

# Comparative Study of Microcrystalline Cellulose for Wet Continuous Manufacturing

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## INTRODUCTION

- In the wet continuous manufacturing method, the raw material supply, hydration, granulation, and drying processes are all performed in the system. Therefore, the point is that there is no stagnation such as clogging of raw materials during the process.
- In addition, physical properties of granules obtained by granulation, particularly the size of granules, must be properly controlled because they affect tablet properties such as API dissolution and weight RSD.
- In this study, we investigated the process compatibility of prescription design focusing on microcrystalline cellulose (MCC) in a wet continuous manufacturing system.
- We compared different types of MCC grades "Ceolus™" to investigate what powder properties contribute to process compatibility and which grade is suitable for the wet continuous manufacturing system.

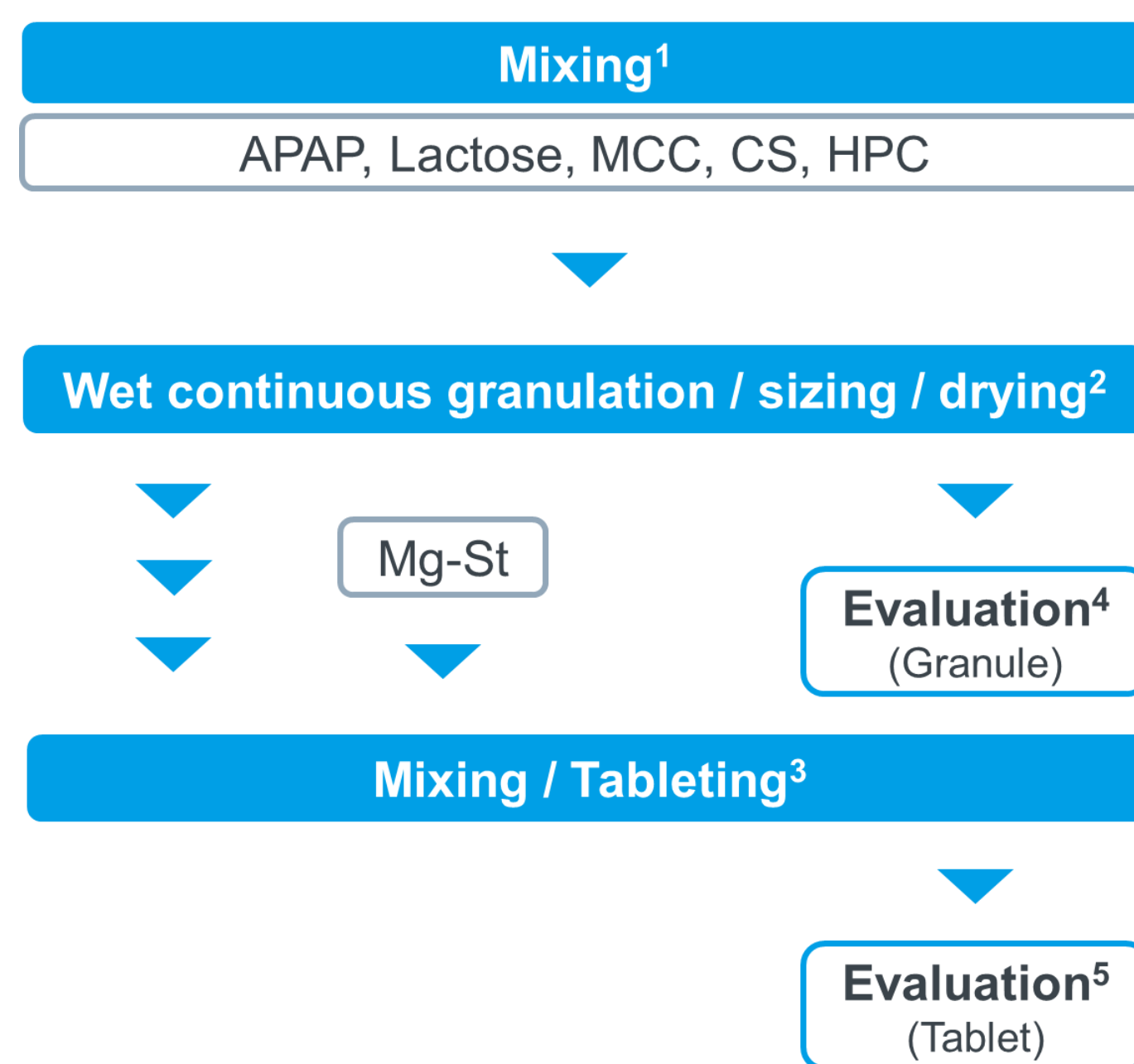
## EXPERIMENTS

Table 1. Powder properties of MCCs used in this study

| Ceolus™ Grades               | PH-101 | UF-702 | UF-711 | KG-802 | KG-1000 |
|------------------------------|--------|--------|--------|--------|---------|
| Particle size D50 (μm)       | 50     | 90     | 50     | 50     | 50      |
| Bulk density (g/mL)          | 0.2    | 0.29   | 0.22   | 0.21   | 0.12    |
| Repose angle (°)             | 45     | 34     | 42     | 49     | 57      |
| Nitrite (μg/g) Maximum value | 0.011  | N.D.   | N.D.   | N.D.   | N.D.    |
| SEM Image (x500)             |        |        |        |        |         |

