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# Utility of Polyplasdone™ crospovidone as a Solubilizer

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## Introduction

Increasing the dissolution rate of poor soluble active pharmaceutical ingredients (APIs) is a major challenge in pharmaceutical formulation development. The goal of this study was evaluate the utility of several superdistegrants in wet-granulation tablet formulations to improve the rate of drug dissolution, using the poorly soluble model drugs meloxicam and fenofibrate.

It was found that, depending on the loading level, the inclusion of Polyplasdone crospovidone in tablet formulations can greatly increase the dissolution rate of the poorly soluble model drugs. The superdisintegrants evaluated in this work included the following:

- 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. The competitive CL and CL-F grades of crospovidone vary only in particle size and are also used interchangeably.

## Methods

***Preparation of 200 mg Meloxicam Tablets by Wet Granulation.*** Plasdone™ K 29/32 povidone was dissolved into a quantity of ethyl alcohol equal to 20% of the batch size (Table 1). The first five ingredients in Table 1 were passed through an 18 mesh screen. The screened materials were mixed for 2 minutes in a Glatt high-shear mixer/granulator, then the povidone-alcohol solution (10% w/v) was sprayed in at 25 g/min, with the impeller at 500 rpm and chopper at 500 rpm. More ethyl alcohol was added as needed, until a suitable endpoint was achieved. The granulation was dried at room temperature to NMT 2% moisture content. The granulations were then milled in a FitzMill with a 0.065" screen, knives forward and medium speed. The milled meloxicam granulation and each superdisintegrant were passed through an 18 mesh screen. Magnesium stearate and silicon dioxide were passed through a 35 mesh screen, added to the granulation, and blended for 3 minutes. The final blend was compressed using 5/16” FFBE tooling on a Manesty Betapress to a tablet weight of 200 mg. Tablet hardness, thickness, friability, and disintegration time were tested.

**Table 1. Meloxicam tablet formulation**

| Ingredients | Tablet formulation (%w/w) | Tablet weight (mg) |
|---|---|---|
| **Intragranular** | | |
| Meloxicam | 7.5 | 15 |
| Superdisintegrant | 5 | 10 |
| Mannitol | 44 | 88 |
| Aspartame | 1 | 2 |
| Spray-dried lactose | 37.5 | 75 |
| Plasdone™ K29/32 povidone | 2 | 4 |
| **Extra-granular** | | |
| Sillicon dioxide | 2 | 4 |
| Magnesium stearate | 1 | 2 |
| Total | 100 | 200 |

***Dissolution.*** Dissolution (n = 3) was conducted in 900 ml pH 7.5 phosphate buffer at 37°C using USP apparatus II at 75 rpm paddle speed (Distek Dissolution System, Model 5100). The amount of meloxicam dissolved was monitored using a UV spectrophotometer (Agilent 8453) at 362 nm. Samples were taken at 7.5, 15, and 30 minutes.

***Preparation of 348 mg ODT Fenofibrate Tablets (20% Superdisintegrant) by Wet Granulation.*** Plasdone K29/32 povidone (Table 2) was dissolved into a quantity of DI water equal to 15% of the batch size, then sodium lauryl sulfate was dissolved in the povidone solution. The remaining intragranular ingredients listed in Table 2 were passed through a 14 mesh screen. The screened materials were mixed for 2 minutes in a Collete high-shear mixer/granulator, then the povidone 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 dried in an oven set to 65°C to NMT 2% moisture. The dried granulation was milled in a 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 blend, and blended for 3 minutes. The final blend was compressed using 3/8" FFBE tooling on a Manesty Betapress, to a tablet weight of 348 mg. Tablet hardness, thickness, friability, and disintegration time were tested.

**Table 2. ODT fenofibrate tablet formulation**

| Ingredients | Granulation formula | Tablet formulation (%w/w) | Tablet weight (mg) |
|---|---|---|---|
| **Intragranular** | | | |
| Fenofibrate | 15.5 | 15.5 | 54 |
| Mannitol | 35 | 35 | 121.94 |
| Microcrystalline cellulose | 24 | 24 | 83.61 |
| Sodium lauryl sulfate | 1.5 | 1.5 | 5.23 |
| Plasdone™ K29/32 povidone | 3 | 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 | 79 | 100 | 348.39 |

***Dissolution.*** Dissolution was carried out in 0.025M sodium lauryl sulfate, 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 precipitation of the API from 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 80A, 250 × 4.6 mm.

***Preparation of 302.5 mg IR Fenofibrate Tablets (8% Superdisintegrant) by Wet Granulation.*** The IR fenofibrate tablets were prepared in the same manner as the ODT fenofibrate tablets. The formulation is shown in Table 3. Dissolution was also tested using the same method as that used for the ODT fenofibrate tablets.

