Excipients
NISSO HPC
APPLICATION NOTE

Hydroxypropyl Cellulose for Orally Disintegrating Film Drug Application[1]

SUMMARY

Hydroxypropyl cellulose (HPC) is a water-soluble polymer that has film formation properties with excellent plasticity. Its hydroxypropyl groups drive the solubilization of the cellulose thus hindering the hydrogen bonding of the hydroxyl groups. In this study, we evaluated the applicability and effectiveness of HPC in Orally Disintegrating Films (ODF's) by varing the API, excipient and molecular weight of HPC. Based on the results of the evaluation, ODFs could by prepared using HPC as the base material.

INTRODUCTION

Oral dosage form is considered the most desirable medication method since it is simple and convenient. The most common forms available are tablets, powders and capsules. However for children, the elderly and others with limited swallowing ability, these dosage forms can be challenging to take by mouth. Orally disintegrating tablets (ODTs), which quickly disintegrate and disperse with a small amount of water in oral cavity, are being developed actively as the dosage form which can be taken easily even by the people who have difficulty swallowing. However, in the case of ODTs, it is difficult to achieve both enough tablet hardness and quick disintegration. In addition, preparation of ODTs is usually complicated and special tablet machine or technology may be required.

Orally Disintegrating Films (ODFs), which also quickly disintegrate and disperse in the oral cavity, are being developed for functional foods such as breath fresheners. Pharmaceutical orally disintegrating films are being developed and many kinds of ODFs are now available in OTC drug market. In comparison with ODTs, ODFs can be an easier oral dosage form, with advantages of durability or portability owing to a thin and flexible form.

HPC is widely used as a binder and a film coating agent for pharmaceutical application owing to its chemically inert nature. HPC has film formation properties with excellent plasticity for easy handling. In this study, we prepared ODFs using several types of HPC as a base material and evaluated the effect of the film properties by formulating drugs and other excipients.

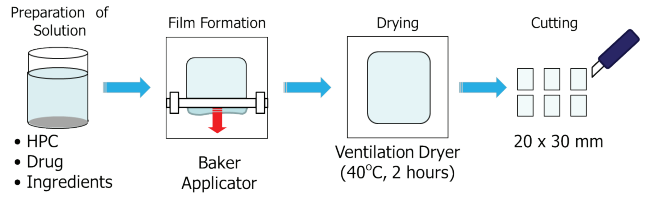
METHODS

Materials

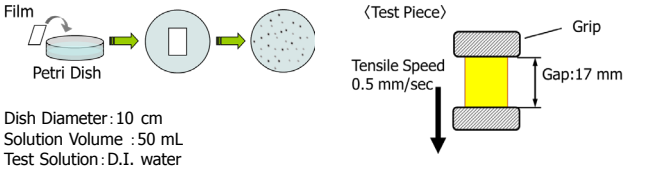
Base Material		Hydroxypropyl Cellulose HPC-SL (Viscosity: 3-5.9 mPa·s at 20°C, 2% aqueous solution)
Model Drug		Ascorbic Acid (VC, Solubility: 40mg/mL) Acetaminopehn (AAP, Solubility: 14mg/mL) Ibuprofen (IBU, Solubility: 0.049mg/mL)
Excipients	Soluble	Erythritol Glucose Trehalose
	Insoluble	Calcium Carbonate ($CaCO^3$) Microcrystalline Cellulose (MCC) Crospovidone (cl-PVP) Croscarmellose Sodium Low-substituted Hydroxypropyl Cellulose (L-HPC)

Experimental Methods

Preparation method for HPC film



Evaluation methods for disintegratability and film strength

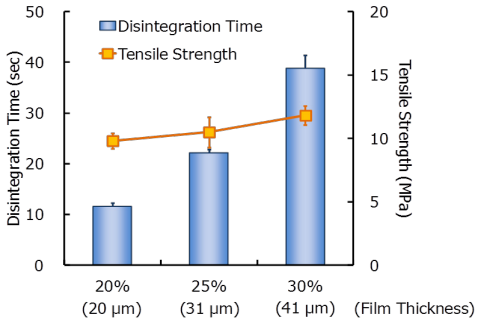


Dish Diameter : 10 cm
Solution Volume : 50 mL
Test Solution : D.I. water
Temperature : RT
Disintegration Time:
Time from film floating until disintegration

$$\text{Tensile Strength (MPa)} = \frac{\text{Max Load (N)}}{\text{Area of Cross Section (mm}^2\text{)}}$$

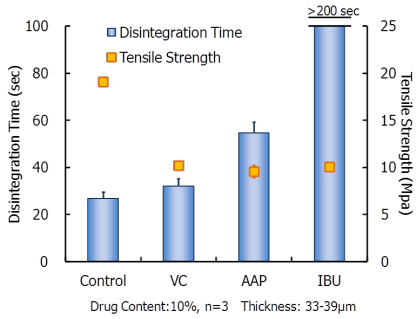
RESULTS AND DISCUSSION

1. Effect of HPC Concentration



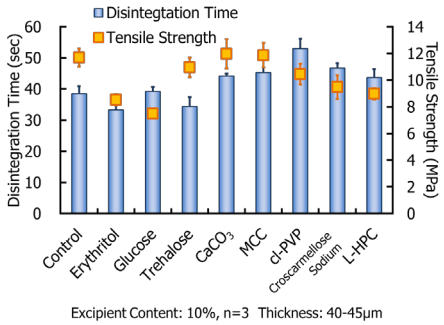
Increasing HPC-SL concentration led to increased disintegration time while tensile strength was not affected (Fig. 1). It was observed that film thickness increased in proportion to HPC concentration.

