PTR 101

Evaluation of different binders for roller compaction

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Objectives

When preparing tablets by roller compaction, managing compactability and friability can be challenging due to the double compression process. Binders are critical functional ingredients in tablets prepared by roller compaction. This study compares binder performance in tablets prepared by roller compaction.

Introduction

Roller compaction is an economical granulation technology that requires fewer processing steps and less processing equipment than wet granulation. Roller compaction can improve flow and density properties that are often lacking in direct compression formulations. It is a good alternative to wet granulation for formulations that have poor flowability. As no water or solvent is added to ingredients, roller compaction is also suitable for APIs that are sensitive to moisture. There are two challenges, however, in preparing tablets by roller compaction; namely compactability and friability, which are adversely impacted by the double compression process. This study evaluates the performance of different binders: hydroxypropylcellulose (Klucel™ EXF HPC), copovidone (Plasdone™ S-630 PVP/VA), hypromellose (Benecel™ E15 HPMC), povidone (Plasdone™ K-29/32 PVP) and ethylcellulose (Aqualon™ T10 EC), in tablets prepared by roller compaction. Metformin HCl and acetaminophen, which are poorly flowable and poorly compactable, were chosen as model drugs in this study.

Experimental methods

Mixtures of 75.8% metformin, different levels of binder (0% or 6%) and mannitol (see Table 1) were roller compacted at a roll pressure of 60 bar (TFG LAB Micro; Freund-Vector Corporation, USA) and then milled, lubricated with magnesium stearate and compressed to 660 mg tablets (8 station, Mini press II; Karnavati Engineering, India) under different compaction forces (10, 15, 20, 25 kN).

Table 1. Metformin formulations

	0% binder		6% binder	
Ingredients	**mg/tablet**	**%**	**mg/tablet**	**%**
Metformin HCl	500	75.8	500	75.8
Mannitol	157	23.8	117.4	17.8
Binder *	0	0	39.6	6
Mg stearate	3	0.4	3	0.4
Total	**660**	**100**	**660**	**100**

Note: This work was presented at the annual meeting of the American Association of Pharmaceutical Scientists, October 25–29, 2015, Orlando, Florida.

Additionally, mixtures of 60% acetaminophen, different levels of binder (0% or 6%), mannitol, Polyplasdone™ XL crospovidone (PVPP) and 0.3% silicon dioxide (see Table 2) were roller compacted at a roll pressure of 60 bar and then milled with the other 0.3% silicon dioxide; lubricated with magnesium stearate, stearate acid and talc and compressed to 500 mg tablets under different compaction forces.

	0% binder		6% binder	
Ingredients	**mg/tablet**	**%**	**mg/tablet**	**%**
Acetaminophen	300	60	300	60
Mannitol	164	32.8	134	26.8
Binder *	0	0	30	6
Polyplasdone™ XL crospovidone	15	3	15	3
Silicon dioxide	3	0.6	3	0.6
Talcum	10	2	10	2
Magnesium stearate	4	0.8	4	0.8
Stearic acid	4	0.8	4	0.8
Total	**500 mg**	**100%**	**500 mg**	**100%**

Breaking force: Breaking force of tablets made with different binders and compaction forces were evaluated using a TBH 300MD (Erweka GmbH, Germany).

Tablet friability: Friability was evaluated using a Tar200 friability tester (Erweka GmbH, Germany).

Dissolution: All dissolution testing was conducted using tablets that were compressed with 20 kN force. Dissolution of metformin tablets was conducted using 1000 mL of pH 6.8 phosphate buffer media with USP Apparatus II at 50 rpm. Dissolution of APAP tablets was conducted using 900 mL of pH 5.8 phosphate buffer media with USP Apparatus II at 50 rpm. Samples were taken at 5, 10, 15, 30 and 45 min and evaluated with UV-Vis.

Materials

Metformin HCl, CP, Shouguang Fukang Pharmaceutical Co. Ltd, Shandong Province, China

Acetaminophen, CP, Hebei Jiheng (Group) Pharmaceutical Co. Ltd, Hebei Province, China

Klucel™ EXF hydroxypropylcellulose (HPC); Plasdone™ S-630 copovidone (PVP/VA); Benecel™ E15 hypromellose (HPMC); Plasdone™ K-29/32 povidone (PVP); Aqualon™ T10 ethylcellulose (EC) and Polyplasdone™ crospovidone (PVPP) all marketed by Ashland Inc., USA.

