

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

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AsahiKASEI

CEOLUS™
Just Pure Performance

Ceolus™ Microcrystalline cellulose (MCC)

Ceolus™ brings unique properties due to their particle shapes.

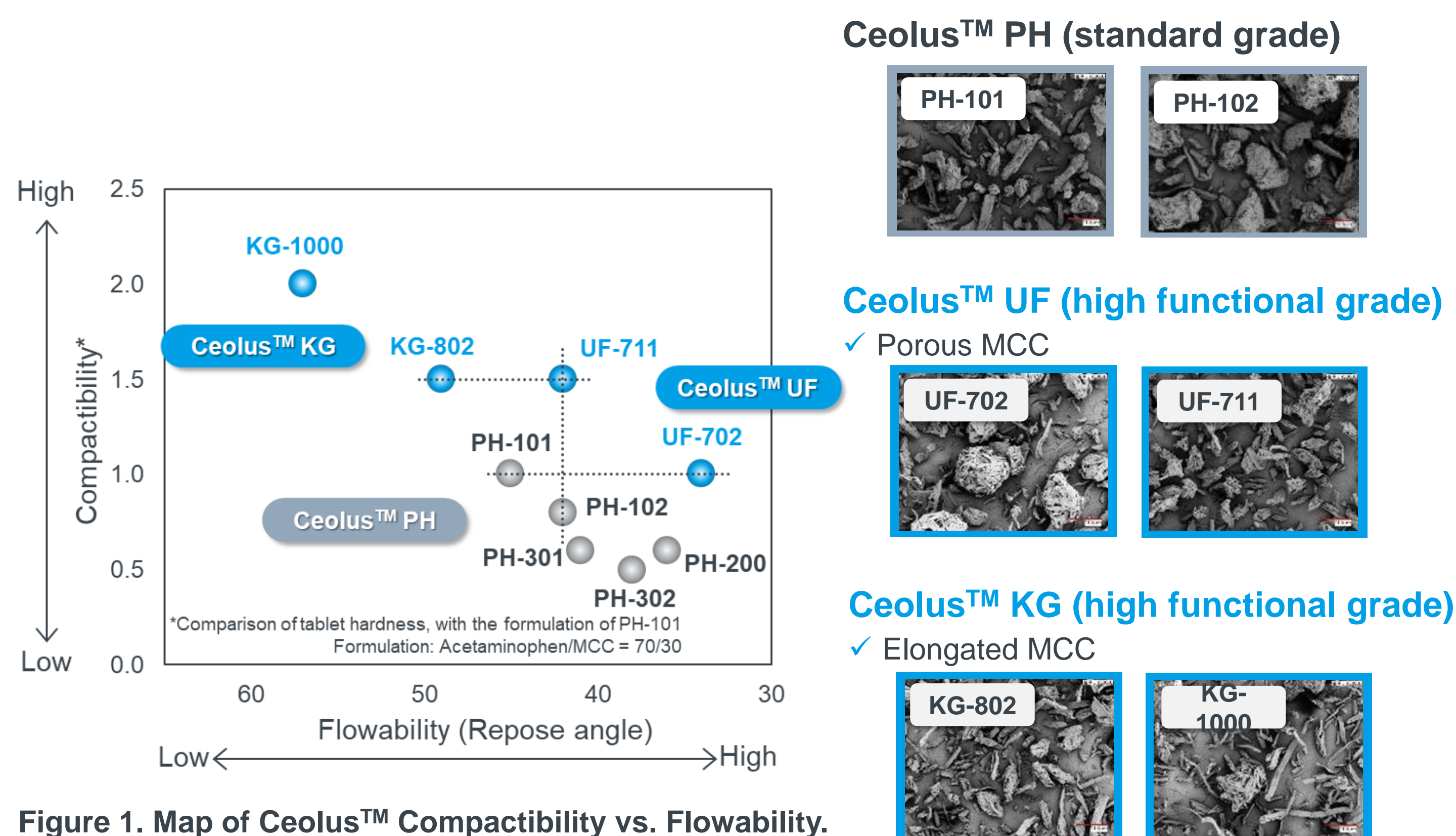
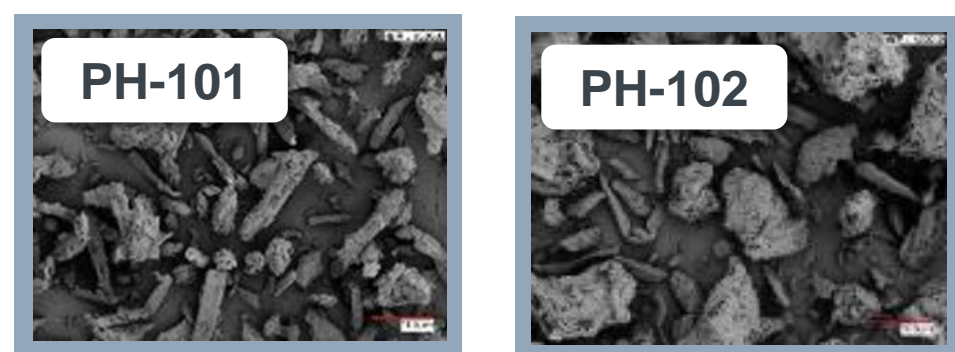
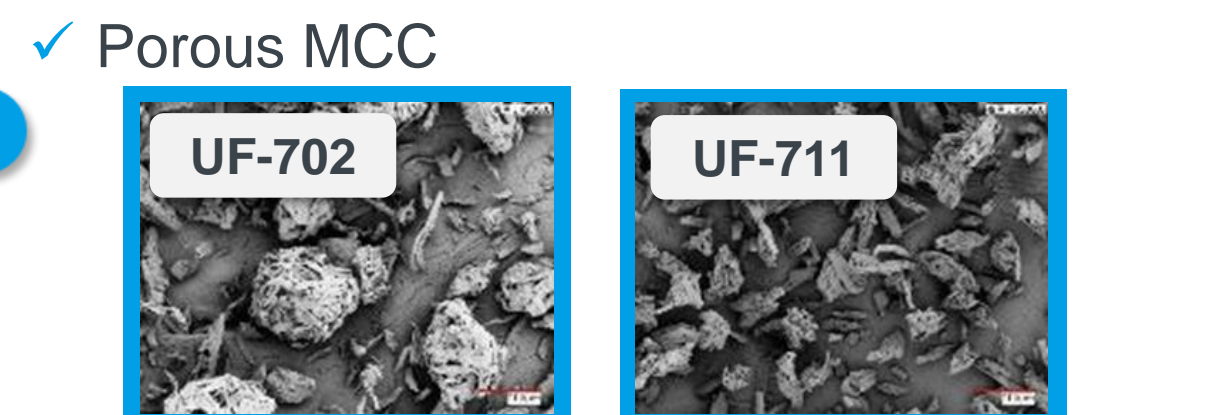


