PTR-097

Utility of Polyplasdone™ crospovidone as a Superdisintegrant

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Introduction

The goal of this study was to evaluate the effects of several superdisintegrants on disintegration time, breaking force, and drug release of different immediate-release (IR) tablet formulations. Ranitidine HCl was used as a model drug for direct compression (DC), and acetaminophen (APAP) was used as a model drug for wet-granulation methods.

It was found that the IR tablets of both formulations made with Polyplasdone XL crospovidones had shorter disintegration times and somewhat faster drug release than tablets made with other polymers. The superdisintegrants evaluated in this study were as follows:

- Polyplasdone crospovidone
- Competitive crospovidone
- Croscarmellose sodium
- Sodium starch glycolate
- L-HPC

Because the XL and Ultra grades of Polyplasdone crospovidone have the same physical and chemical properties (the only difference being in the level of impurities) these grades are used interchangeably in this study (see Table 1). The competitive CL and CL-F grades of crospovidone vary only in particle size and are also used interchangeably.

Table 1. Particle size distributions and peroxide levels of various superdisintegrants

Polymer Type	D10 (µm)	D50 (µm)	D90 (µm)	Mean (µm)	Peroxide (ppm)
Polyplasdone™ XL crospovidone	32.9	109.3	285	135.8	29
Polyplasdone XL-10 crospovidone	9.2	22.4	49.6	28	55.3
Polyplasdone Ultra crospovidone	51.4	113.3	234.3	131.6	9.2
Polyplasdone Ultra-10 crospovidone	9.9	24.6	51.2	28.6	22
Competitive CL crospovidone	16.1	68.5	185.6	86.5	151
Competitive CL-F crospovidone	12.1	34.8	103.1	47.7	217
Croscarmellose sodium	18.6	43.2	109.3	55.5	N/A
Sodium starch glycolate	21.3	41.8	67.3	43.3	N/A
L-HPC	15.2	50.7	135.2	65.8	N/A

Methods

Preparation of 600 mg IR Ranitidine HCl Tablets by Direct Compression. The first four ingredients in Table 2 were blended for 10 minutes in a V-blender. A mixture of silicon dioxide and magnesium stearate was passed through 35 mesh screen. This blend was combined with the first four ingredients and also blended in a V-blender, for 3 minutes. The final blend was compressed on a Manesty Betapress using 7/16" FFBE tooling, to a tablet weight of 600 mg. Tablet hardness, thickness, friability, and disintegration time were tested.

Table 2. IR Ranitidine HCl tablet formulation

Ingredients	Tablet formulation (% w/w)	Tablet weight (mg)
Ranitidine HCl	60	360
Microcrystalline cellulose	27.5	165
Benecel™ E6 HPMC	6	36
Superdisintegrant	5	30
Silicon dioxide	1	6
Magnesium stearate	0.5	3
Total	100	600

Dissolution. Dissolution (n = 6) was conducted in 900 ml DI water at 37°C using the USP apparatus II at 50 rpm paddle speed (Distek Dissolution System, Model 5100). The amount of ranitidine dissolved was monitored using a UV spectrophotometer (Agilent 8453) at 220 nm. Samples were taken at 7.5, 15, 30, and 45 minutes.

Preparation of 650mg Acetaminophen (APAP) Tablets by Wet Granulation. The intragranular ingredients listed in Table 3 were passed through a 14 mesh screen. The screened materials were mixed in a Collete high-shear mixer/granulator for 2 minutes. Purified water was sprayed in at 50 g/min, with the impeller at 295 rpm and chopper at 3554 rpm, until a suitable endpoint was achieved. The granulation was then put in an oven set to 65°C, and dried to NMT 2% moisture. The dried granulations were milled in a FitzMill with a 0.065" screen, knives forward and medium speed. The milled acetaminophen granulation and each superdisintegrant were passed through an 18 mesh screen and blended for 10 minutes. The magnesium stearate was passed through a 35 mesh screen, added to the blend, then blended for 3 minutes. The final blend was compressed on a Manesty Betapress using 7/16" FFBE tooling, to a tablet weight of 650 mg. Tablet hardness, thickness, friability, and disintegration time were tested.

Table 3. Acetaminophen tablet formulation

Ingredients	Tablet formulation (%w/w)	Tablet weight (mg)
Intragranular		
Acetaminophen (dense powder)	50	325
Lactose, regular, NF	21.8	141.4
Calcium sulfate hydrous, NF	21.8	141.4
Klucel™ EXF HPC	3	19.5
Extragranular		
Superdisintegrant	3	19.5
Magnesium stearate	0.5	3.3
Total	100	650

Dissolution. Dissolution (n = 3) was conducted in 900 ml pH 5.8 phosphate buffer at 37°C using USP apparatus II at 50 rpm paddle speed (Distek Dissolution System, Model 5100). The amount of acetaminophen dissolved was monitored using a UV spectrophotometer (Agilent 8453) at 314 nm. Samples were taken at 7.5, 15, 30, and 45 minutes.