Mannitol: Pearlitol™ SD200, Roquette Inc., France

Results and Discussion

Klucel EXF HPC provided better compactability than other binders for both metformin and acetaminophen formulations (see Figures 1 and 2). For acetaminophen formulations, Plasdone S-630 PVP/VA also performed very well. The effect of roll pressure was studied for acetaminophen tablets with 6% of Klucel™ EXF HPC or Plasdone™ S-630 PVP/VA (see Figure 3). Increasing roll pressure from 50 bar to 70 bar has little effect on compactability of the acetaminophen formulation with Plasdone S-630 PVP/VA in this study. For Klucel EXF HPC, lower roll pressure achieved higher tablet breaking forces.

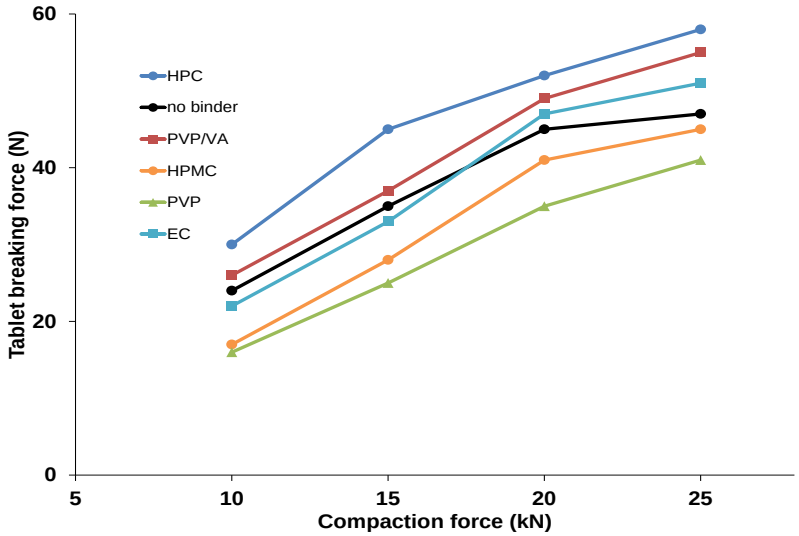

Figure 1. Tablet breaking force of metformin formulations with 0% or 6% binder

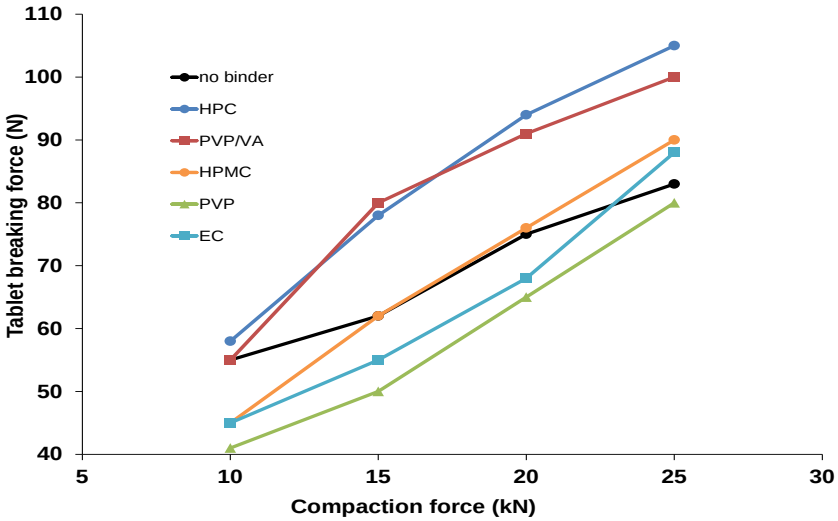

Figure 2. Tablet breaking force of acetaminophen formulations with 0% or 6% binder