Table 2. Tested formulation in this study

| Ingredients  | Loading (%) |
|--|-------------|
| Acetaminophen (APAP)                                 | 1           |
| Spray-dried lactose (Lactose)                        | 62          |
| MCC : CEOLUS™ (KG-1000,KG-802,UF-711, UF-702,PH-101) | 10          |
| Cornstarch (CS)                                      | 27          |
| Hydroxypropyl cellulose (HPC)                        | 3.5         |
| Magnesium stearate (Mg-St)                           | 0.5         |



- Tumbler mixer TMS-36S (Seiwa giken)  
Charge amount: 10 kg, Rotation: 100rpm, Time: 5min.
- Wet Continuous Manufacturing Process System: Granuformer® Gf-2050 (FREUND CORPORATION)  
Processing speed: 15 kg/h  
Kneading paddle: 40 pieces, Paddle spin-speed: 100 rpm  
Water content: 30-40%  
Sizing: 1000rpm, Screen size: φ3 mm  
Drying temp.: 120 °C Flow rate: 8.5 m³/min
- Mixing condition: PE bag, Mixing time: 30 sec.  
Tableting machine: LIBRA2(Kikusui Seisakusho)  
Open feeder, 12/36 punch  
Turntable rotation speed: 30 rpm  
Tablet size: 200 mg, φ8 mm - 12R  
Main Compression Force: 6-17 kN
- Granule size
- API content RSD, tablet hardness, friability, disintegration and dissolution