Figure 1. Map of Ceolus™ Compactivity vs. Flowability.

Ceolus™ PH (standard grade)



Ceolus™ UF (high functional grade)



Ceolus™ KG (high functional grade)

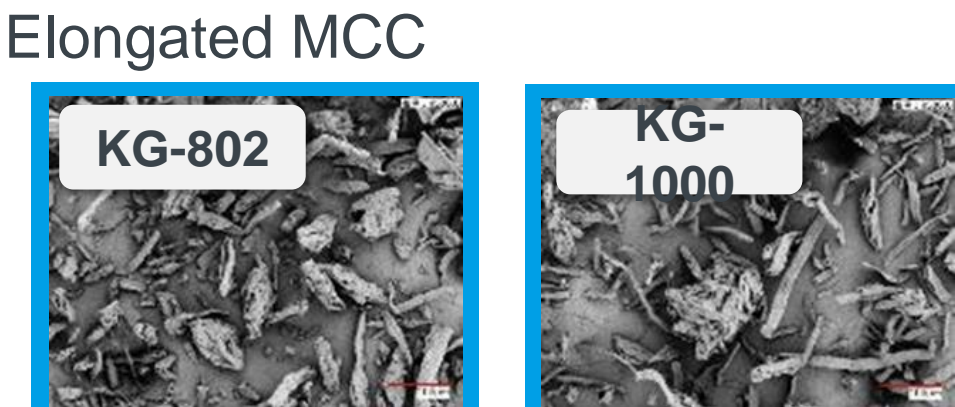


Figure 2. SEM images of Ceolus™ particles.

Ceolus™ KG

Ceolus™ KG is a highly compactible MCC with elongated particles.

