Effect of Hydroxypropyl Cellulose Grade on the Tablet Characteristics in Continuous Granulation

Yuta Yamauchi[1], Toshiaki Okado[1], Edmont Stoyanov[2]
1,NIPPON SODA, Japan, 2,NISSO Chemical Europe, Germany
E-mail: y.yamauchi@nissogr.com

Excipients
NISSO HPC
Hydroxypropyl Cellulose
for Pharmaceutical

CTAC
CELLULOSE TECHNICAL APPLICATION CENTER

Introduction

Hydroxypropyl cellulose (HPC) is a nonionic cellulosic ether with high solubility in water and polar organic solvents. This amphiphilic polymer is used as a thickener and stabilizer, tablet binder, controlled released matrix, drug solubilizer in nanosuspensions, amorphous solid dispersions and 3D-printing excipient[1-4]. HPC is available in different molecular weights and particle sizes, that needs a precise grade selection for specific applications. While we have previously evaluated the effects of HPC molecular weight and particle size on tablet properties in fluid bed granulation and high shear wet granulation, the impact in continuous manufacturing has not been investigated. Nowadays, continuous manufacturing is gaining attention in pharmaceutical production as a novel approach that enables consistent manufacturing of high-quality products. In this study, we have evaluated the effects of different HPC grades on tablet properties in continuous granulation processing.

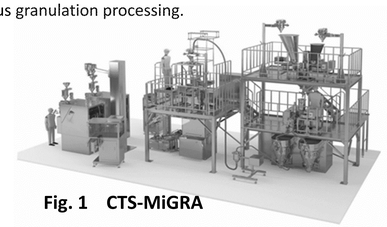

Fig. 1 CTS-MiGRA

Method

Powder mixing
Powders except NISSO SSF (sodium stearyl fumarate, Nippon Soda Corp., Japan) were added to a high shear granulator (VG-100 , Powrex Corp., Japan) according to Table 1 and mixed for 3 minutes. Three grades of HPC (Nippon Soda Corp., Japan) with different molecular weights and particle sizes were used (Table 2). The blade rotation speed was 190 min^{-1} and the cross screw rotation speed was 3000 min^{-1}.

Continuous granulation
Using a continuous process equipment (CTS-MiGRA , Powrex Corp., Japan, Fig. 1), 12% water was added to each powder mixture for granulation. The granules were then dried at an inlet air temperature of 80° C and air flow rate of 1.0 m^3/min. When the product temperature reached 45° C, the granules were discharged by pneumatic conveying. Subsequently, the granules were milled and sized using a Comill, and the granulated product was collected.

Tableting
NISSO SSF (lubricant) was added to the granules and mixed by hand. The powder mixture was then compressed using a tablet press (VERA-5, Kikusui Seisakusho Co., Ltd.,Japan) at a compression force of 7.5 kN. The tablets were compressed under the conditions of Φ8 mmR12. The tablet properties were evaluated in accordance with the Japanese Pharmacopoeia 18.

Table 1. Formulation

Component	Content (% w/w)
Paracetamol	10.0
Pharmatose 200M	58.5
Corn starch	25.0
Silica	0.5
NISSO HPC	5.0
NISSO SSF	1.0

Table 2. HPC grades used in the study

grade	particle size	molecular weight
HPC−L FP	80-110	140,000
HPC-SL FP	80-110	100,000
HPC-SSL	85	40,000
HPC-SSL SFP	20	40,000

Result

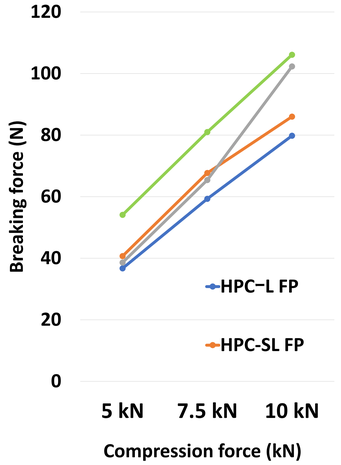

Fig. 2. Breaking force by HPC grade

●The smaller the HPC particle size, the higher the breaking force (Fig.2).