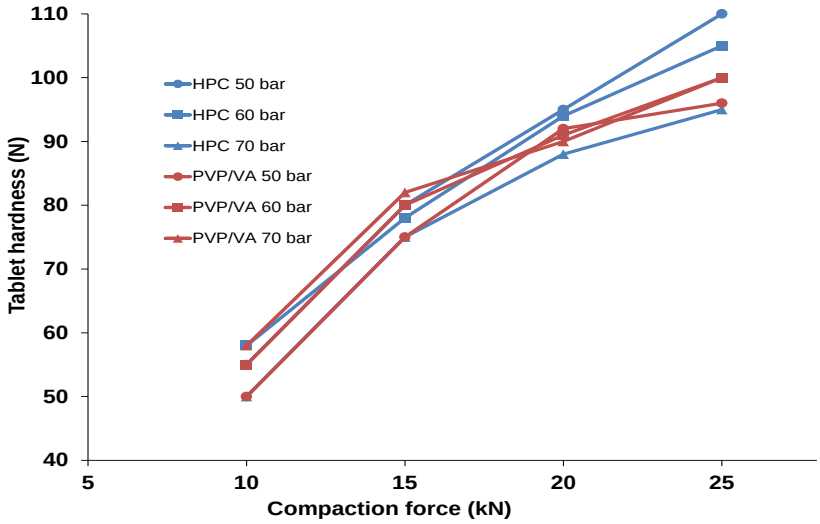

Figure 3. Tablet breaking force of acetaminophen formulations with HPC or PVP/VA at various roll pressure

As seen in Figures 4 and 5, Klucel™ EXF HPC provided the lowest friability for both metformin and acetaminophen formulations. No capping occurred during friability testing with Klucel EXF in formulations compressed at 10–25 kN. For other binders, capping occurred during friability testing for tablets compressed at very low or very high compression forces.

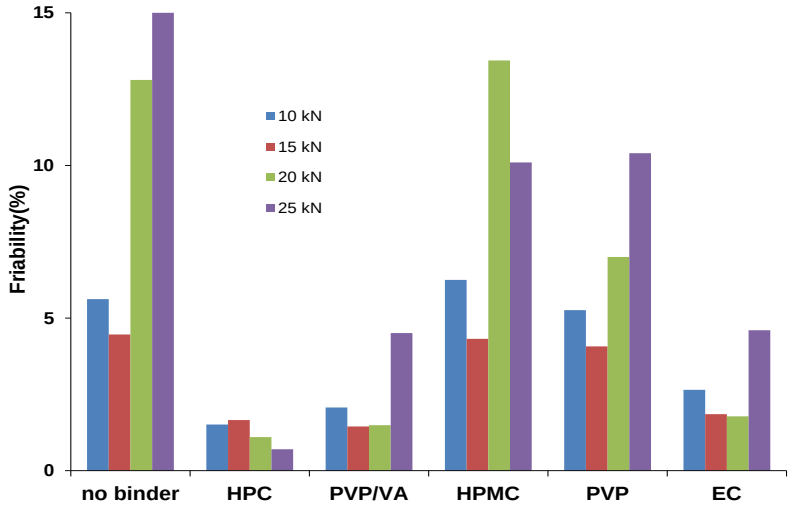

Fig 4 Friability of Metformin formulations with 0% or 6% binder

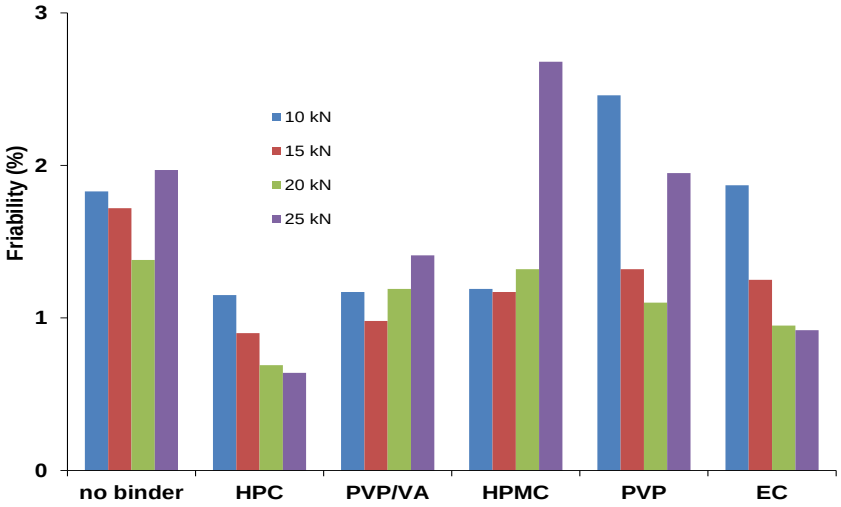

Fig 5. Friability of acetaminophen formulations with 0% or 6% binder

The dissolution results for metformin tablets and acetaminophen tablets with different binders were all acceptable and similar to one another (see Figures 6 and 7).

