Study of MCC Powder property toward application in Continuous Direct Compression System

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PURPOSE

- To compare different type of Microcrystalline cellulose (MCC) as an excipient for Continuous Direct Compression system (CDC)
- To clarify the key parameter for CDC system

✓ MCCs with different particle sizes, bulk densities, and shapes were used (Table 1)

★ Include trace impurity information (max or average of 6~10lots) as reference information since nitrosamine-related substances are important for pharmaceutical.

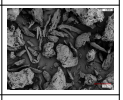
	KG-1000	KG-802	UF711	PH-102
Shapes	Fibrous	Fibrous	Amorphous (Porous)	Amorphous
Particle size D50 (μm)	50	50	50	90
Bulk density (g/mL)	0.12	0.21	0.22	0.30
Repose angle (°)	57	49	42	42
SEM Image (×500)				
★ Nitrite (μg/g) Maximum value	N.D.	N.D.	N.D	0.012
★ Nitrate (μg/g) Average value	0.112	0.106	0.109	0.082

Table 1. Properties of MCCs used In this study.

EXPERIMENT METHODS AND RESULTS

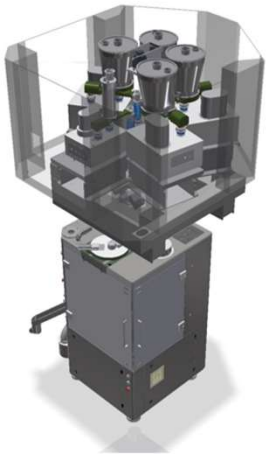


Figure 1. Image of CDC system (CRA-RIS SYSTEM).

No.	1	2	3	4
Formulation	KG-1000	KG-802	UF-711	PH-102
Acetaminophen (APAP)	40	40	40	40
Spray-dried lactose (Lactose)	41	37	37	37
MCC: CEOLUS™	15	20	20	20
Croscarmellose sodium (CCS)	2	1	1	1
Silicon dioxide (SiO_2)	1	1	1	1
Magnesium stearate (Mg-St)	1	1	1	1
Bulk density (g/mL)	0.416	0.433	0.440	0.470
Repose angle (°)	46	43	42	42

Table 2. Formulation and properties of powder mix.

Tableting conditions
Tool: CRA-RIS SYSTEM (Kikusui Seisakusho)
45 punches, Turntable rotation speed: 41.2 rpm
Force feeder rotation speed: 45 rpm
CRATER screen diameter: φ3.0 mm (KG-1000), φ2.0 mm (KG-802, UF-711, PH-102)
Tablet size: 180 mg, φ8 mm - 12R
Run time: 60 min
Sampling time: 0, 2, 4, 6, 8, 10, 15, 30, 45, 60 min
Compression Force: (Main compression) 12 kN, (Pre-compression) 6 kN

Loss-in-Weight (LIW) feeders*

POLARIS2 (20)		POLARIS5 (20)	
Lactose	37-41 wt%	APAP	40 wt%
CCS	1 wt%	SiO_2	1 wt%
POLARIS4 (20)		POLARIS3 (12)	
MCC	15-20 wt%	Mg-St	1 wt%

* Due to the limited number of LIW feeders, lactose and CCS, APAP and SiO_2 are premixed and set in the LIW feeder.

Continuous blending / tableting

No.		1	2	3	4
Items	Target	KG-1000	KG-802	UF-711	PH-102
Tablet Weight RSD	<2.0%	1.0%	1.0%	1.3%	1.0%
API content RSD	<2.0%	0.81%	1.36%	1.29%	1.87%
Tablet Hardness	>50N	100 N	91 N	93 N	81 N
Tablet Hardness RSD	-	7%	8%	7%	10%
Friability	<0.20%	0.15%	0.17%	0.17%	0.22%
Disintegrating Time	<30 min	1.9 min	2.1 min	2.0 min	1.5 min
Dissolution rate After 15 min	>85%	100%	100%	100%	99.7%

Figure 2. Experiment procedure and date summary

➢ KG-1000 showed the best performance among all MCC, especially API contents RSD was good.

DYNAMIC FLOWABILITY : BASIC FLOW ENERGY (BFE)

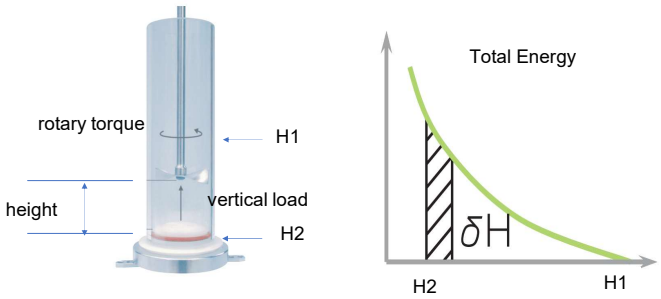


Figure 3. Illustration of measurement principle of powder rheometer FT-4.

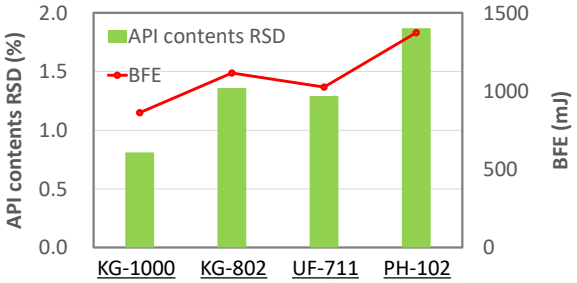


Figure 4. API contents RSD and BFE data by MCC type.

➢ There were good correlation between API contents RSD and BFE.

FEED RATE STABILITY AND LONG RUN TEST

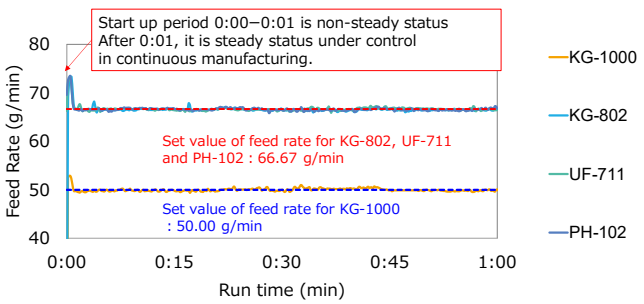


Figure 5. Feed rate of each CEOLUS™ grades during the run time.

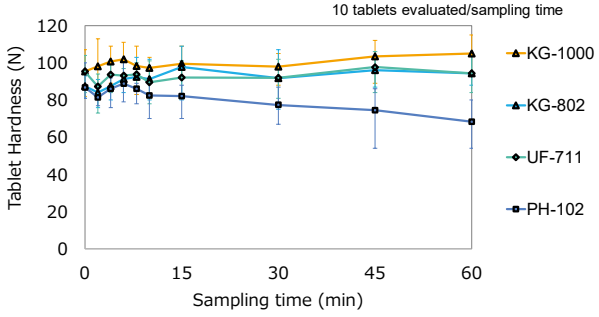


Figure 6. Tablet hardness at each sampling time.

ACKNOWLEDEGMENT
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