◆ Solves tableting issues

Insufficient hardness, sticking, capping, high friability

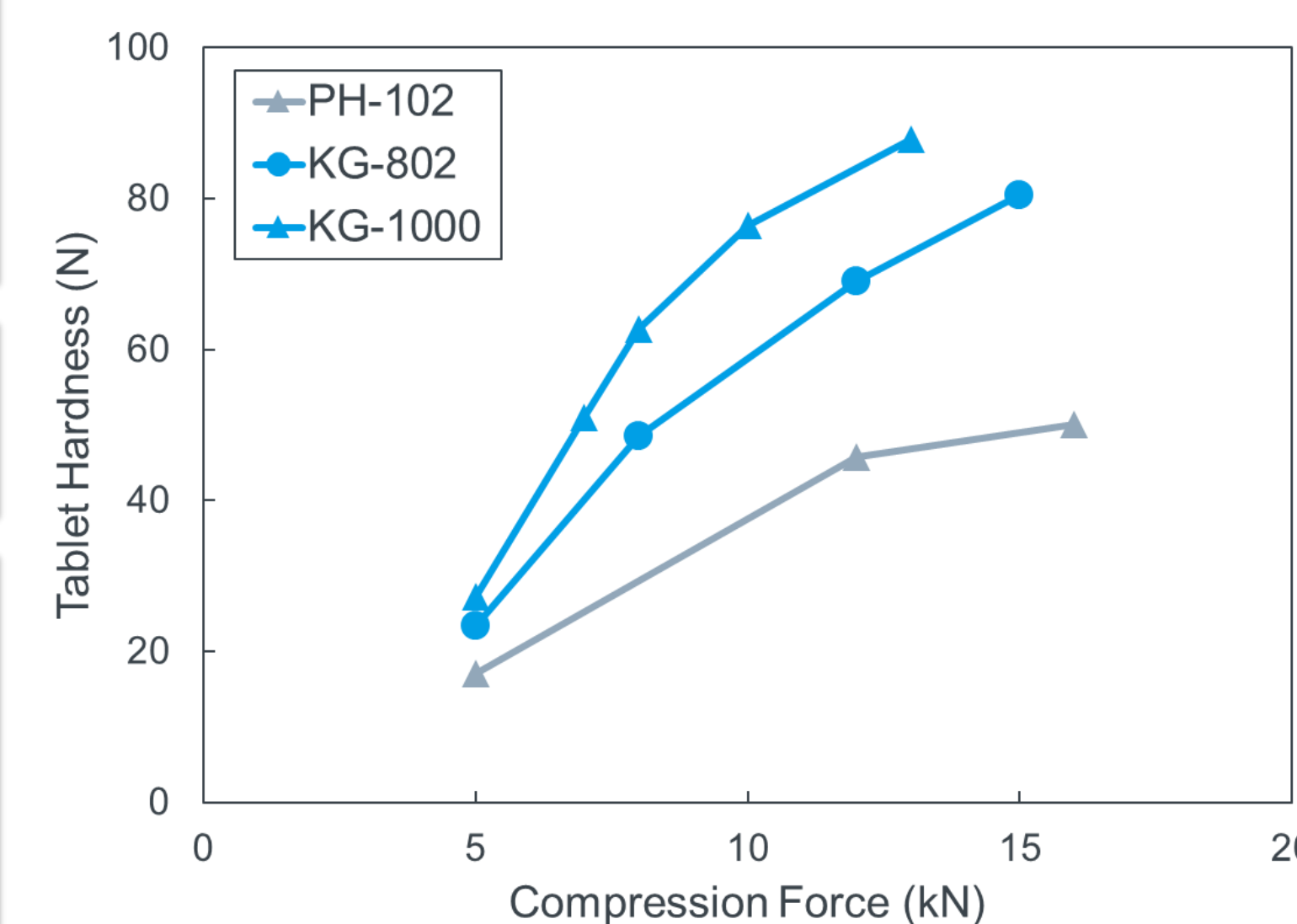
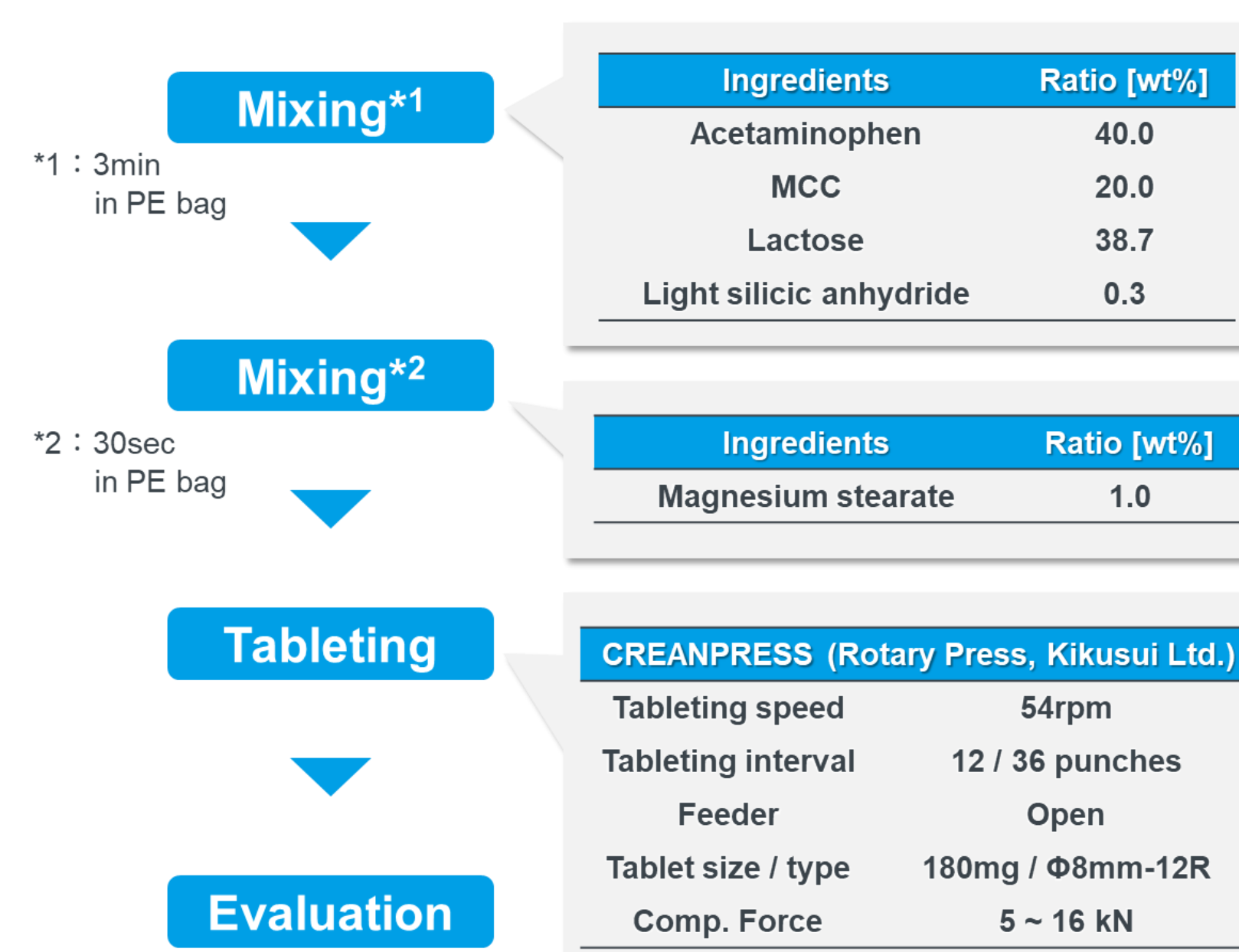


