The Influences of Various Binders on the Film Properties of Pseudoephedrine HCl-layered Pellets in Wurster Coating System

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PURPOSE

In order to get formulations once-daily containing the high dose(120mg) of pseudoephedrine HCl(PE), the multiparticulate system was developed through Wurster coating system.

METHODS

After the mixture of PE and various binders were stored under stress conditions (40˚C/75% RH) for 4 weeks, the contents of PE were evaluated using HPLC and the candidates were selected. After polyvinylpyrrolidone (PVP) and hypromellose(HPMC) were applied as a binder with PE in the 1st layer respectively in various manufacturing conditions, ethylcellulose(EC) was layered on the 1st layer as a dissolution-controlling membrane. The surface of the coated pellets was identified with FE-SEM analysis.

FORMULATION AND PROCESS CONDITIONS

Formulation

Layer	Function	Composition
1st Drug Layer	Seed	Sugar spheres 25-30(Paular)
	API	Pseudoepherdine hydrochloride(MALLADI)
	Binder	Polyvinylpyrrolidone(BASF) / Hypromellose(Shinetsu)
	Glidant	Aerosil 200(Evonik)
2nd Barrier Membrane	Polymer	Aquacoat ECD-30(FMC Biopolymer)
	Plasticizer	Triethyl citrate(BASF)
	Pore former	Kollicoat IR(BASF)

Process

Parameter	1st Drug Layer	2nd Barrier membrane
Air volume(CMH)	32	30
Product temperature(℃)	38	33
Feed rate(g/min)	20	6
Atomizing air(bar)	1.5	1.7
Final batch size(g)	1,200	850

RESULTS

FINAL PRODUCT CHARACTERISTICS

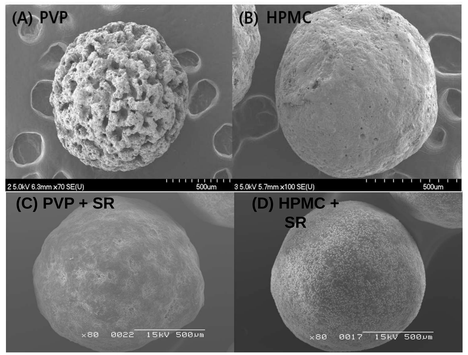

Figure 1. Influence of type of binder on the surface smoothness of pseudoephedrine coated layer
A) Binder : PVP, B) Binder : HPMC, C) SR coated pellet (A), D) SR coated pellet(B)

SUSTAINED RELEASE DISSOLUTION PROFILE

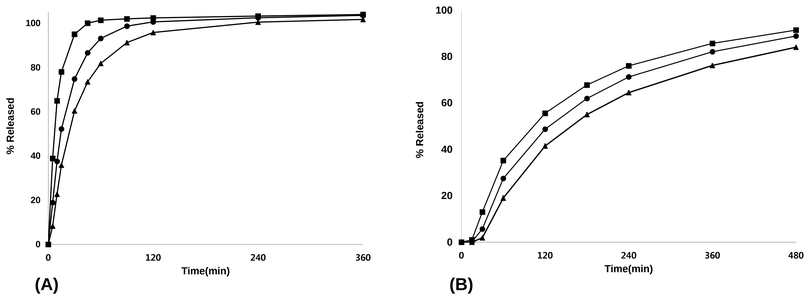

Figure 2. Drug release profiles from the ethylcellulose layered pellets containing different binders in the 1st drug layer; 15% wt. gain(■); 20% wt. gain(●); 25% wt. gain(▲)
A) Binder : PVP, B) Binder : HPMC

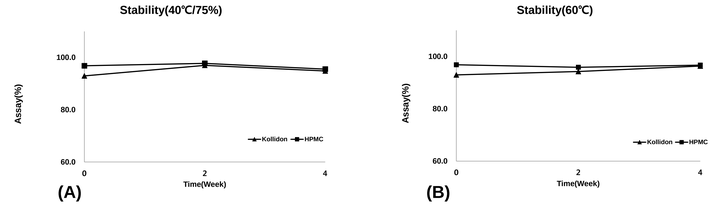

Figure3. Compatibility test of Pseudoephedrine HCl with different binders
A) 40℃, 75%RH, B) 60℃ storage chamber

Under stress conditions, PVP and HPMC did not show any chemical interaction with PE. The pellets coated with PVP as a binder showed much higher variation of dissolution than those with HPMC. And the mean dissolution rates of PVP-coated pellets also were higher by more than 10%(Figure 2). FE-SEM analysis explained that such differences were caused by the surface roughness of the 1st layered pellets which was dependent on the kind of binders(Figure 1). Although the effects of process variables such as air flow, atomizing air pressure, air temperature, and air humidity were evaluated respectively, significant improvement of the surface smoothness and variation of dissolution was not shown. This suggested that HPMC worked much better than PVP as a plasticizer as well as a binder in the coating with PE and supplied the suitable surface roughness to get a reliable EC-coated layer giving the reproducible release rates.

CONCLUSIONS

Though both of HPMC and PVP were showed no chemical interaction with PE under stress conditions, HPMC in the coated PE played an important role in the surface smoothness as a plasticizer as well as a binder which made 2nd EC-coated layer's release well controlled. The various manufacturing conditions in Wurster coating system could not control the weakness of PVP coated layer.

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