**Table 3. IR fenofibrate tablet formulation**

| Ingredients | Tablet formulation (%w/w) | Tablet weight (mg) |
|---|---|---|
| **Intragranular** | | |
| Fenofibrate | 17.85 | 54 |
| Mannitol | 40.31 | 121.94 |
| Microcrystalline cellulose | 27.64 | 83.61 |
| Sodium lauryl sulfate | 1.73 | 5.23 |
| Plasdone™ K29/32 povidone | 3.47 | 10.48 |
| **Extragranular** | | |
| Peppermint flavor | 0.2 | 0.61 |
| Superdisintegrant | 8 | 24.2 |
| Silicon dioxide | 0.4 | 1.21 |
| Magnesium stearate | 0.4 | 1.21 |
| Total | 100 | 302.51 |

## Results and Discussion

***Meloxicam Tablets.*** The dissolution profiles of meloxicam tablets show that all tablets with superdisintegrants easily achieved the USP acceptance criterion of 70% drug release within 30 minutes; the tablets without superdisintegrant had the slowest drug release. Tablets made with Polyplasdone XL-10 crospovidone gave the fastest drug release in phosphate buffer pH 7.5 compared with the other formulations.

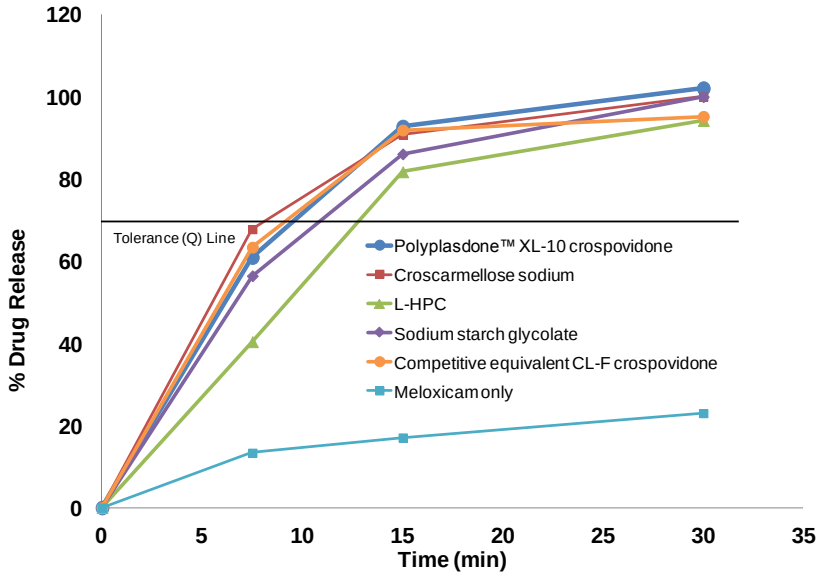


**Figure 1. Dissolution profiles of meloxicam tablets in pH 7.5 phosphate buffer**

***ODT Fenofibrate Tablets.*** The dissolution profiles of ODT fenofibrate tablets shown in Figure 2 demonstrate that all tablets with superdisintegrants easily achieved the USP acceptance criterion of 70% drug release within 60 minutes; the tablets without any superdisintegrant had the slowest release. Also, tablets made with Polyplasdone™ Ultra crospovidone had the highest percent drug release of all.

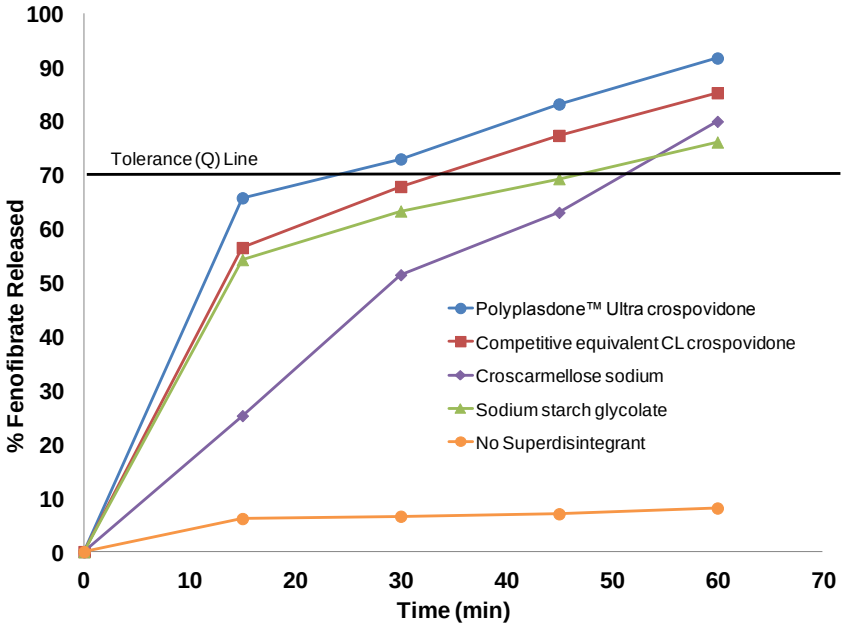


**Figure 2. Dissolution profile of ODT fenofibrate tablets in 0.025M sodium lauryl sulfate**

Figure 3 shows that the IR fenofibrate tablets did not meet the USP acceptance criterion of 70% drug release in 60 minutes. Figure 4 shows that the ODT fenofibrate tablets had greater percent drug release after 60 minutes than the IR tablets, which have lower levels of superdisintegrants.