Figure 3. Experimental example of using Ceolus™ KG.

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™ PH, Ceolus™ KG) to investigate their applicability in tablets containing candesartan cilexetil (CC) as a model pressure-sensitive drug [1].

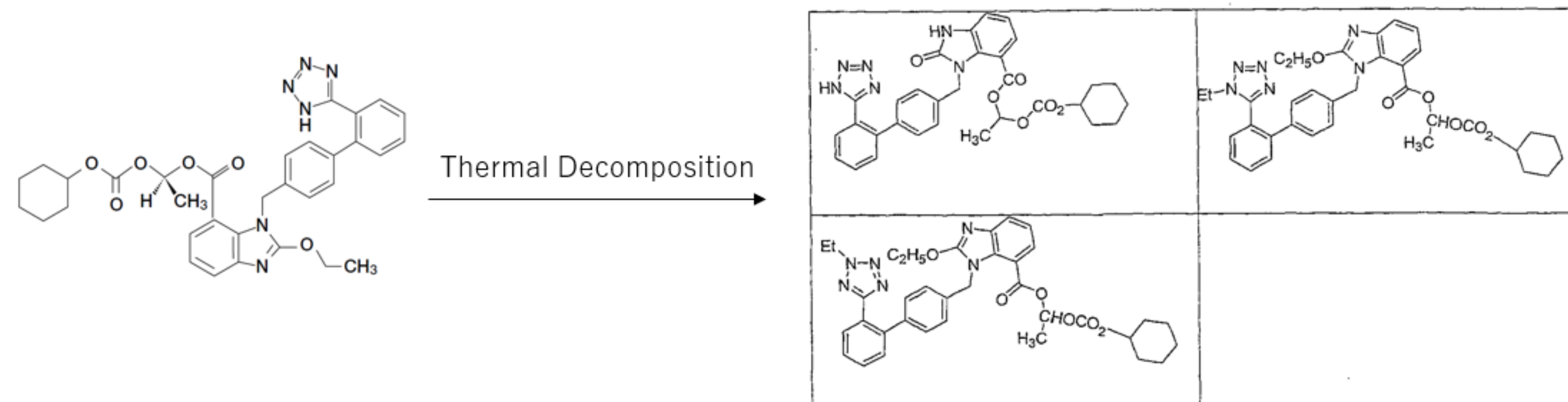


Figure 4. CC and its related substances.

EXPERIMENTS

Table 1. Properties of MCCs used in this study.

