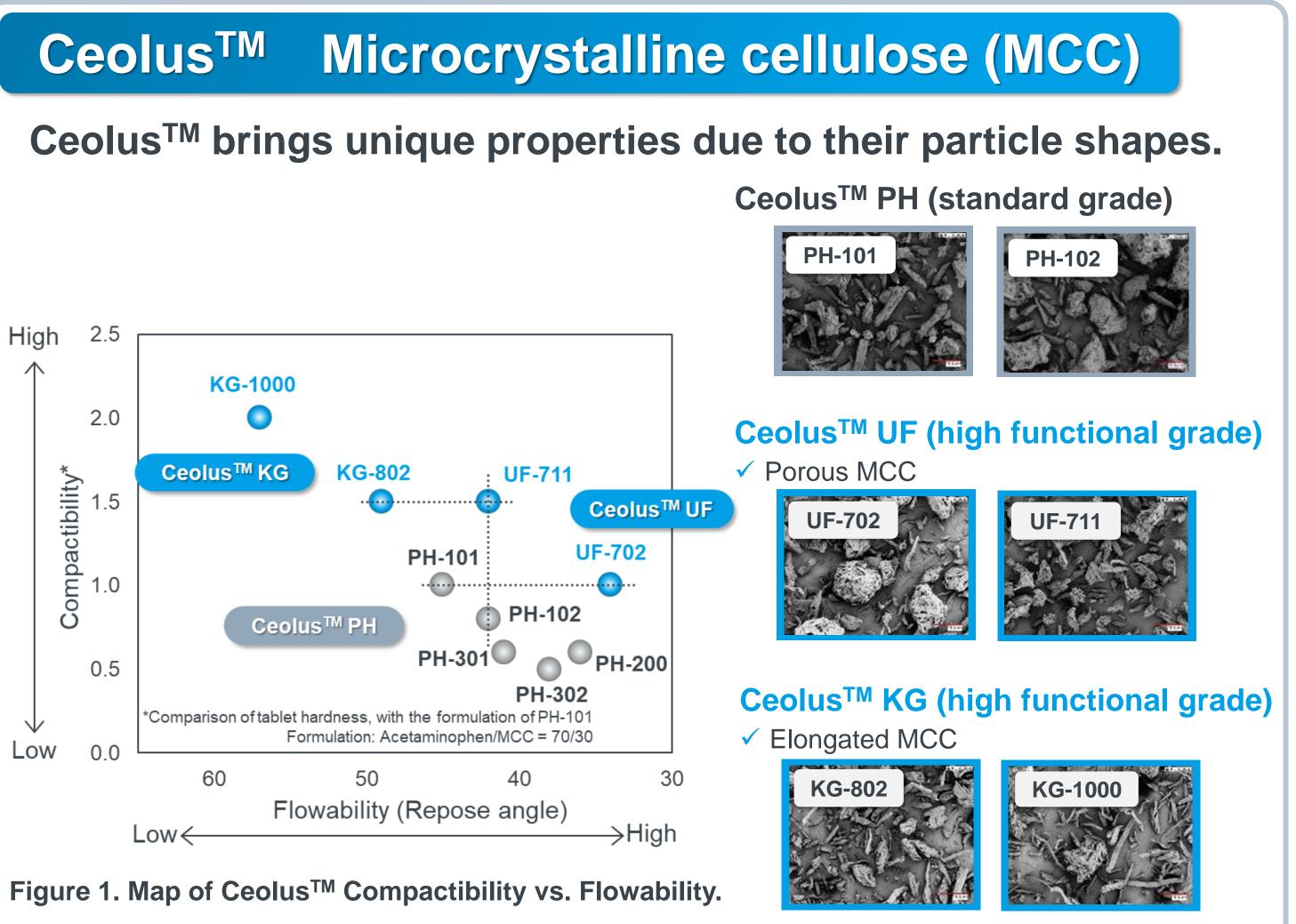
# **Suppression of Related Substance in Tablets Containing Pressure-Sensitive Drugs with Elongated Microcrystalline Cellulose**







#### Ceolus<sup>TM</sup> KG Ceolus<sup>TM</sup> KG is a highly compactible MCC with elongated particles. Solves tableting issues Insufficient hardness, sticking, capping, high friability Ratio [wt%] Ingredients Mixing\*1 Acetaminophen \*1:3min →PH-102 **→**KG-802 **→**KG-1000 Light silicic anhydride Mixing\*2 60 \*2:30sec Ingredients Ratio [wt% Magnesium stearate **Tableting** CREANPRESS (Rotary Press, Kikusui Ltd.) 20 **Tableting speed** 12 / 36 punches Tableting interval Feeder 180mg / Ф8mm-12R Tablet size / type **Evaluation** Compression Force (kN) Comp. Force 5 ~ 16 kN

Figure 3. Experimental example of using Ceolus™ KG.