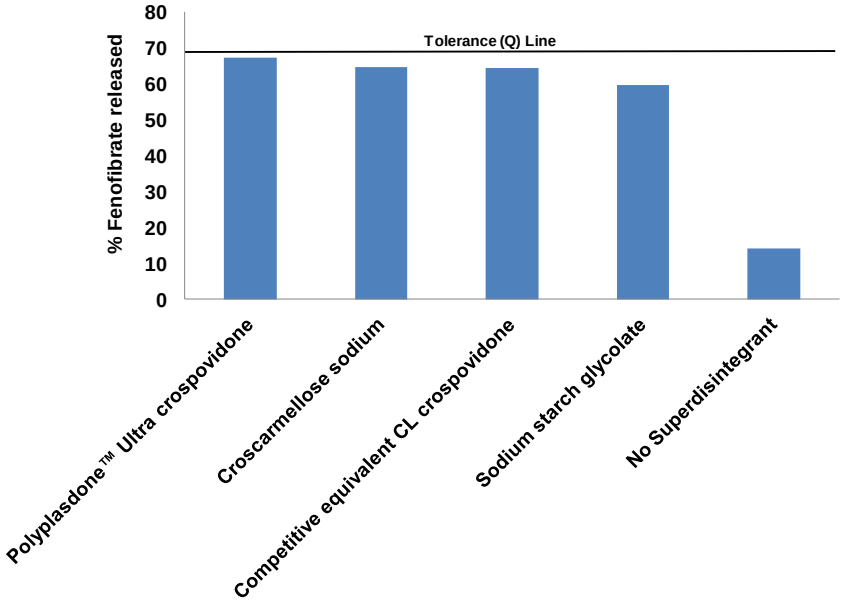


**Figure 3. Dissolution of IR fenofibrate tablets after 60 minutes in 0.025M SLS media**

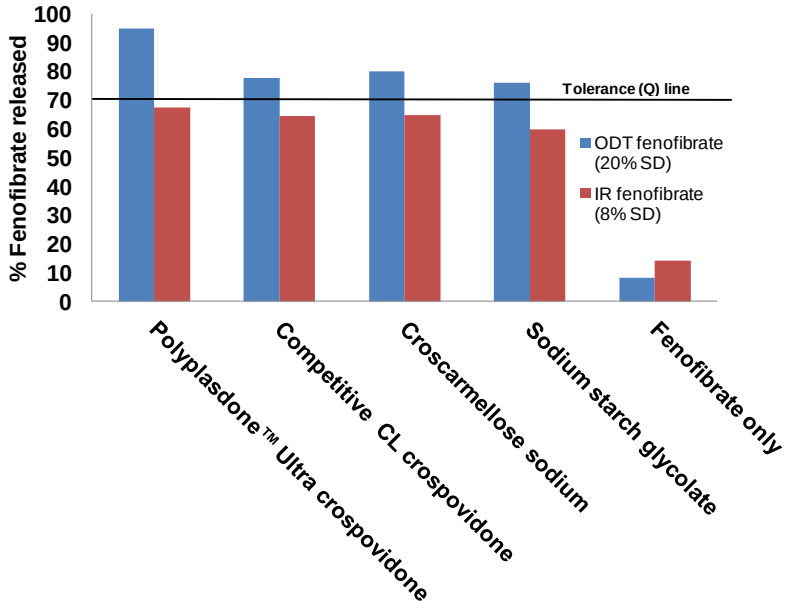


**Figure 4. Dissolution Comparison Between ODT (20%) and 8% Superdisintegrant Tablet Formulations**

## Conclusions

The dissolution rates of both poorly soluble APIs (meloxicam and fenofibrate) were increased greatly when formulated with superdisintegrants. Also, tablet formulations of both drugs made with Polyplasdone crospovidone had faster drug release than tablets made with other superdisintegrants. In addition, fenofibrate tablets with higher levels of Polyplasdone show better percent drug release than tablets with lower levels. On the basis of the data presented here, we conclude that Polyplasdone crospovidone can be used as a solubilizer to improve the dissolution of poorly soluble drugs.