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

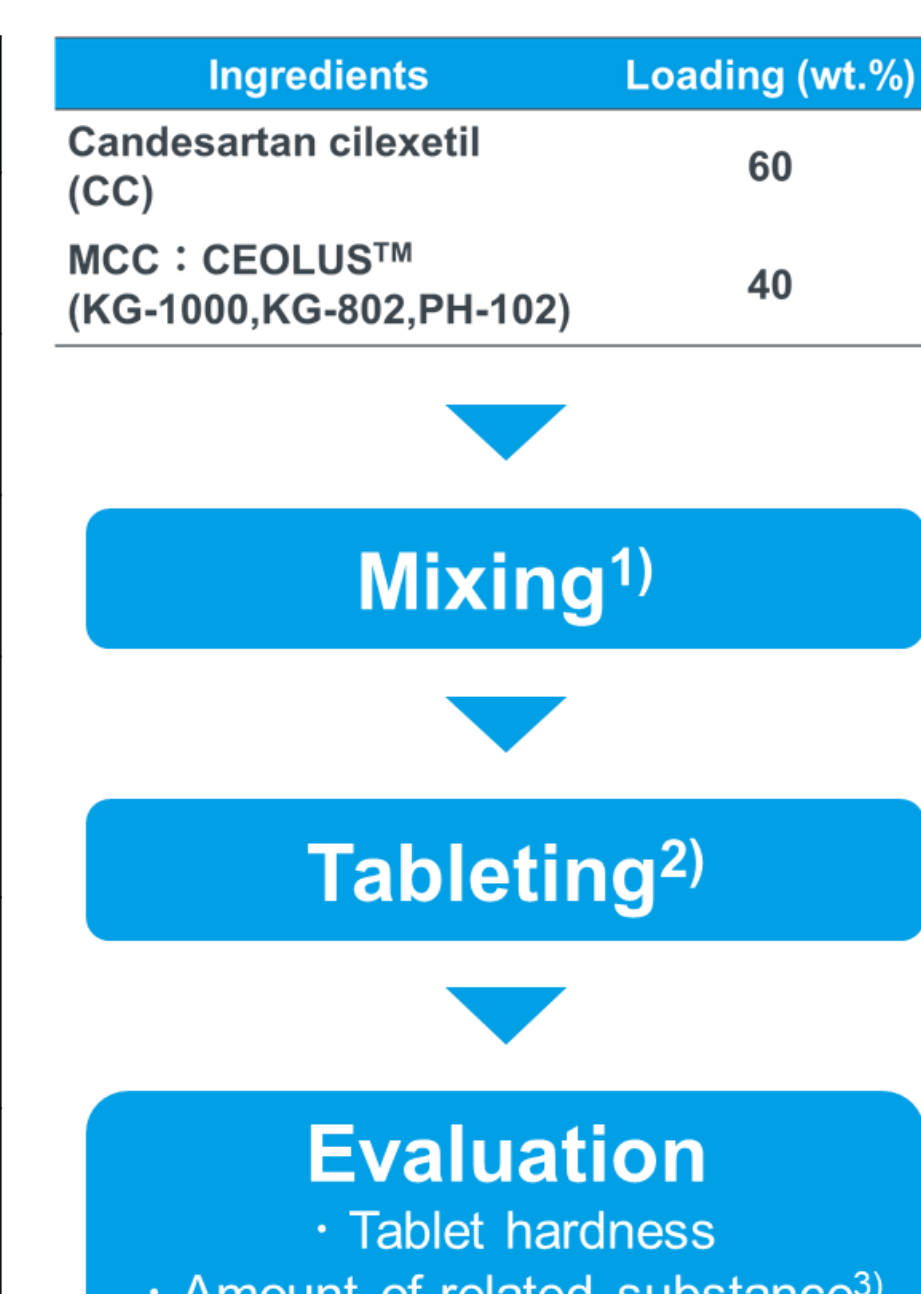


Figure 5. Experimental procedure.

