Consumer Specialties
ashland.com

PTR-098

Utility of Polyplasdone™ crospovidone in Orally Disintegrating Tablet Formulations

Quyen Schwing, Marvin Davis, Divya Tewari, Thomas Dürig
Ashland Specialty Ingredients, Wilmington, Delaware 19808, USA

Introduction

The goal of this study was to evaluate the effect of several superdisintegrants on disintegration time, breaking force, and drug release of different orally disintegrating tablet (ODT) formulations. Acetaminophen (APAP) and fenofibrate were used as model drugs for wet granulation methods. The superdisintegrants tested were as follows:

- Polyplasdone crospovidone
- Competitive crospovidone
- Croscamellose 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. The competitive CL and CL-F grades of crospovidone vary only in particle size and are also used interchangeably. It was found that orally disintegrating tablets made with Polyplasdone XL and Ultra crospovidones have shorter disintegration times, lower friability, and faster drug release than tablets made with other polymers.

Methods

Preparation of 650 mg Acetaminophen (APAP) ODT by Wet Granulation. Passed the intragranular ingredients (Table 1) through a 14 mesh screen, Placed the screened materials into the Collete high-shear mixer/granulator and mixed for 2 minutes, then started spraying purified water at 50 g/min, with the impeller at 295 RPM and chopper at 3554 RPM, until a suitable endpoint was achieved. The granulation was placed in the oven with the temperature set at 65°C, and dried to NMT 2% moisture. Then the granulation was milled in the FitzMill with a 0.065" screen, knives forward, at medium speed. The milled APAP granulation and each superdisintegrant was screened through mesh 18 and blended for 10 minutes. Passed the magnesium stearate through a 35 mesh screen, added to the blend, and blended for 3 minutes. Collected the final blend and compressed on a Manesty Betapress using 7/16" FFBE tooling, to a tablet weight of 650 mg.

Table 1. Acetaminophen ODT formulation

Ingredients	Tablet formulation (%w/w)	Tablet weight (mg)
Intragranular		
Acetaminophen (dense powder)	50	325
Lactose, regular, NF	18.3	118.6
Calcium sulfate hydrous, NF	18.3	118.6
Klucel™ EXF hydroxypropylcellulose	3	19.5
Extragranular		
Superdisintegrant	10	65
Magnesium stearate	0.5	3.3
Total	100	650

For each tablet formulation we tested hardness, thickness, friability, and disintegration time.

Dissolution of APAP ODT Formulation. Dissolution (n = 3) was conducted in 900 ml pH 5.8 phosphate buffer media 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 220 nm. Samples were taken at 7.5, 15, 30, and 45 minutes.

Preparation of 348 mg Fenofibrate ODT by Wet Granulation. Dissolved Plasdone™ K29/32 povidone (Table 2) into a quantity of DI water calculated to be 15% of batch size, then dissolved sodium lauryl sulfate (SLS) completely in the povidone solution. The remaining intra-granular ingredients were passed through a 14 mesh screen. The screened materials were placed into the Collete high-shear mixer/granulator and mixed for 2 minutes, then the povidone-SLS solution 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 placed in the oven set to 65°C, and dried to NMT 2% moisture. The dried granulation was passed through the FitzMill with a 0.065" screen, knives forward and medium speed.

The milled fenofibrate granulation, each superdisintegrant and peppermint flavor were passed through an 18 mesh screen, and blended for 10 minutes. Magnesium stearate and silicon dioxide were passed through a 35 mesh screen, added to the fenofibrate blend, and blended for 3 minutes. The final blend was compressed on a Manesty Betapress using 3/8" FFBE tooling, to a tablet weight of 348 mg.