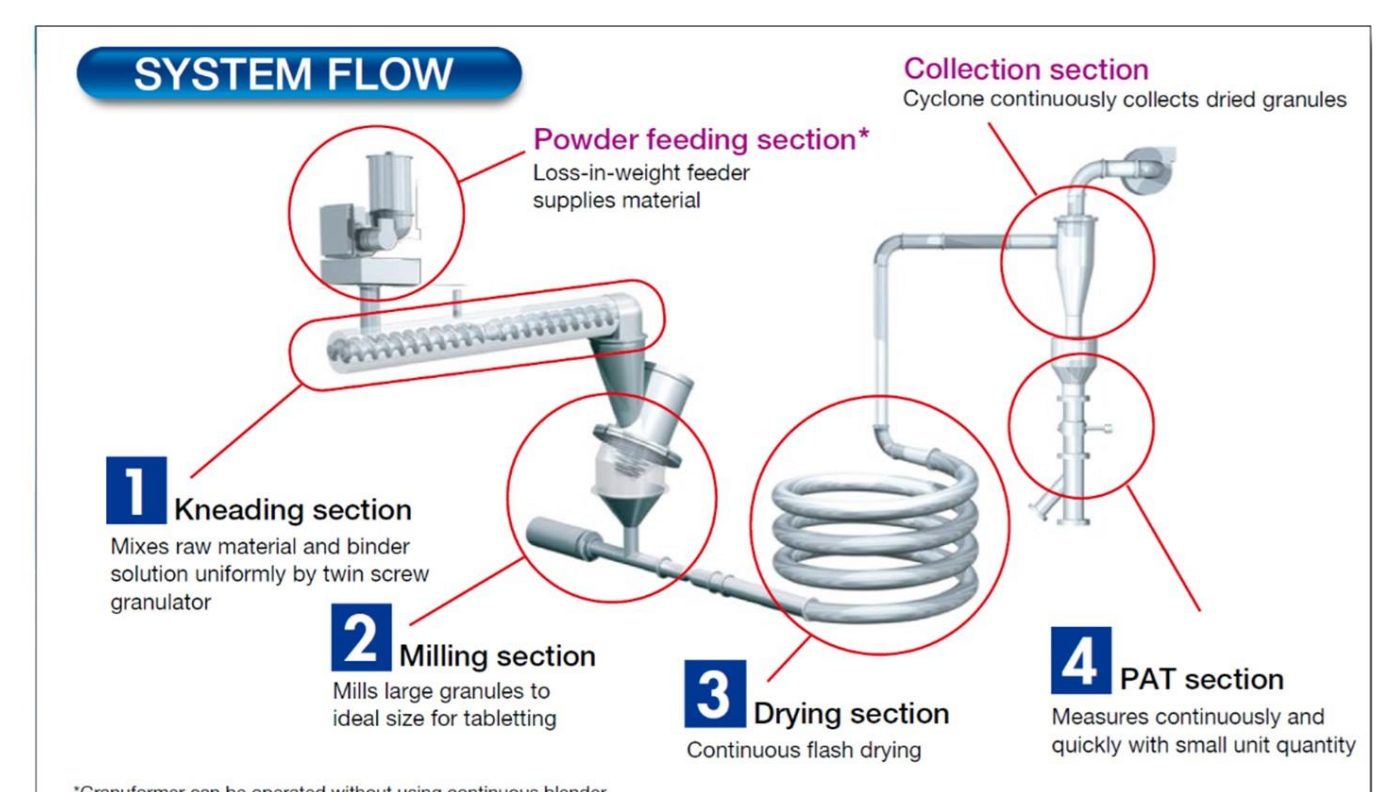


Figure 2. System overview of Granuformer®-2050

Figure 1. Procedure of wet continuous manufacturing

## RESULTS

Table 3. Clogging tendency at the sizing screen

| Ceolus™ Grades | The amount of the added water (%) |      |     |     | Water absorption of MCCs (%) |
|----------------|-----------------------------------|------|-----|-----|------------------------------|
|                | 30                                | 35   | 37  | 40  |                              |
| PH-101         | ****                              | **** | N/A | *   | 200                          |
| KG-802         | ****                              | **** | *   | N/A | 230                          |
| UF-702         | ****                              | **** | **  | N/A | 240                          |
| UF-711         | ****                              | **** | N/A | **  | 240                          |
| KG-1000        | ****                              | **** | N/A | *** | 290                          |

Clogging time from the start  
\*\*\*\* : 16min- (No Clogging), \*\*\* : 11-16min, \*\* : 6-11min, \* : 0-6min

- At the range of water amount 37-40%, while KG-1000 showed clogging at the late stage of granulation, other MCCs showed clogging at the early stage of granulation process.

