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IMPACT OF CROSCARMELLOSE SODIUM FROM DIFFERENT MANUFACTURER ON IN-VITRO ANALYSIS OF S(-)PANTOPRAZOLE TABLETS

PIMPLE S, MAURYA P, SINGH R, JOSHI A, GURJAR M, SHAH M
Formulation and Development (R&D), Emcure Pharmaceuticals Ltd. Bhosari, Pune, Maharashtra, India.

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Abstract: The pivotal objective of this study was to investigate the effect of manufacture specific Croscarmellose sodium on disintegration and drug dissolution parameters of S (-) Pantoprazole tablet. The study of Croscarmellose sodium was done, by considering two suppliers, FMC Biopolymer and DFE (Previously known as DMV Fonterra) in the formulations. The dissolution was carried out in USP apparatus II at 75 rpm in 0.1N HCl followed by 6.8 phosphate buffer as dissolution medium. The dissolution rate of the S (-) Pantoprazole was found highly dependent on the manufacturer of Croscarmellose sodium when used in same concentration. No effect of the diluents on the disintegration of tablet observed. Different formulations in which Croscarmellose sodium added intra or extra granularly have no significant effect on disintegration time and dissolution of S (-) Pantoprazole tablet. However when Croscarmellose sodium of different supplier in same concentration used shows drastic change in disintegration time and dissolution of S (-) Pantoprazole tablet. Similarity factor was calculated between % drug release of formulations of both suppliers and these results indicate that the dissolution of the formulation containing same concentration of Croscarmellose sodium of different supplier having remarkable change in rate of drug release from S (-) Pantoprazole tablet.

Keywords: S (-) Pantoprazole sodium; Disintegrants; Croscarmellose sodium (CCNa); FMC Biopolymer; DFE, Dissolution profile

Corresponding Author: MR. SRIKANT PIMPLE

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INTRODUCTION

Convenience of administration and patient compliance are gaining significant importance in design of dosage form. Disintegrants are substances or mixture of substances added in the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants[1,4]. The inclusion of right disintegrants is a prerequisite to get optimal bioavailability in tablets and capsules. The objectives behind addition of disintegrants are to increase surface area of the tablet fragments and to overcome cohesive forces that keep particles together in a tablet. The demand for faster disintegrating formulation is increased as per time. So, pharmaceutical manufacturers needs to formulate fast disintegrating dosage forms by employing superdisintegrants which are effective at low concentrations and have greater disintegrating efficiency and are more effective intra granularly. But the major drawback is their hygroscopic nature, therefore not used with moisture sensitive drugs[5]. The choice of superdisintegrant for a tablet formulation depends largely on the nature of the drug being used. For example, the solubility of the drug component could affect the rate and mechanism of tablet disintegration. Superdisintegrants such as Croscarmellose sodium, sodium starch glycolate (SSG), and Crospovidone are now frequently used in tablet formulations to improve the rate and extent of tablet disintegration and thus improve the rate of drug dissolution[11].

S (-) Pantoprazole is a proton pump inhibitor, belongs to group of benzimidazole, used for the treatment of gastric and duodenum ulcers. Chirally pure S (-) Pantoprazole is more potent and cycloprotective, it has consistent pharmacokinetics and half dose of racemate is required for treatment. It offers lesser potential for drug interaction in comparison to racemic Pantoprazole. S (-) Pantoprazole undergoes degradation in acid medium of the stomach, can be coated with enteric coating polymer that will safely deliver the drug in the small intestine. An enteric coating is a barrier applied to oral medication that controls the location in the digestive system where it is absorbed. Most enteric coatings work by presenting a surface that is stable at the highly acidic pH found in the stomach, but breaks down rapidly at a less acidic (relatively more basic) pH. An Ideal enteric polymer should possess a hydrophilic and hydrophobic monomeric unit. Methacrylic acid and methyl methacrylate could make an ideal hydrophilic and hydrophobic unit respectively. Such compositions of polymer are essentially insoluble in gastric fluids and may help transportation of drugs across the proximal alimentary tract without degradation.

It accumulates in the acidic compartment of parietal cells and is converted to the active form, a sulphanilamide, which binds to hydrogen-potassium-ATP-ase at the secretory surface of gastric parietal cells. Inhibition of hydrogen-potassium-ATP-ase blocks the final step of gastric acid production, leading to inhibition of both basal and stimulated acid secretion. The duration of

inhibition of acid secretion does not correlate with the much shorter elimination half-life of PTZ[2, 9, 10, 12]. S (-) Pantoprazole is well absorbed when administered as an enteric-coated, delayed release tablet, with an oral bioavailability of 77%. It is hepatically metabolized via cytochrome P2C19 to hydroxypantoprazole, an inactive metabolite that subsequently undergoes sulphate conjugation. The elimination half-life ranges from 0.9 to 1.9 hours and is independent of dose[3].

MATERIALS AND METHODS:

Materials

Materials used in this study were S (-) Pantoprazole sodium obtained from Emcure Pharmaceuticals limited Pune, Mannitol from Roquette Pharma, Croscarmellose sodium from FMC Biopolymers and DFE (Previously known as DMV Fonterra), Sodium Carbonate Anhydrous from Kronox Lab Sciences, PVP K 90 from BASF, Crospovidone (Polyplasdone XL) from ISP Pharmaceuticals, Calcium stearate from Ferro and purified water.