Table 2. Fenofibrate ODT tablet formulation

Ingredients	**Tablet Formulation (% w/w)**	**Tablet Weight (mg)**
Intragranular		
Fenofibrate	15.5	54
Mannitol	35	121.94
Microcrystalline cellulose	24	83.61
Sodium lauryl sulfate (SLS)	1.5	5.23
Plasdone™ K29/32 povidone	3	10.45
Extragranular		
Peppermint flavor	0.2	0.7
Superdisintegrant	20	69.68
Silicon dioxide	0.4	1.39
Magnesium stearate	0.4	1.39
Total	100	348.39

For each tablet formulation we tested hardness, thickness, friability, and disintegration time.

Dissolution of Fenofibrate ODT Formulations. Dissolution was carried out in 0.05M SLS, USP Apparatus II at 75 rpm for 60 minutes. Samples were withdrawn at 15, 30, 45, and 60 minutes and immediately diluted with methanol to prevent supersaturation solubility of the API in SLS solution. The diluted samples were filtered through a 0.45 µm nylon membrane and quantitated by HPLC with UV detection at 286 nm. Column: Synergi 4 µm Hydro-RP 80 Å, 250 × 4.6 mm.

Results and Discussion

Orally Disintegrating Acetaminophen Tablets. Figures 1 and 2 show that both Polyplasdone™ crospovidone and L-HPC yielded harder tablets with lower friability than other polymers; Figure 3 shows that tablets made with Polyplasdone XL crospovidone had the shortest disintegration time. The prolonged disintegration time in tablets made with L-HPC and croscamellose sodium can be related to their fibrous structure, which forms a gel-like mass upon hydration. The behavior of sodium starch glycolate tablets can be related to the main characteristics of starch, swelling and gelling. The dissolution profiles in Figure 4 show that all tablet formulations with superdisintegrants have similar percent drug release in phosphate pH 5.8 medium. However, tablets made with sodium starch glycolate gave the fastest drug release, due to the soft tablets breaking apart in ionic solution faster.