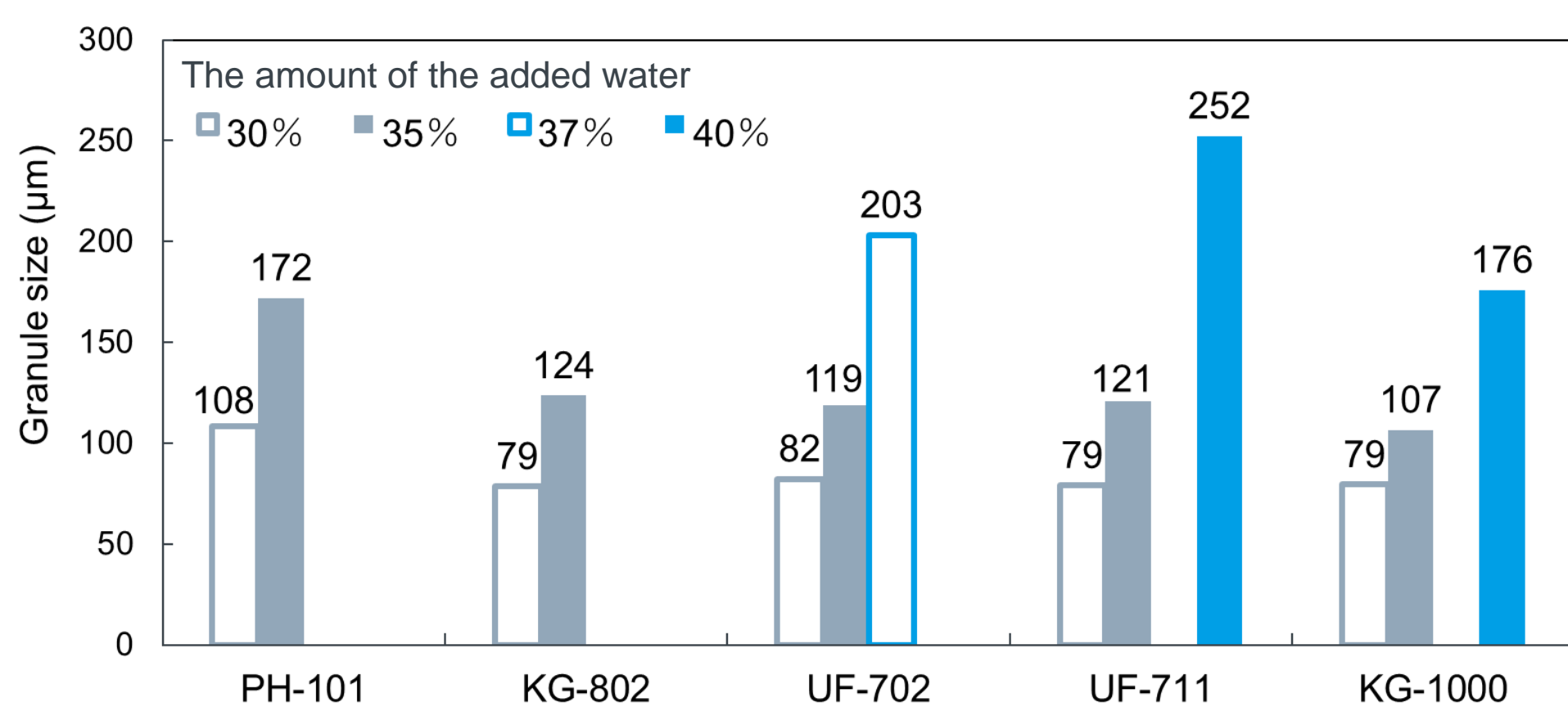


Figure 3. Size of granules of each grade with respect to water added.

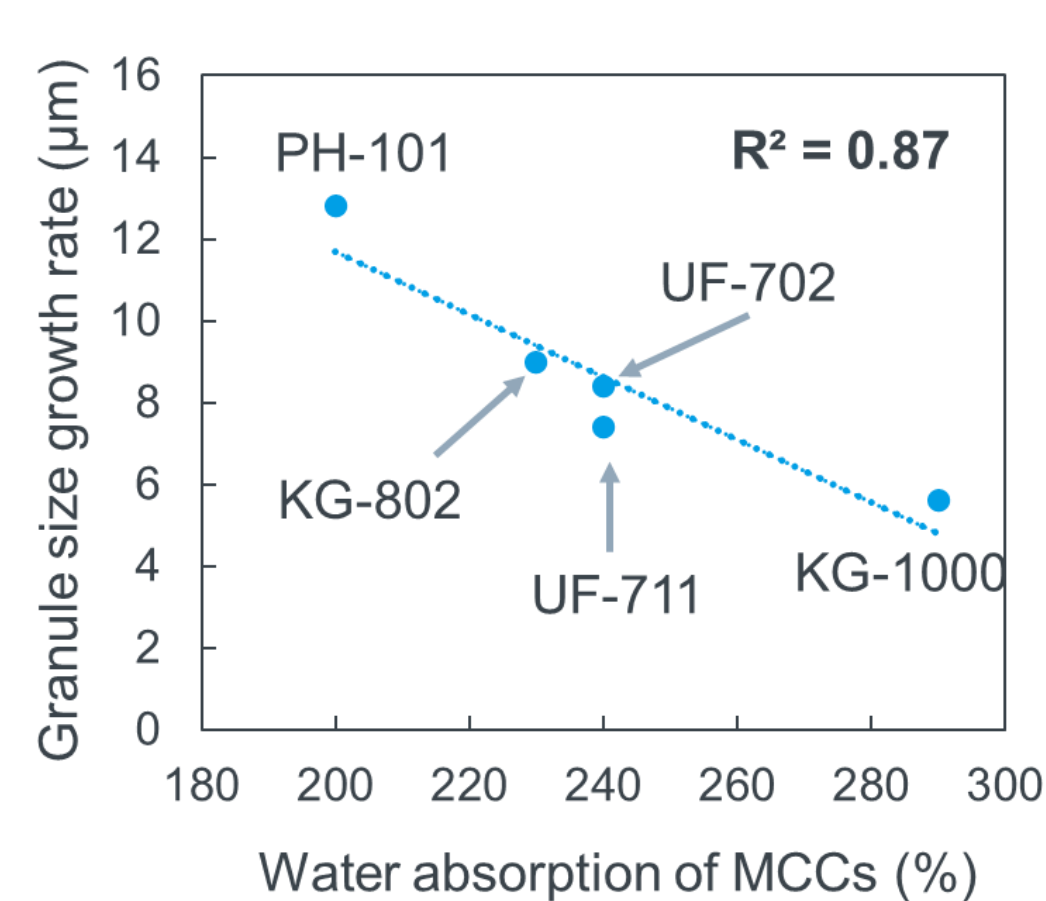


Figure 4. Granule size growth by 1% of water added (Range of water added : 30-35%)