RESULTS

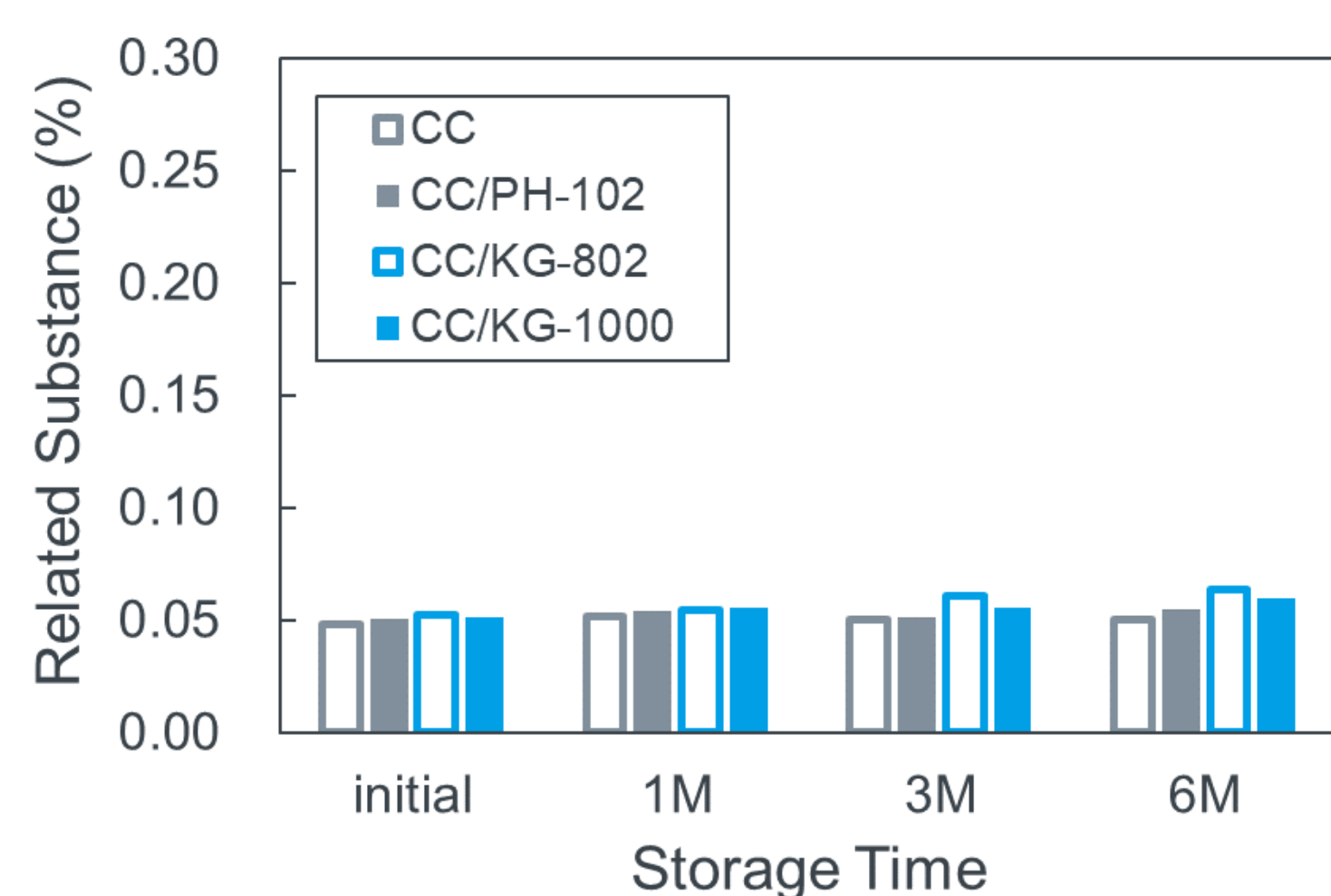


Figure 6. Changes in related substance in powders.

