Optimization of Solid Dispersion Formulation by VCM

Kohei Tahara, Ph. D. Professor Laboratory of Pharmaceutical Engineering Gifu Pharmaceutical University

Purpose

One method to improve the solubility of drugs having poor water solubility is preparing these drugs as solid dispersions. Solid dispersions are formulated by uniformly dispersing the target drug as molecules or fine particles within a carrier. Recent reports showed solubility can be improved in drugs having poor water solubility by preparing them as solid dispersions utilizing water-soluble polyvinyl alcohol (PVA) as a carrier by applying hot melt extrusion (HME) or electrospinning methods[1, 2].

The physical properties of PVA approved as pharmaceutical excipients are determined by the degree of hydrolysis (ratio of hydroxyl groups to acetyl groups) and the degree of polymerization. Since there are various PVA grades with different levels of these parameters, selecting the best possible PVA is essential. In this study, we screened solid dispersion bases using MeltPrep's Vacuum Compression Molding (VCM), which can prepare samples on the milligram scale by vacuum compression molding, assuming that the HME process is used to produce the solid dispersions.

Experiment

Indomethacin (IND) was utilized as the model drug. Various PVAs with different degrees of polymerization and hydrolysis were utilized from the GOHSENOL™ series manufactured by Mitsubishi Chemical Corporation (Table 1). PVA powder and IND powder were mixed in a ratio of 7:3 using a pestle and mortar. After filling the VCM with the mixed powder, the melting process was carried out at 230°C for 5 min[3].

PVA/IND pellets were collected from the VCM and processed into powder by grinding in a freezer mill for 5 min. IND dissolution from solid dispersion was evaluated by the dissolution test (paddle method) described in Japanese Pharmacopoeia.

Table 1: PVAs with different degrees of polymerization and hydrolysis utilized in this study.

Grade Name	Degree of polymerization	Degree of hydrolysis (mol%)
NK-05R	500	72
KL-05	500	80
EG-05P	500	88
KH-20	2400	80
EG-40P	2400	88

Result

The results from IND dissolution of the PVA/IND solid dispersions prepared by VCM are shown in Figure 1. In the PVA/IND solid dispersions, improvement of IND solubility was confirmed when using any grade of PVA. Powder X-ray diffractometry and thermal analysis showed that IND was amorphous in PVA/IND solid dispersions, suggesting that amorphization of IND improved the solubility. Different IND dissolution patterns were observed depending on the PVA grade. The highest IND dissolution was observed with solid dispersions using NK-05R or KL-05, both of which have a relatively low degree of polymerization and hydrolysis.

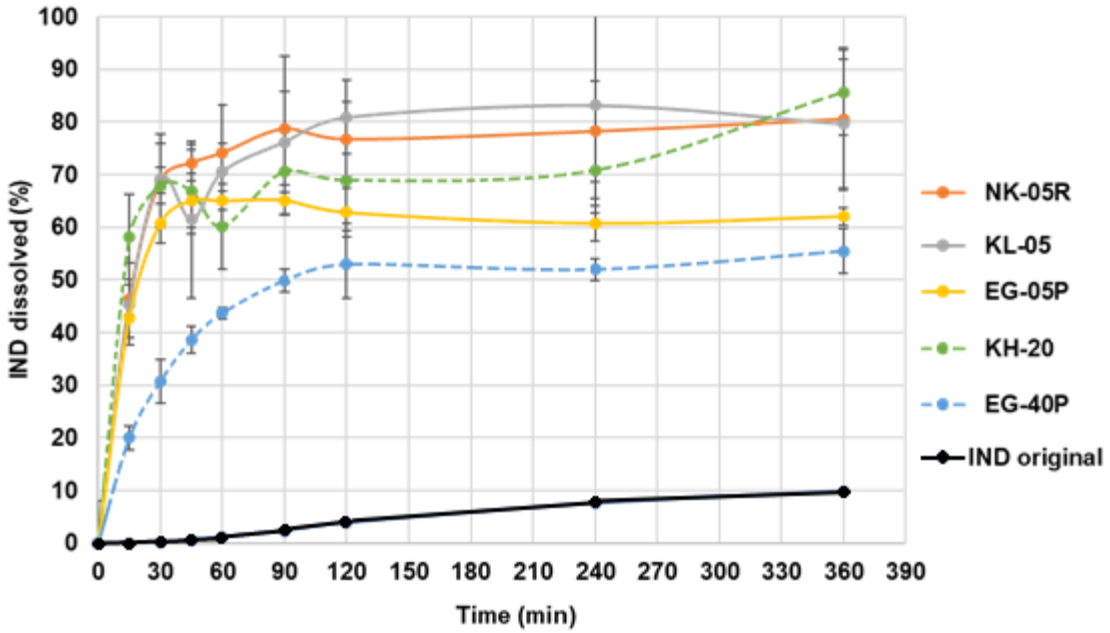

Fig. 1 IND dissolution profiles from cryo-milled PVA/IND solid dispersions prepared by VCM (n=3, mean ± standard deviation)

Conclusion

These results demonstrated the necessity for selecting the appropriate degree of polymerization and hydrolysis when using PVA as a solid dispersion carrier. Furthermore, proper selection of the PVA grade according to the drug could achieve the targeted release pattern, showing the importance of screening in the formulation design for solid dispersion carriers.

Bibliography

1) Mori Y, Motoyama K, Ishida M, Onodera R, Higashi T, Arima H. Theoretical and practical evaluation of lowly hydrolyzed polyvinyl alcohol as a potential Theoretical and practical evaluation of lowly hydrolyzed polyvinyl alcohol as a potential carrier for hot-melt extrusion. Int J Pharm. 555:124-134. 2019
2) Shibata T, Yoshimura N, Kobayashi A, Ito T, Hara K, Tahara K. Emulsion-electrospun polyvinyl alcohol nanofibers as a solid dispersion system to improve Emulsion-electrospun polyvinyl alcohol nanofibers as a solid dispersion system to improve solubility and control the release of probucol, a poorly water-soluble drug. J Drug Deliv Sci Technol.102953. 2021
3) Shadambikar G, Kipping T, Di-Gallo N, Elia A-G, Knüttel A-N, Treffer D, Repka MA. Vacuum Compression Molding as a Screening Tool to Investigate Carrier Suitability for Hot-Melt Extrusion Formulations. Pharmaceutics. 12(11):1019. 2020