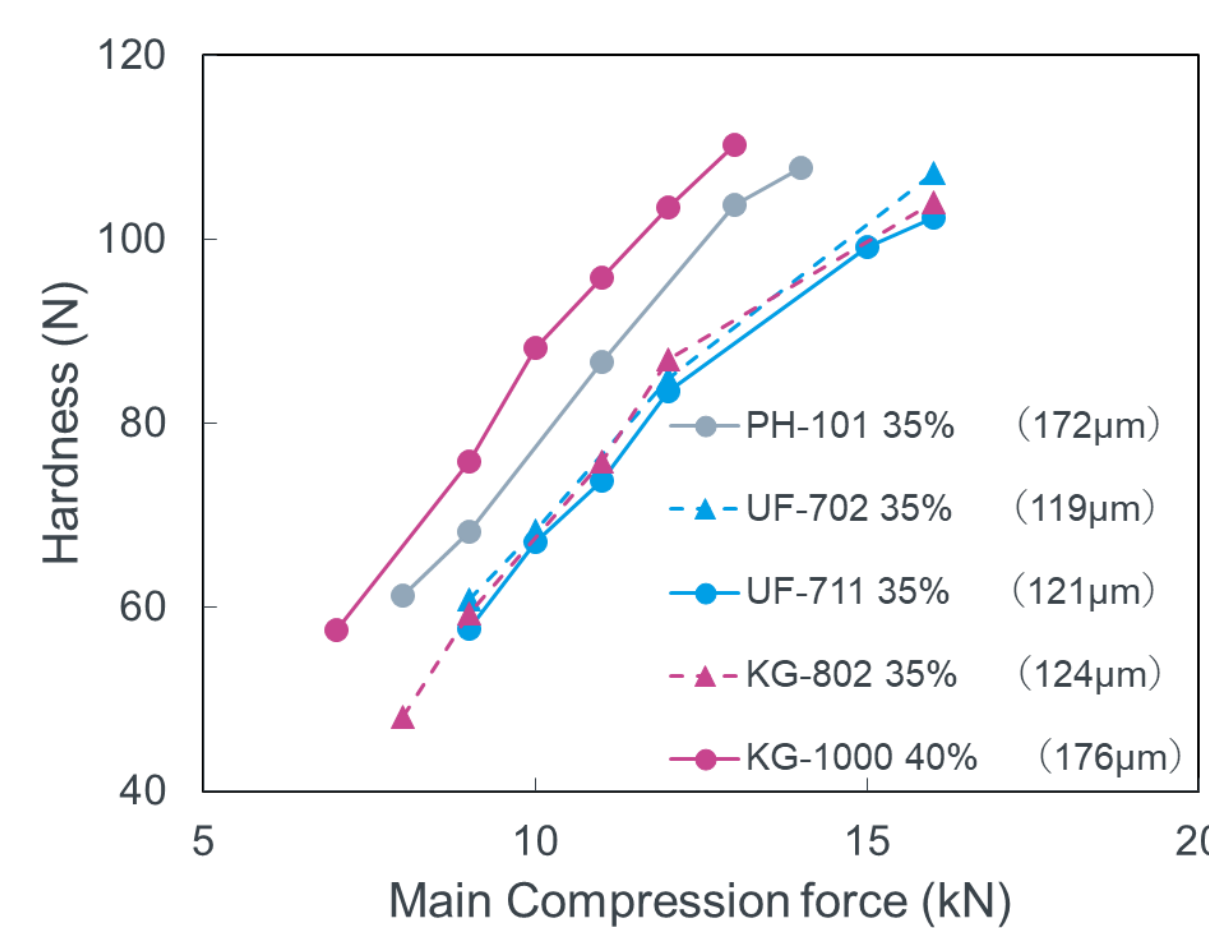


Figure 5. Tablet hardness

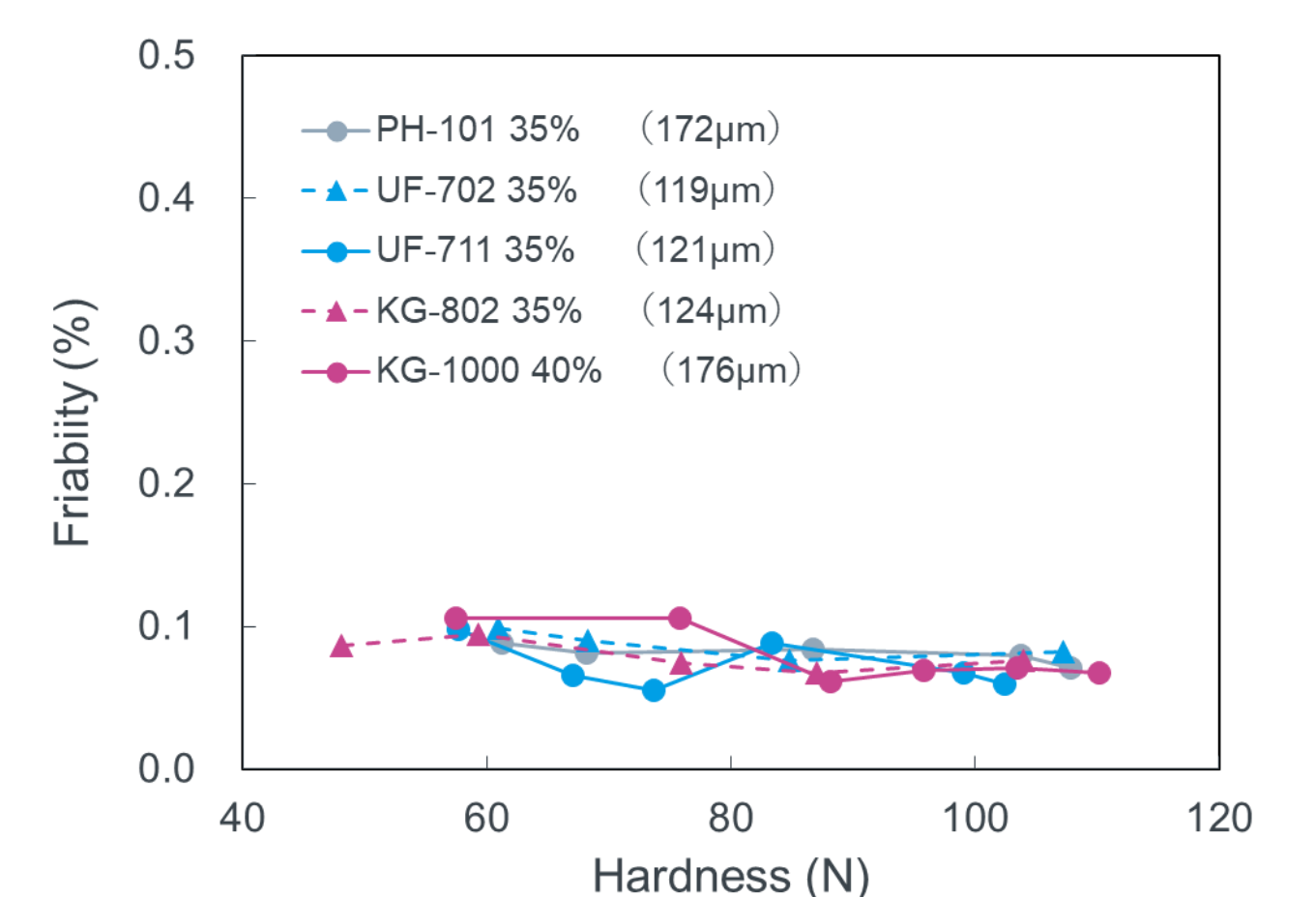


Figure 6. Friability

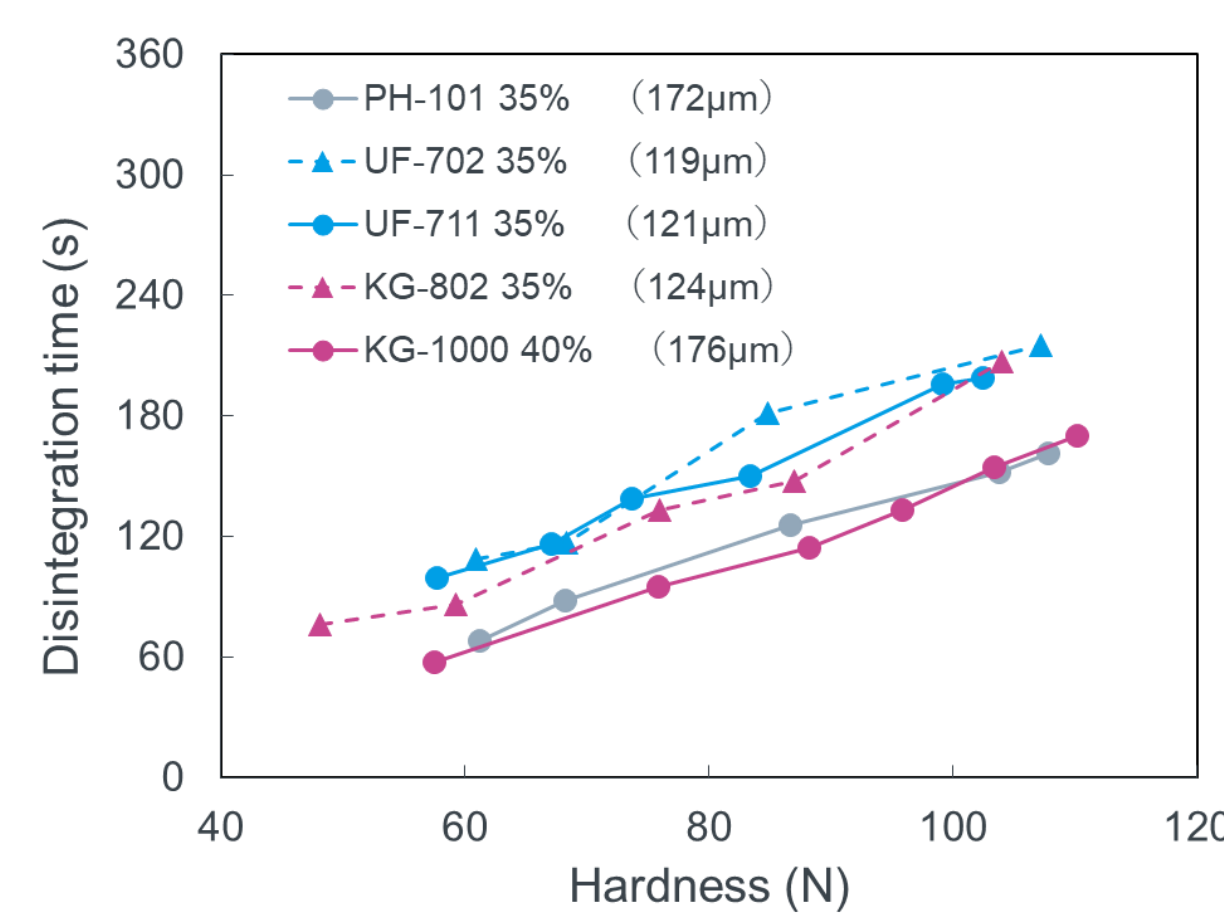


Figure 7. Disintegration time

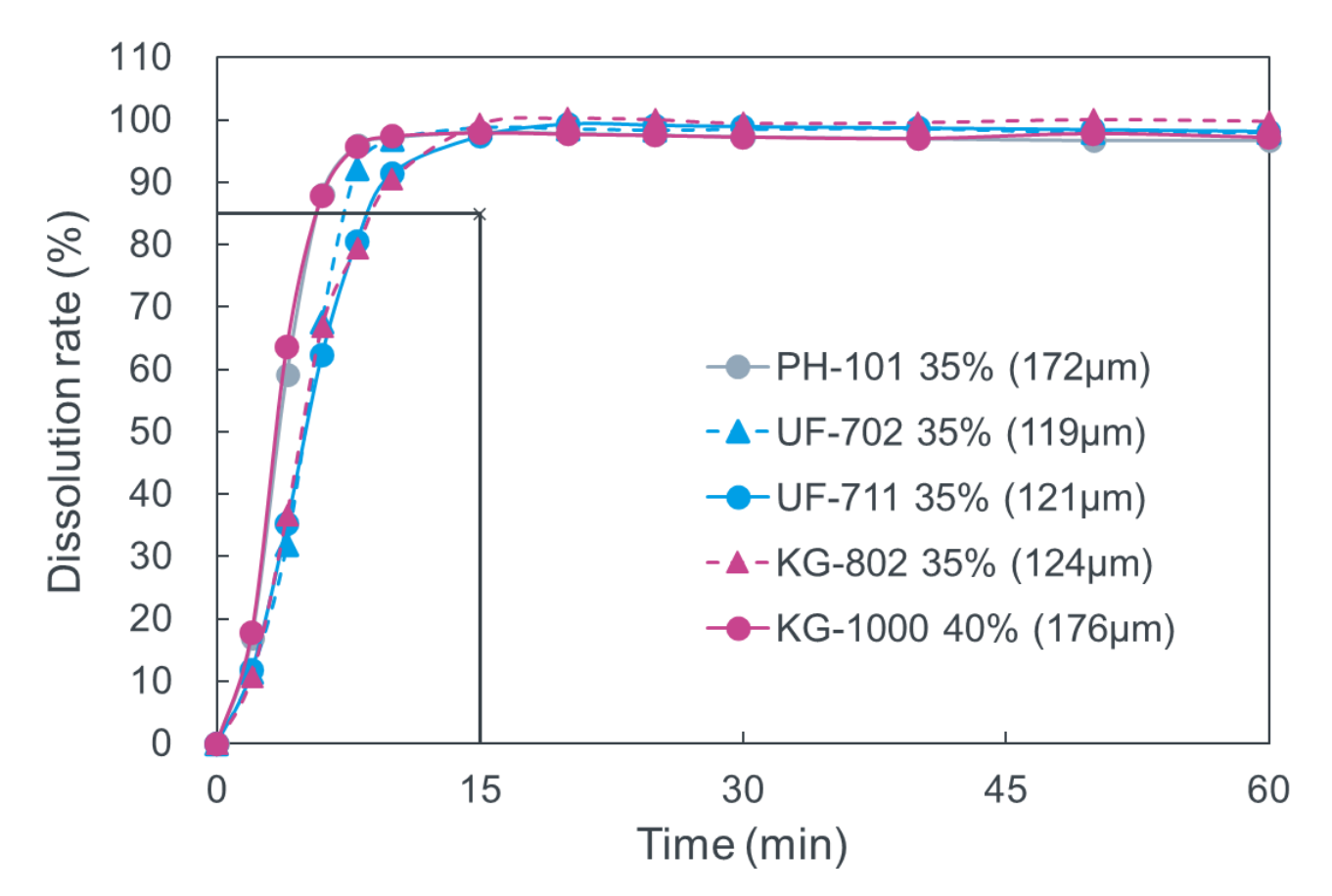


Figure 8. Dissolution profile with 1st fluid