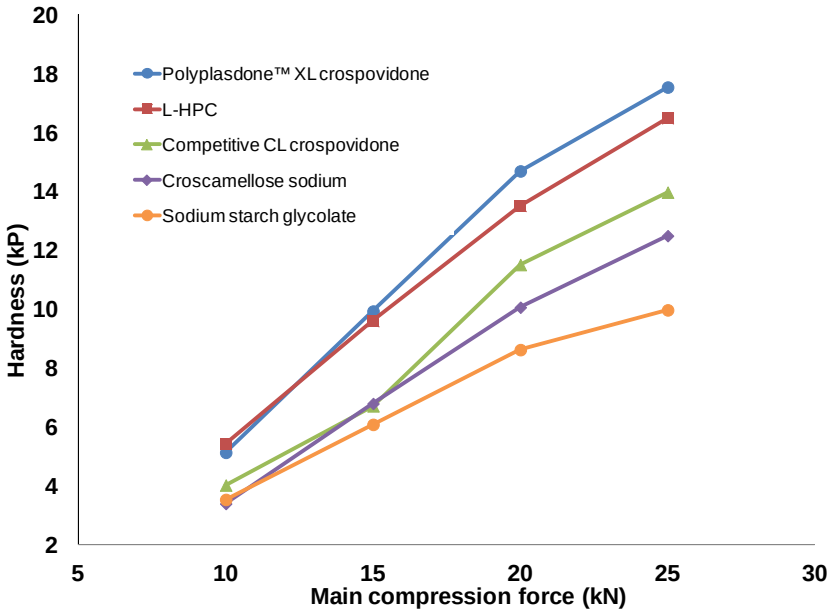

Figure 1. Effect of compression force on hardness of acetaminophen ODTs

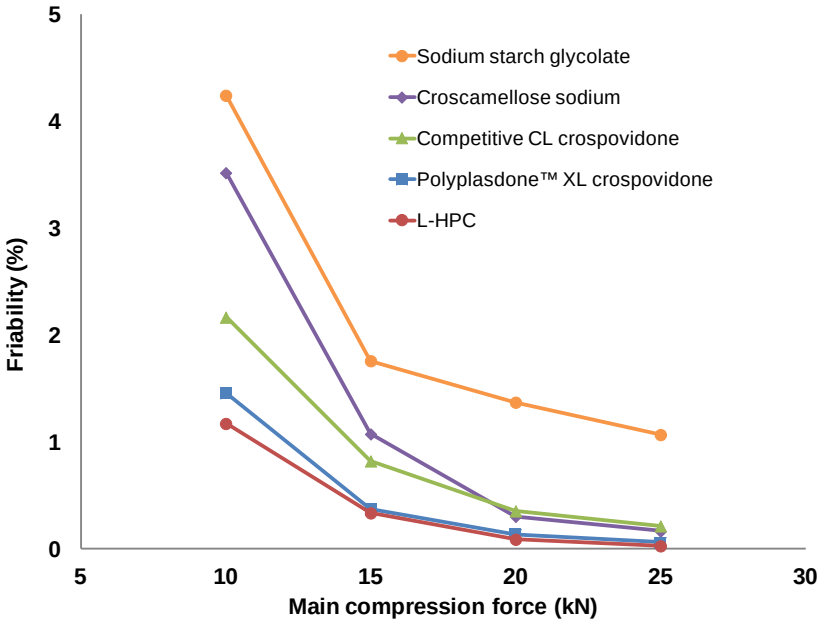

Figure 2. Effect of compression force on friability of acetaminophen ODTs

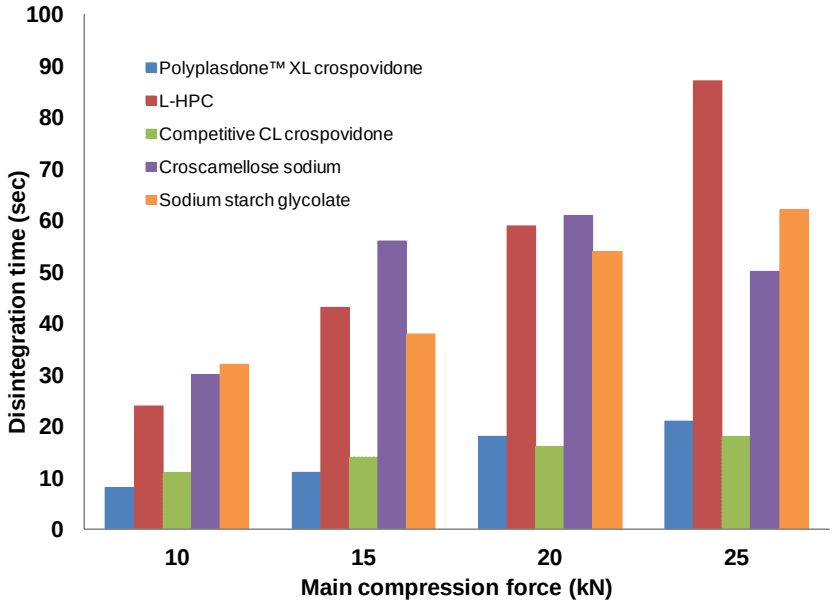

Figure 3. Effect of compression force on disintegration time of acetaminophen ODTs