#### INTRODUCTION

- ◆ It is known that the pressure, friction, heat, etc. applied during compression molding of some drugs causes crystal distortion and destabilization.
- When dealing with such kinds of substances, excipient selection is important.
- ◆ In this study, we report the use of different types of MCCs (Ceolus<sup>™</sup> PH, Ceolus<sup>™</sup> KG) to investigate their applicability in tablets containing candesartan cilexetil (CC) as a model pressure-sensitive drug [1].

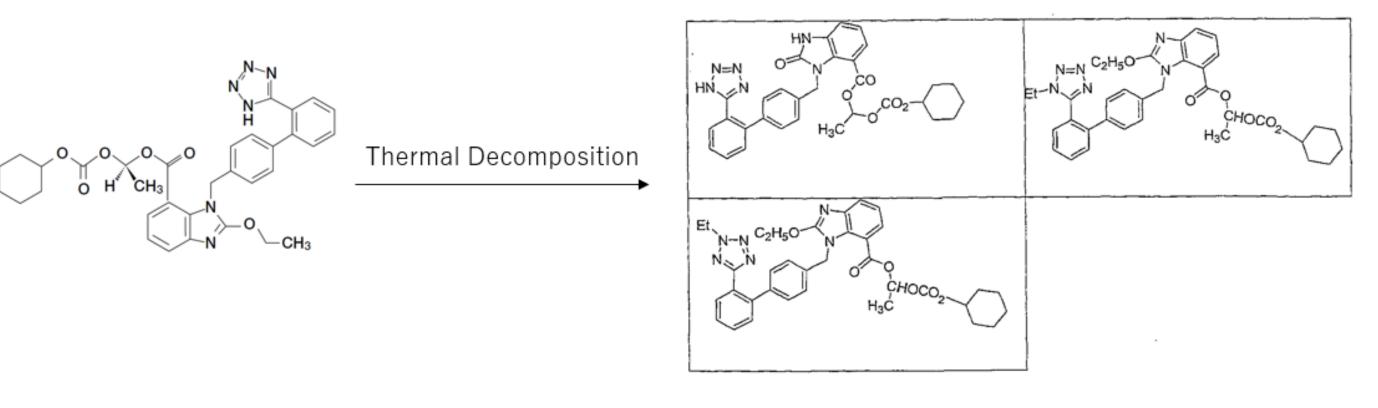


Figure 4. CC and its related substances.

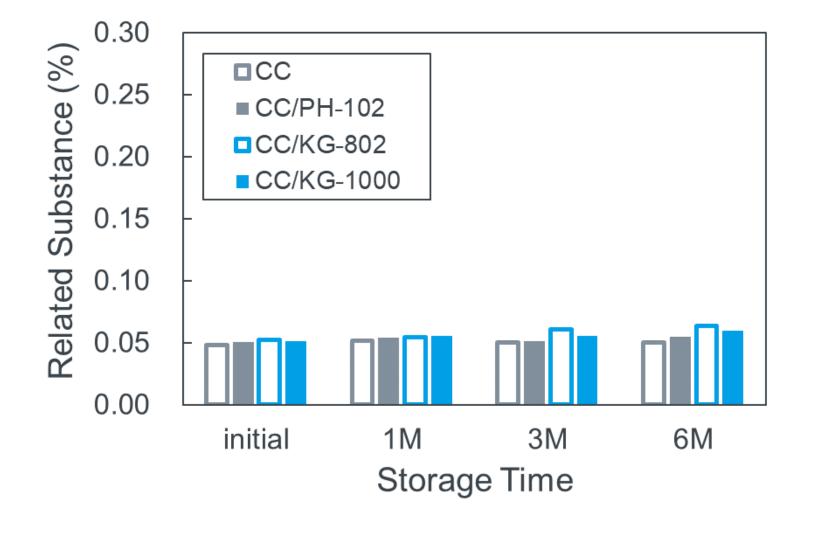
### **EXPERIMENTS**

Table 1. Properties of MCCs used in this study.

		KG-802	KG-1000	Ingredients	Loading (wt.%)	vt %)	
	PH-102			Candesartan cilexetil			
Particle size D50 (µm)	90	50	50	(CC) MCC : CEOLUS <sup>™</sup> (KG-1000,KG-802,PH-102)	60 40		
Bulk density (g/mL)	0.30	0.21	0.12				
Repose angle (°)	42	49	57	Mixing	1)	1)Mixing condition: PE bag, Mixing time: 3 min	
SEM Image (×500)				Tableting <sup>2)</sup>		2)Tool: MODEL-1011 CREEP, AIKOH ENGINEE Tablet size: 200mg, 8mmΦ-30R *Tableting was carried out under the static condi (10 sec of creep holding time). *Compression force was adjusted to obtain the thardness of 50 N that is practically required value.	
Nitrite (μg/g) Maximum value	0.012	N.D.	N.D				
Nitrate (µg/g) Average value	0.082	0.106	0.112	Evaluati  · Tablet hard  · Amount of related	ness	3)Tool: Model LC-10ADVP, Shimadzu Corpora *The tablets were dissolved in a mobile phase drug concentration of 160 mg/L, then filtered to 0.45 µm filter.	
						*The ratio of related compounds was quantified peak area ratio of CC and its related-compour	

Figure 5. Experimental procedure.

