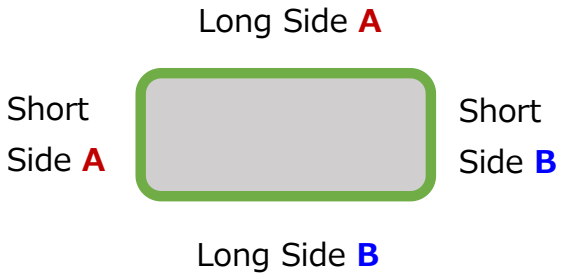


Results Film Thickness



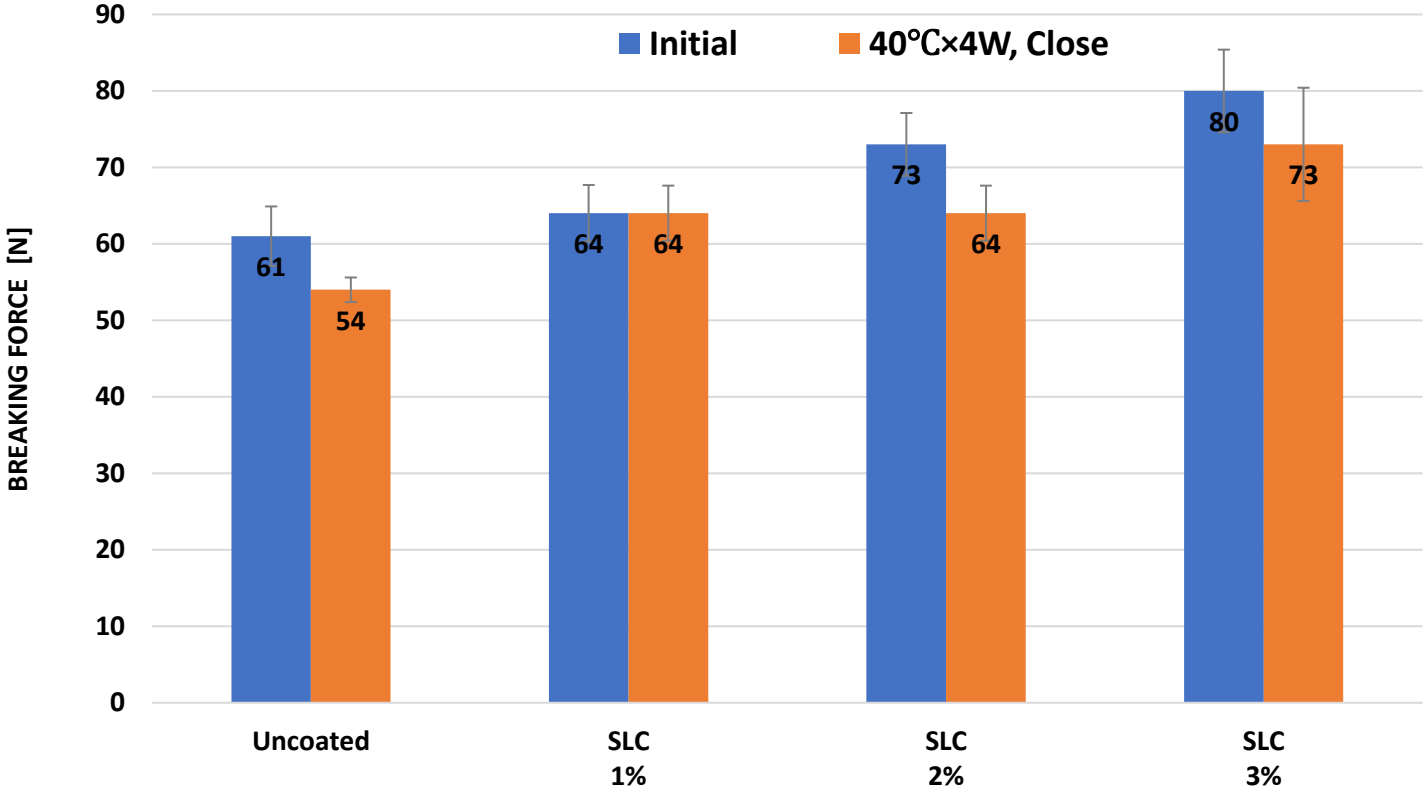
- Homogeneous SLC film thickness over the tablet surface
- No film damages were observed

[Film thickness : green line]



Results Stability Test: Tablet Breaking Force

The coated scored tablets were placed in closed glass containers and stored at 40℃ 75%RH for 4 weeks; Then, tablet breaking force (BF) and disintegration time (DT) were measured.