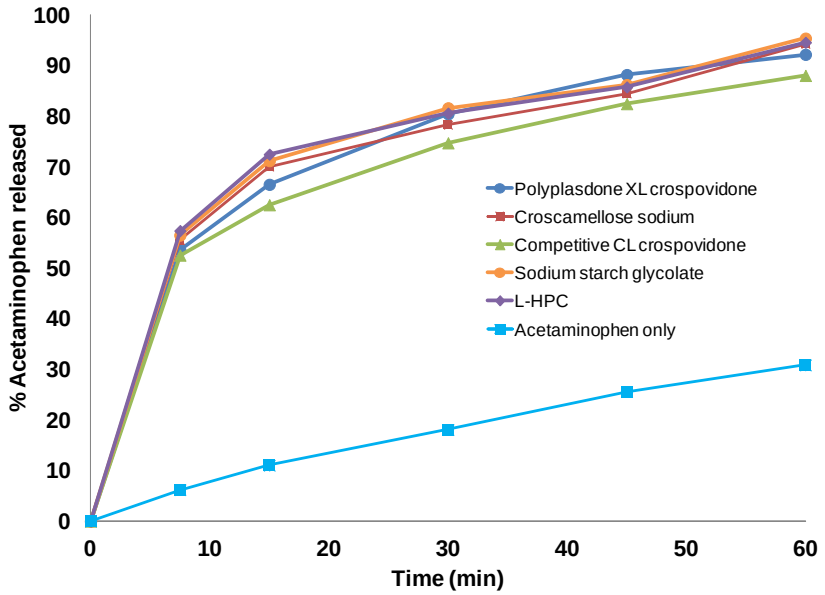

Figure 4. Dissolution profile of acetaminophen ODT in pH 5.8 phosphate buffer

Orally Disintegrating Fenofibrate Tablets. Figure 5 shows that fenofibrate ODTs made with Polyplasdone™ Ultra crospovidone have the highest breaking force. In addition, tablets made with croscamellose sodium and sodium starch glycolate had the longest disintegration times in DI water (Figure 6). These results may be related to the high level of free carboxylic groups within the disintegrants, which results in the formation of a gel layer, preventing further penetration of water into deeper parts of the tablets. Both Polyplasdone crospovidone and the competitive crospovidone showed much shorter disintegration times due to their wicking and swelling properties, which maintain the multiparticulate structure with a high surface area. Tablets made with Polyplasdone Ultra crospovidone had the shortest disintegration time.