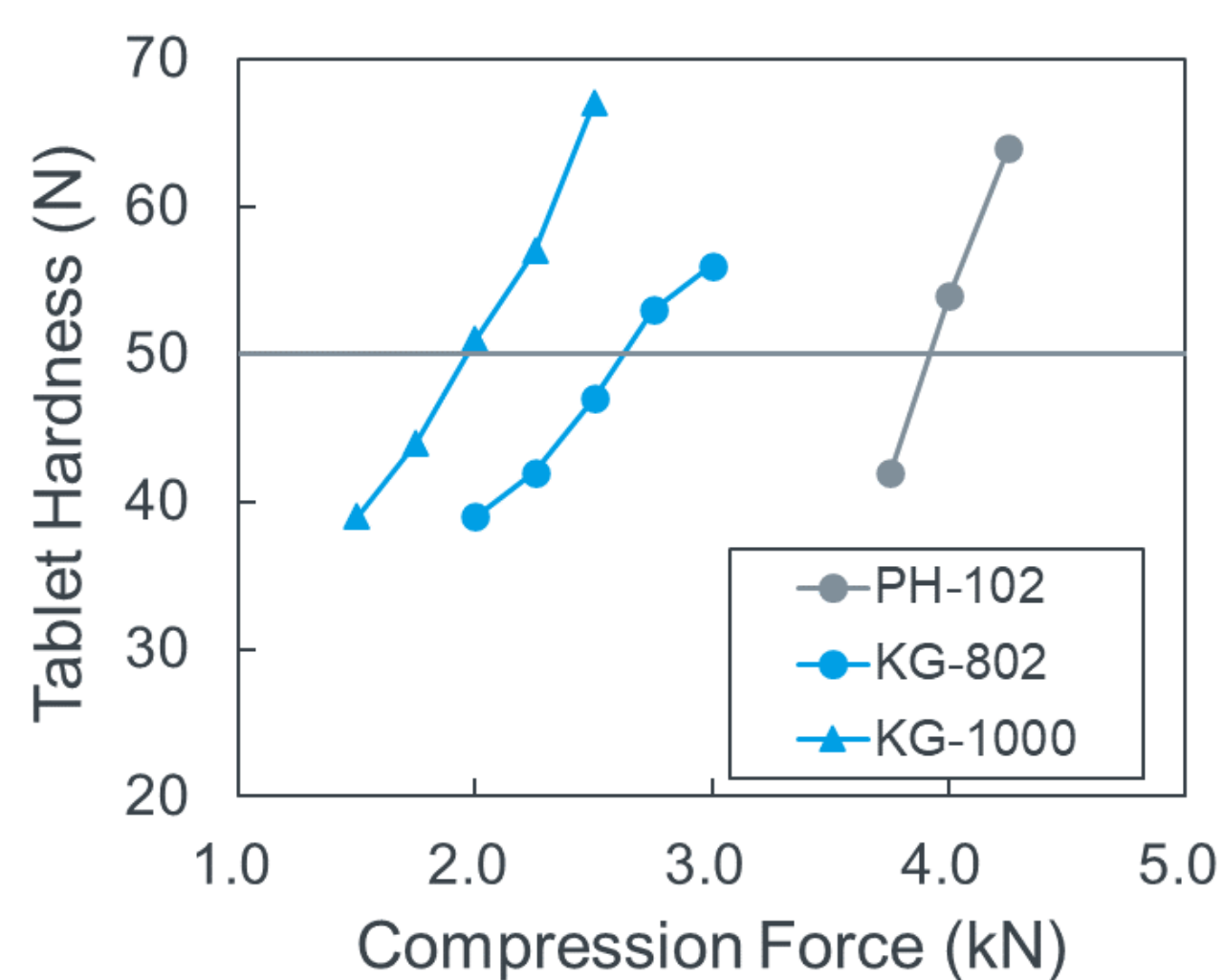


Figure 7. Tablet hardness of each formulation.