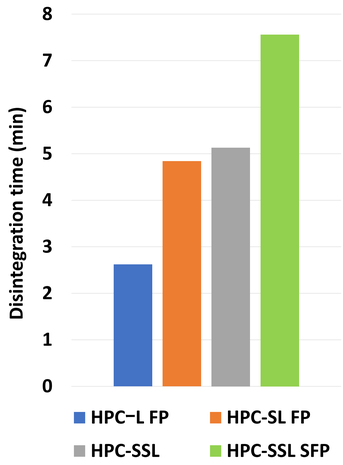

Fig. 3. Disintegration time by HPC grade
※Breaking force ranged from 102N to 111N

●Higher HPC molecular weight decreases disintegration time (Fig.3).

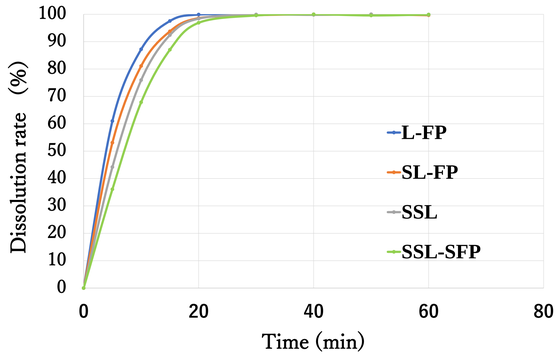

Fig. 4. Dissolution rate by HPC grade
※Breaking force ranged from 60N to 80N

●Higher HPC molecular weight shows faster dissolution (Fig.4).

This trend suggests that the disintegration mechanism may differ depending on the molecular weight of HPC[4]

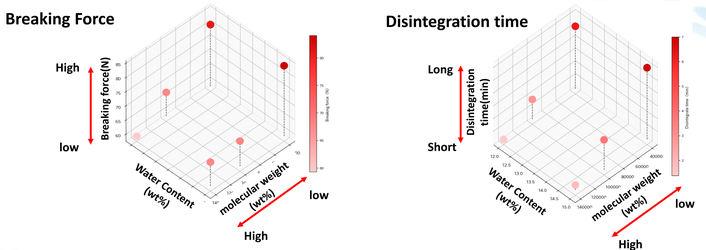

Fig.5 Plot chart of continuous wet granulation data

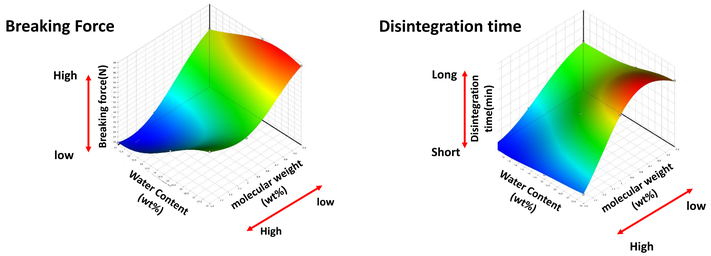

Fig.6 Response surface plot of high shear granulation data

Comparison with high shear granulation results

● The relationship between molecular weight and tablet hardness/disintegration time correlated with response surface analysis results from wet granulation (high shear granulation)(Figs. 5 and 6).

Conclusion

- High tablet breaking forces are produced with smaller particle size binder grade. HPC-SSL SFP demonstrated the highest tablet breaking force.
- Higher molecular weight binder produced slightly quicker drug dissolution. In this formulation, HPC-L demonstrated the fastest drug dissolution rate.
- Twin-screw granulation results showed similar trends to fluid bed granulation and high shear wet granulation.

References

1. Ito, A., Konnerth, C., Schmidt, J., Peukert, W. – "Effect of polymer species and concentration on he production of mefenamic acid nanoparticles by media milling"Eur. J. Pharm. Biopharm. 2016, 98, 98-107.
2. Luebbert, C., Stoyanov, E., Sadowski, G. – "Phase behavior of ASDs based on hydroxypropyl cellulose" Int. J. Pharm. X 2021, 3, 100070
3. Stoyanov, E., Okada, K., Ohashi, T., Serizawa, R.— "HPC-SLC Benefits for Film-Coating of Sustained Release Matrix Tablets: Impact on the Drug Release in Hydroalcoholic Conditions", CRS, 2023
4. Stoyanov, E., Ehlig, B., Tanev, W. – "Eye on Excipients" Tablets & Capsules 2018, January. CSC Publishing