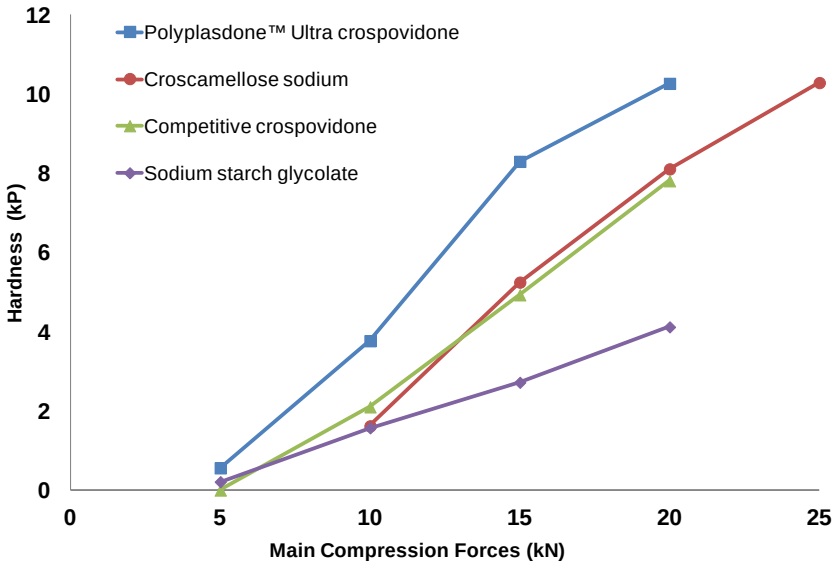

Figure 5. Effect of compression force on hardness of fenofibrate ODTs

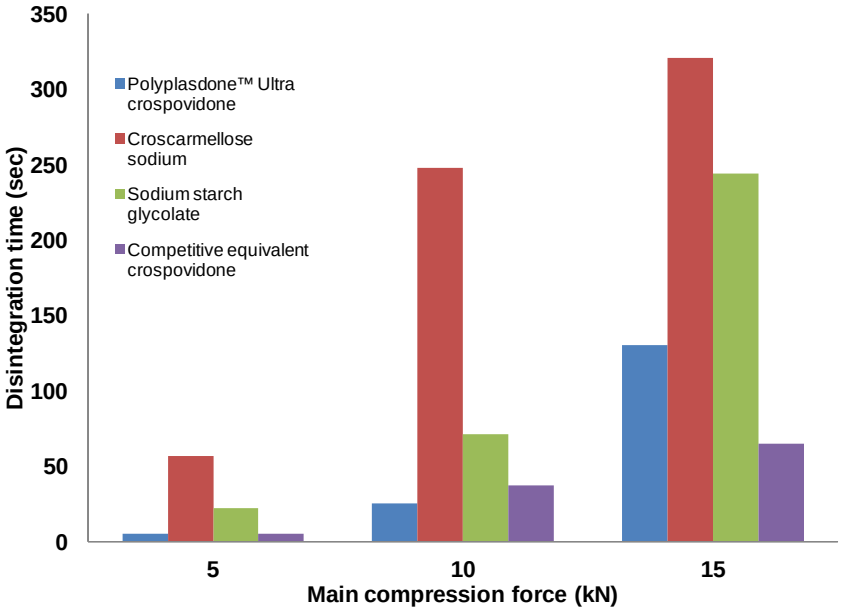

Figure 6. Effect of compression force on disintegration time of fenofibrate ODTs

The dissolution profiles of fenofibrate tablets show the tablets made with Polyplasdone Ultra crospovidone had the fastest drug release, when compared with the other tablets (Figure 7). Both sodium starch Glycolate and Croscamellose Sodium tablets showed slower drug release, which may be correlated with the prolonged disintegration time discussed above.

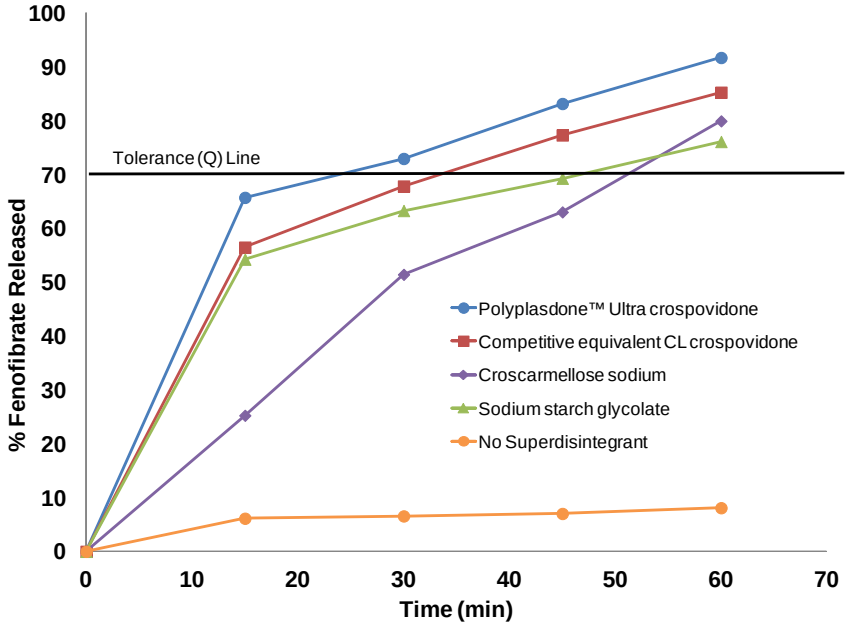

Figure 1. Dissolution profile of fenofibrate tablets (at initial time) in 0.025M SLS medium

Conclusions

From the results discussed above, and due to the physical and chemical properties of the various polymers, it was found that orally-disintegrating tablets of formulations made with Polyplasdone XL and Ultra crospovidones had shorter disintegration times and better friability than tablets made with other polymers.