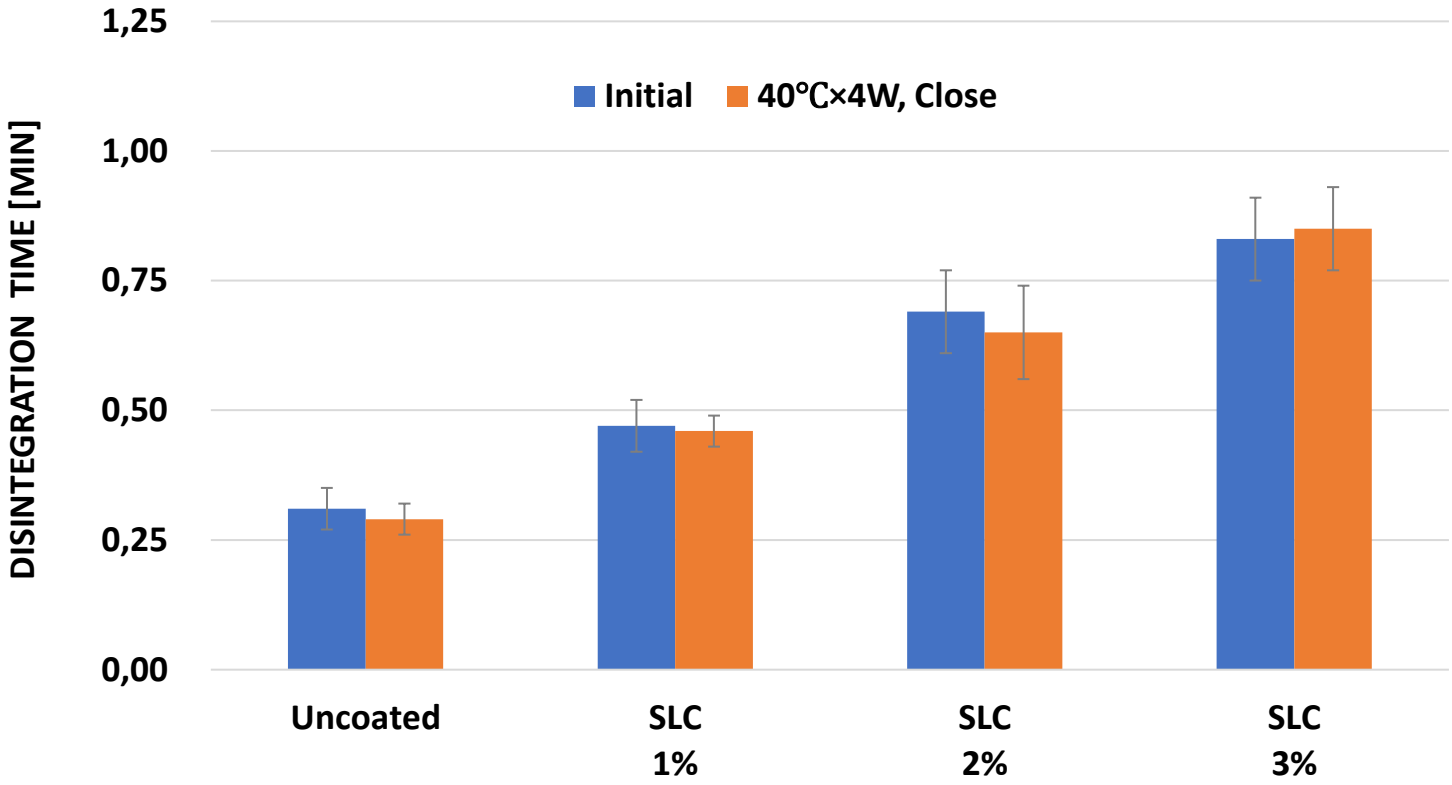


- Improved breaking force at SLC weight gain > 2 %
- Good BF stability after 4 weeks at 40°C/75 % RH

Results Stability Test: Tablet Disintegration Time

The coated scored tablets were placed in closed glass containers and stored at 40℃ 75%RH for 4 weeks;

Then, tablet breaking force and disintegration time were measured.



- Minimal disintegration time increase at SLC weight gain > 2 %; all below 60 sec
- Good DT stability after 4 weeks at 40°C/75 % RH

THANK YOU VERY MUCH FOR YOUR ATTENTION!

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