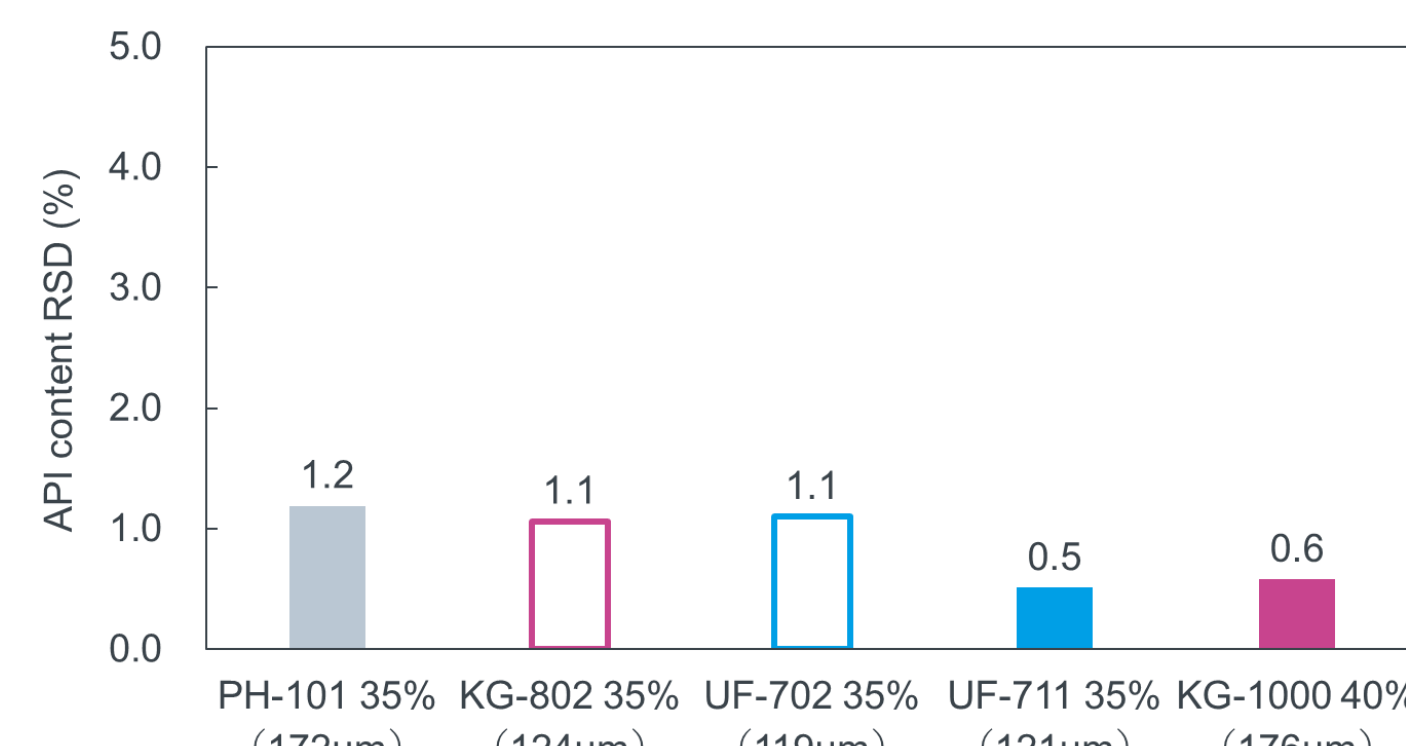


Figure 9. API content RSD

- As results, KG-1000 showed the best with respect to tablet hardness among all, while keeping good disintegration time and dissolution.

## CONCLUSION

- We compared different types of MCC grades "Ceolus™" to investigate what powder properties contribute to process compatibility with the continuous manufacturing system "Granuformer® Gf-2050."
- We observed correlation between water absorption properties of MCCs and the increment of granule size with amount of water added.
- Among all MCC, KG-1000 which possesses the highest water absorption property showed the least clogging tendency and the most moderate particle growth with respect to the amount of water added during granulation process.

## ACKNOWLEDGEMENT

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