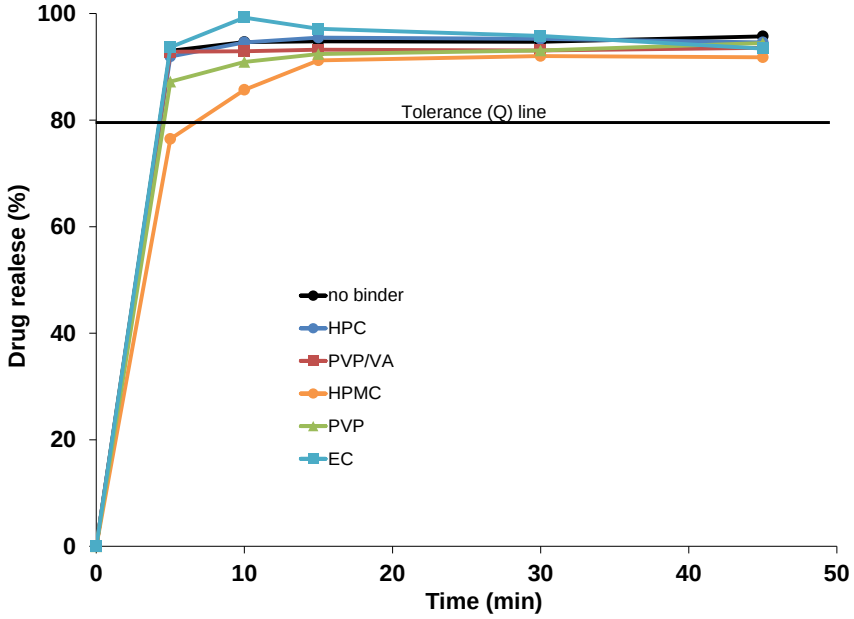

Fig 6. Dissolution of metformin formulations with 0% or 6% binder

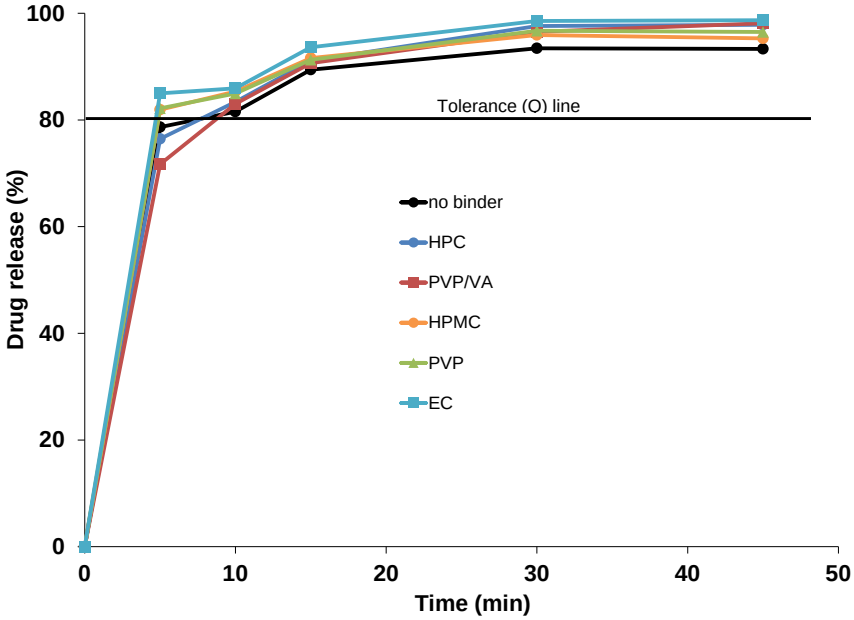

Fig 7. Dissolution of acetaminophen formulations with 0% or 6% binder

Conclusions

Klucel™ EXF HPC is a very effective binder for roller compaction, which provides consistently higher tablet strength and lower friability than many other binders. No capping occurred during tablet compaction and friability testing for formulations including Klucel EXF HPC.