Results and Discussion

IR Ranitidine HCl Tablets. Figure 1 shows both Polyplasdone™ and L-HPC yielded harder tablets than other polymers; however, in Figure 2, L-HPC is seen to have the slowest drug release. Sodium starch glycolate not only yielded the softest tablets but also had slower drug release.

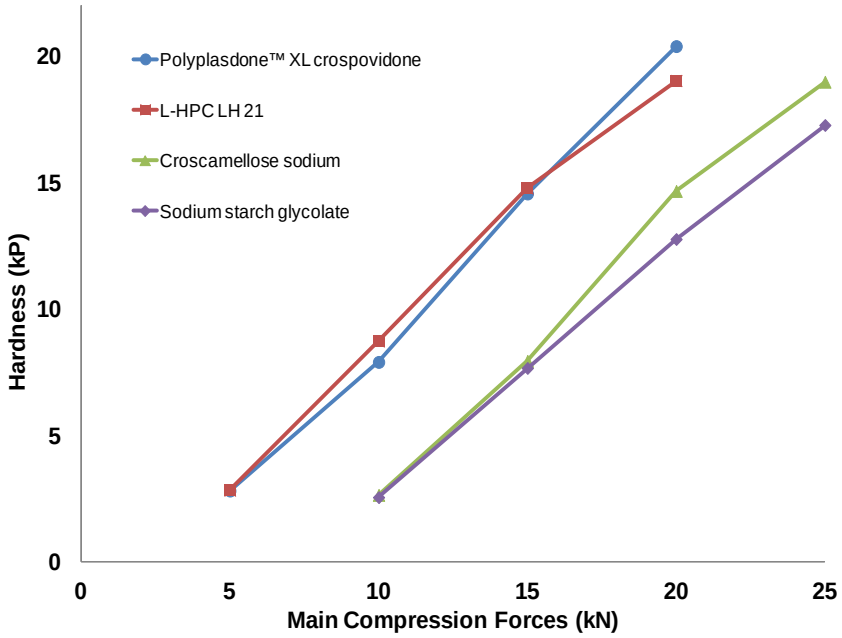

Figure 1. Effect of compression force on hardness of IR ranitidine HCl tablets

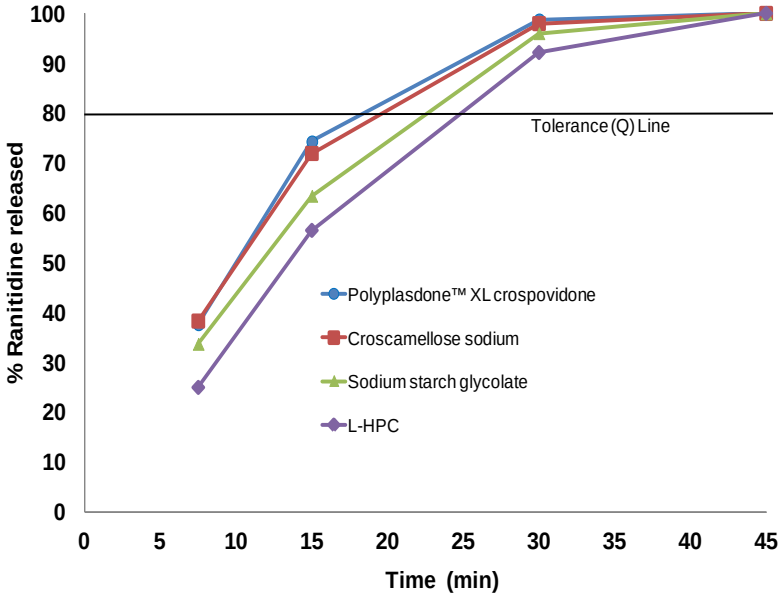

Figure 2. Dissolution profile of ranitidine tablets in DI water

IR Acetaminophen (APAP) Tablets. At low compression forces (10 and 15 kN), most tablets yielded similar hardness results, but at higher compression forces, the tablets with Polyplasdone™ XL crospovidone or croscamellose sodium yielded harder tablets than other polymers (Figure 3). However, Figure 4 shows that tablets with L-HPC or croscamellose sodium had longer disintegration times than the tablets made with Polyplasdone crospovidone.