# RESULTS



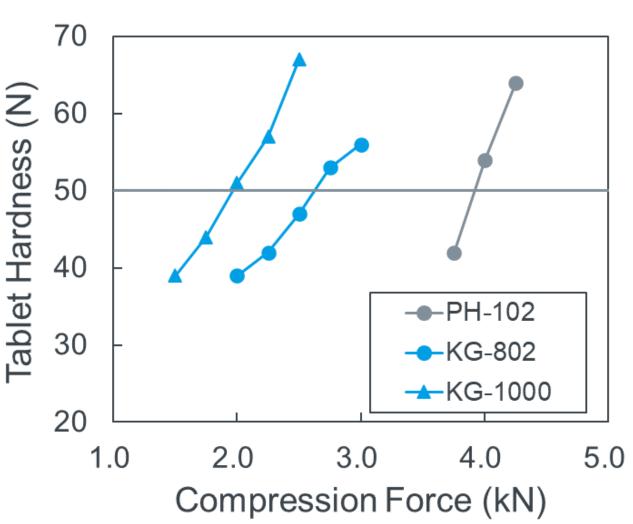
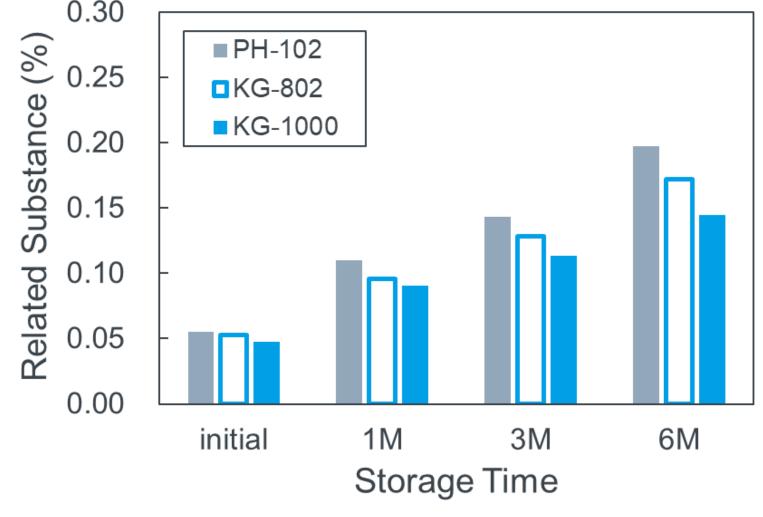


Figure 2. SEM images of Ceolus<sup>™</sup> particles.



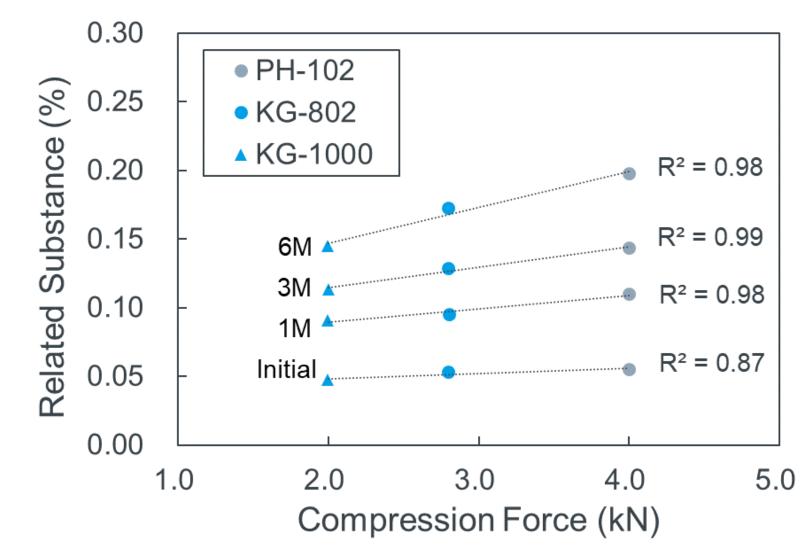


Figure 6. Changes in related substance in powders.

Figure 7 Tablet hardness of each formulation.

Figure 8. Changes in related substance in tablets.

Figure 9. Relationship between amount of related substance in tablets and compression force.

\* The formulation powders and the tablets were stored in a sealed glass bottle at 25°C. and 58% RH for 6 months.

# CONCLUSION

- ◆The tableting pressure to obtain tablets of the same hardness could be decreased with applying elongated-shaped MCCs (KG-1000 and KG-802) compared to amorphous-shaped MCC (PH-102).
- ♦ The lower the compression force was applied, the less the amount of related substance generated.
- **♦ KG-1000** showed the least amount of related substance.

#### REFERENCES

[1] Japanese Patent Publication 2008-505935A.

[2] Lei, J., Zhang, X., Zhuo, Z., Zhu, K., Sun, P., and Fan, Q., HPLC-UV simultaneous determination of candesartan cilexetil and hydrochlorothiazide in compound candesartan cilexetil tablets, Yaow u Fenxi Zazhi, 27 (4), 566-568 (2007).