2. Effect of Drug



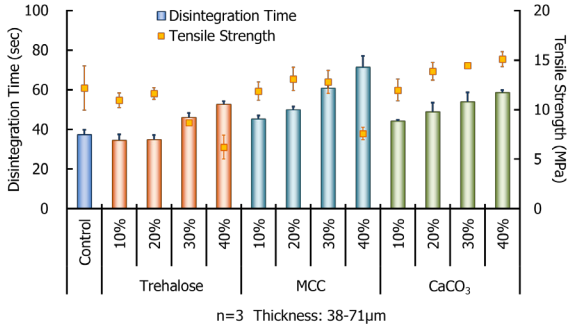
When drugs were added, tensile strength of HPC film reduced. This is perhaps caused by the hindered binding strength between HPC molecules by drug molecules. Also, disintegration time increased when AAP and IBU were added, while it did not change in the case of VC was added (Fig. 2).

3. Effect of Excipients



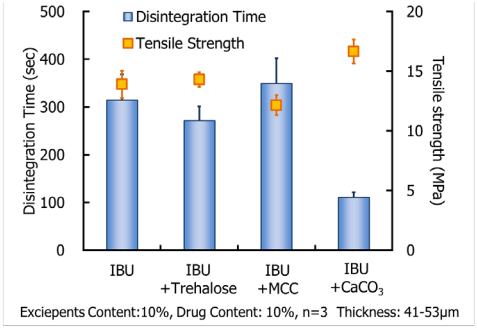
Remarkable improvement in disintegration time was not seen in when excipients were added. On the other hand, tensile strength was not affected, or reduced by addition of excipients (Fig 3).

4. Effect of Excipients Content



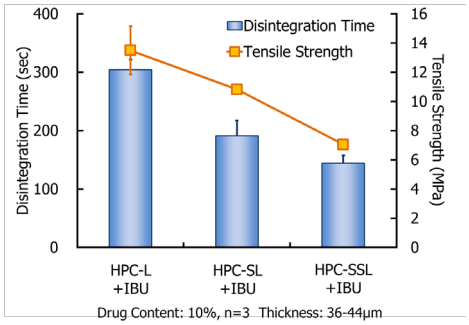
When $CaCO^3$ was added, tensile strength increased in proportion to its content in the range of 10-40%, while it reduced in the case of Trehalose and MCC. On the other hand, disintegration time increased in proportion to excipient contents in all case (Fig. 4).

5. Effect of Excipients on HPC Film containing Ibuprofen



When $CaCO^3$ was added, disintegration time reduced by 1/3 while tensile strength improved. Not much difference was seen for both disintegration time and tensile strength when trehalose and MCC were added (Fig. 5).

6. Effect of HPC Molecular Weight



In the case of HPC-L, which is higher molecular weight grade than HPC-SL, both disintegration time and tensile strength increased. On the other hand, in the case of HPC-SSL, which is the lowest molecular weight grade of HPC, disintegratability improved while tensile strength reduced (Fig. 6).

CONCLUSIONS

- It was observed that disintegration time of HPC film tended to increase in proportion to film thickness increasing depending on HPC contents, while tensile strength was independent.
- Disintegration time of film was much increased when formulating IBU, which is the most hydrophobic drug tested in this study.
- Disintegratability of HPC film containing IBU was improved by addition of $CaCO^3$.
- The film with lower molecular weight HPC (HPC-SSL) showed the faster disintegration and moderate tensile strength.

Based on these results it was suggested that ODF could be designed and prepared by using HPC as base material.

REFERENCES

1. Umemura, K.; Yamakawa, R.; Takeuchi, Y. and Takeuchi, H. Usability of PVA Co-polymer as a New Type of Film Former for Orally Disintegrating Film Dosage Form. The 25th Annual Meeting of the Academy of Pharmaceutical Science and Technology, Japan (2010).
2. Takeuchi, H.; Yamakawa, R.; Nishimatsu, T.; Takeuchi, Y.; Hayakawa, K. and Maruyama, N. Design of rapidly disintegrating drug delivery films for oral doses with hydoxypropyl methylcellulose. J. DRUG DEL. SCI. TECH., 23 (5), 471-475 (2013).
3. NISSO HPC Technical Data: www.nissoexcipients.com

[1]This data was originally presented at the 41st Annual Meeting of the Controlled Release Society as the poster: "Evaluation of Hydroxypropyl Cellulose for Orally Disintegrating Film Drug Application" by
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