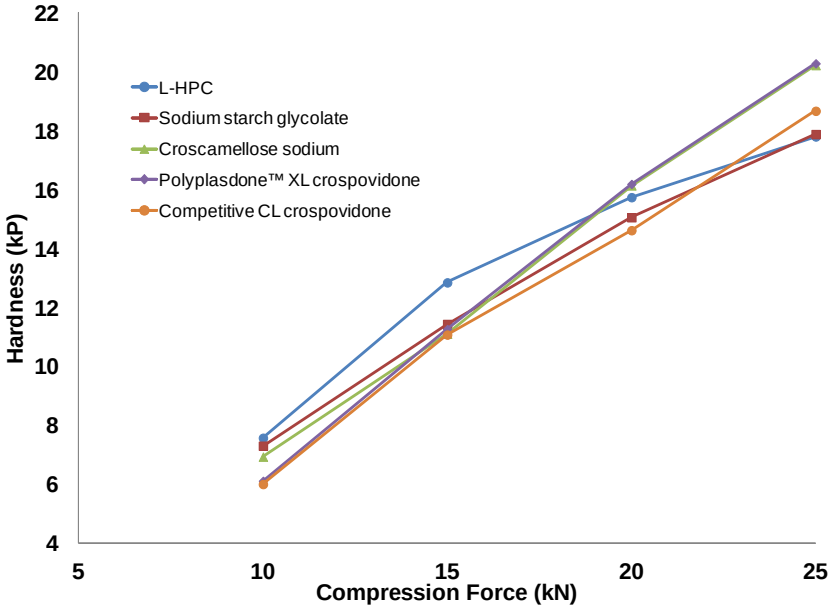

Figure 3. Effect of compression force on hardness of IR acetaminophen tablets

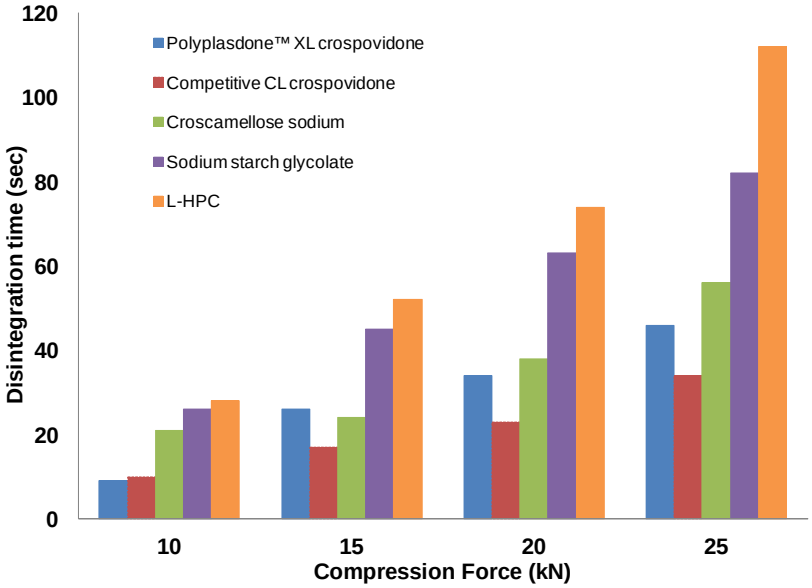

Figure 4. Disintegration time of IR acetaminophen tablets

The dissolution profiles of APAP tablets (Figure 5) show that all tablets with superdisintegrants easily achieved the USP acceptance criteria of 80% drug release within 60 minutes; the tablets without a superdisintegrant had the slowest drug release rate. Tablets made with a competitive crospovidone had the shortest disintegration time (Figure 4) but much softer tablets (Figure 3), and gave the slowest drug release (Figure 5) compared with the other superdisintegrants evaluated here.

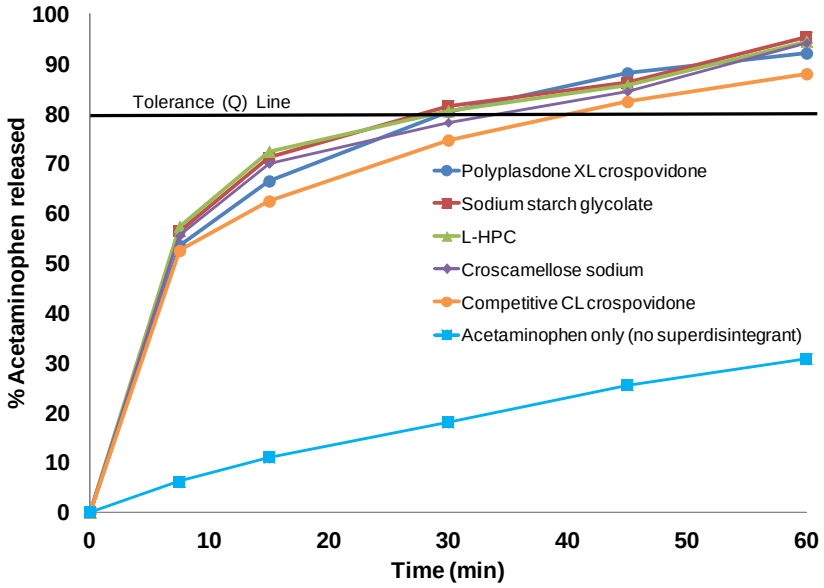

Figure 5. Dissolution profile of acetaminophen tablets in pH 5.8 phosphate buffer

Conclusions

Immediate-release tablets of both formulations made with Polyplasdone™ XL crospovidones had shorter disintegration times and somewhat faster drug release than tablets made with other superdisintegrants. This results from the fact that Polyplasdone XL crospovidone has the largest PSD and is close to the average particle size of common active and inactive ingredients, thereby yielding better content uniformity than the other polymers.