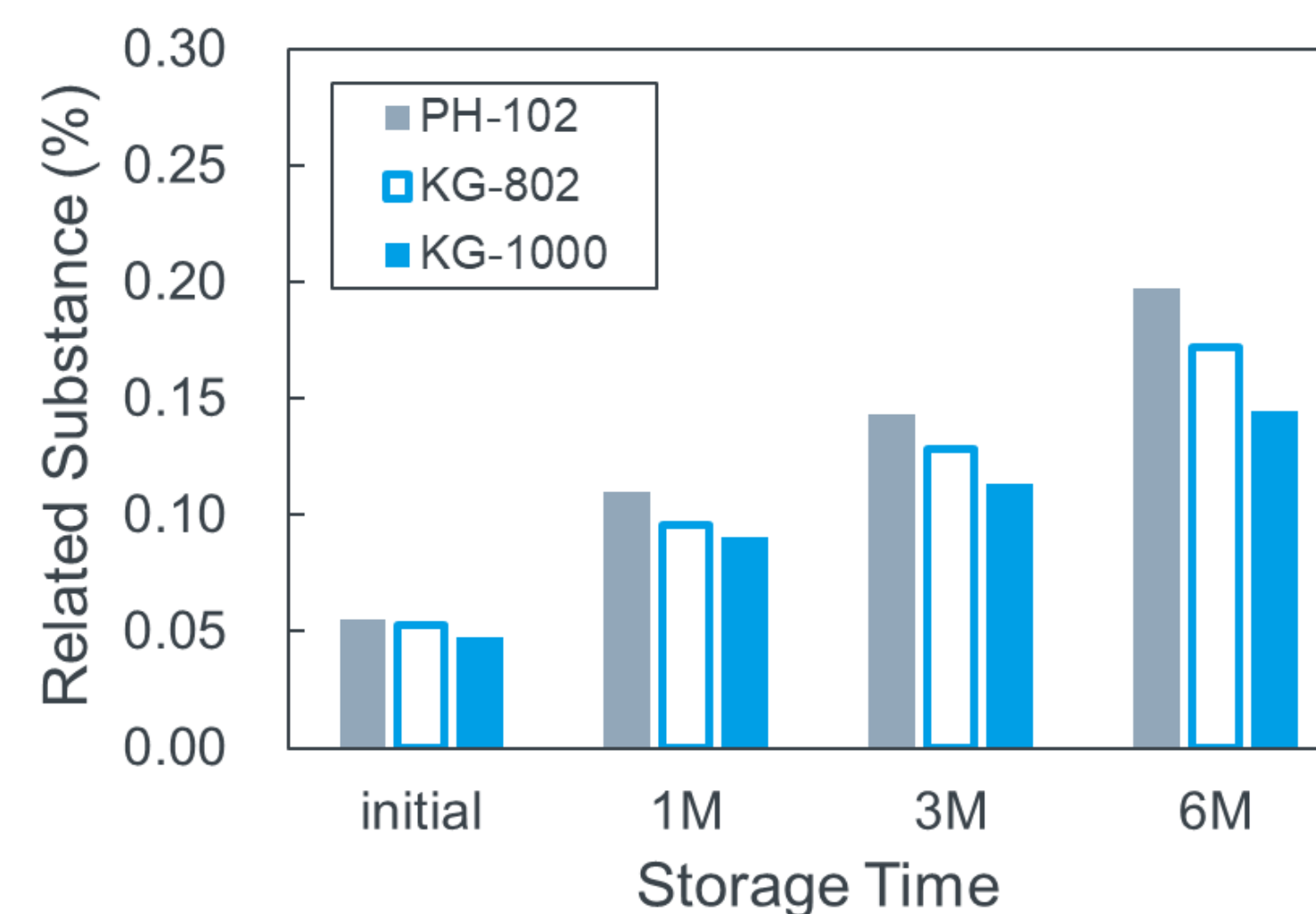


Figure 8. Changes in related substance in tablets.

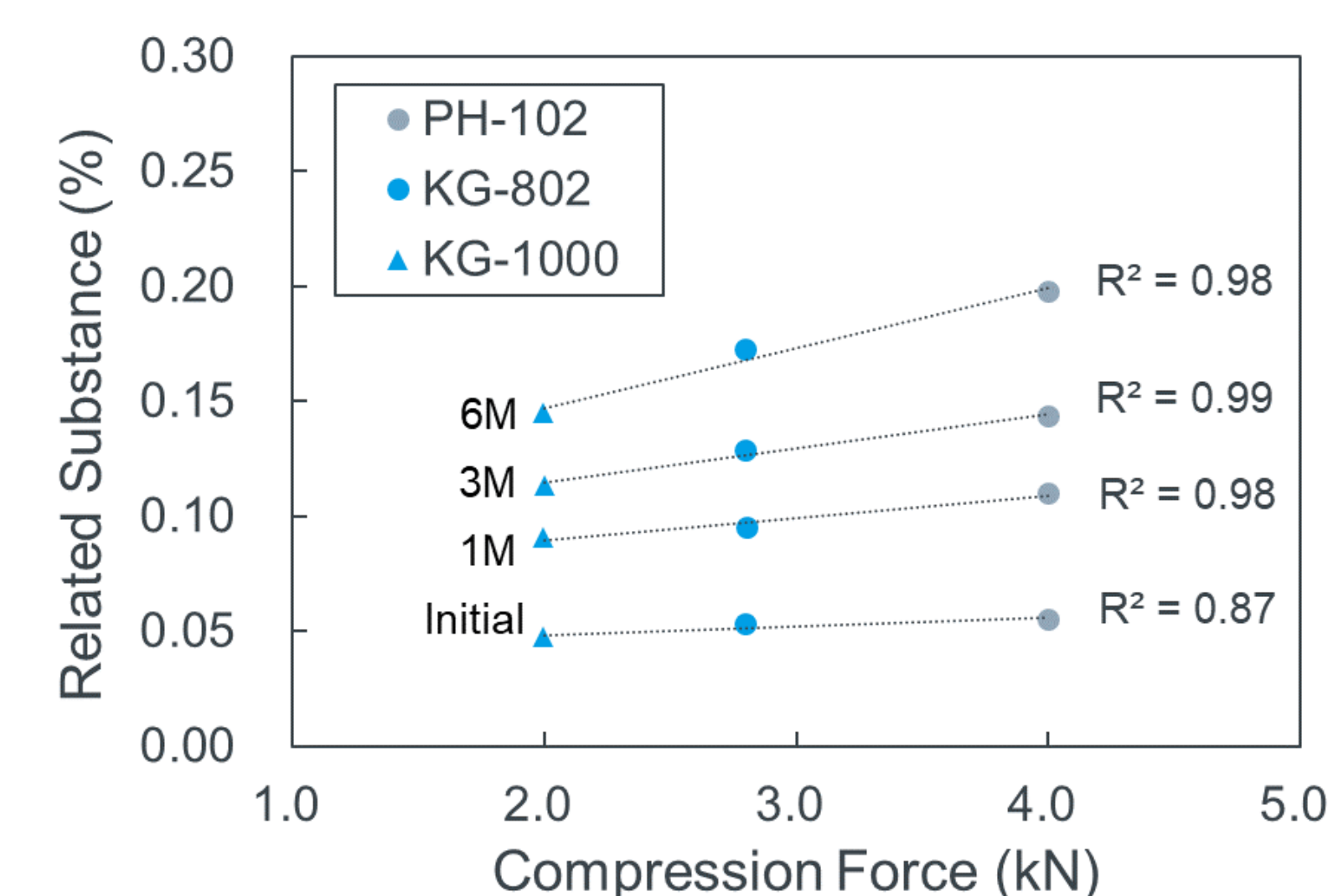


Figure 9. Relationship between amount of related substance in tablets and compression force.

* 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).