Methods

Accurately weighed quantities of S (-) Pantoprazole Sodium, Croscarmellose Sodium & Mannitol were shifted from 40 # sieve. Sodium carbonate anhydrous was milled through the Multimill & passed through 60 # sieve. Above sifted materials were transferred in a rapid mixer granulator and mixed for about 10 minutes. Binder solution of PVPK-90 in purified water was prepared and added to above mixture to get wet mass. The wet mass passed through 10mm screen and dried in FBD. Polyplasdone XL and Croscarmellose Sodium were sifted through 40 # sieve and mixed with dried granules for about 15 minutes. Calcium Stearate was sifted through 60 # sieve and mix with above granules for about 5 minutes. The lubricated granules were compressed into tablets by using 7.4 mm standard concave punch having average weight 140 mg and hardness about 5 kp. Same procedure was followed for all the formulation as given in Table 1.

RESULT AND DISCUSSION:

Six formulations of S (-) Pantoprazole sodium were prepared by wet granulation technique with different batches of S (-) Pantoprazole sodium and Croscarmellose sodium from two different suppliers. Core and coated tablet of S (-) Pantoprazole was evaluated for various parameters like hardness, thickness, friability, disintegration and dissolution. Results obtained from different trials were shown in Table 2, and were found well within acceptable limit except the disintegration time as disintegration time of formulations with Croscarmellose sodium from FMC was on higher side. Viscosity of Croscarmellose sodium from two different manufacturers was evaluated by Ostwald viscometer. It was observed that Croscarmellose sodium from FMC Biopolymer showed higher viscosity in comparison with DFE when used in same concentration.

The disintegration time for formulations (F1, F2, & F5) with Croscarmellose sodium from FMC was similar. Disintegration time of formulations (F3&F4) having Croscarmellose sodium from DFE was same. In-vitro dissolution test was performed for all formulations. Dissolution of core tablet of formulations F3&F4 has average dissolution 84.31% and 90.62% respectively in 45 minutes. However formulation F1, F2, & F5 having dissolution 36.17%, 32.88%, 21.00% respectively in 45 minutes. The graph were plotted against tablet and % drug release (Figure 1). It was also observed that addition of disintegrants extra granularly leads to slightly improved drug release. From the results it was observed that formulation having Croscarmellose sodium of FMC (F1, F2, & F5) swell in the dissolution vessel, form matrix and release of drug was retarded. However formulations F3 & F4 having Croscarmellose sodium of DFE disintegrate completely by erosion and give 100% release.

CONCLUSION:

Different trials were taken to study the behaviour of Croscarmellose Sodium of two different suppliers. It was observed that different formulations having same excipients and Croscarmellose sodium of different supplier shows a drastic change in disintegration and in-vitro drug release. However to confirm this S (-) Pantoprazole sodium of different batch was used to see the effect of Croscarmellose sodium. Results showed no effect of API on disintegration time and dissolution of the tablets. All the batches of S (-) Pantoprazole tablets shows a remarkable reduction in % drug release when formulated with Croscarmellose Sodium from FMC Biopolymer. Whereas when same batches were taken with Croscarmellose Sodium from DFE then it shows a remarkable increase in % drug release. From viscosity study it was observed that Croscarmellose sodium of FMC was more viscous as compare to Croscarmellose sodium of DFE when used in same concentration, which directly affect the disintegration and dissolution of drug product. Disintegration time by using Croscarmellose sodium of FMC was 20-23 minutes which is very higher than Croscarmellose sodium of DFE which is 4-5 minutes. From the above study it can also be concluded that reduced quantity of Croscarmellose sodium from FMC Biopolymer can be used to obtain the desired results and optimization of the quantity of Croscarmellose sodium from FMC Biopolymer can be done.

Table 1: Comparison of Different Formulation of S (-) Pantoprazole Sodium Tablet

Ingredients	F1	F2	F3	F4	F5
Formulations	Batch with CCNa from FMC	Batch with CCNa from FMC	Batch with CCNa from DFE intra granularly	Batch with CCNa from DFE extra granularly	Batch with CCNa from FMC extra granularly
S(-) Pantoprazole Sodium [Batch No. 1]	20.0	20.0	20.0	20.0	20.0

S(-) Pantoprazole Sodium [Batch No. 2]	-	-	-	-	-
Mannitol	70.0	70.0	70.0	70.0	70.0
Sodium Carbonate [Anhydrous]	20.0	20.0	20.0	20.0	20.0
Croscarmellose Sodium [FMC Biopolymer]	10.0	10.0	-	-	-
Croscarmellose Sodium [DMV Fonterra]	-	-	10.0	-	-
Povidone [PVP K- 90]	2.0	2.0	2.0	2.0	2.0
Purified Water	40.0	20.0	20.0	20.0	20.0
Croscarmellose Sodium [DMV Fonterra]	-	-	-	10.0	-
Croscarmellose Sodium [FMC Biopolymer]	-	-	-	-	10.0
Crospovidone [Polyplasdone XL]	15.0	15.0	15.0	15.0	15.0
Calcium Stearate	3.2	3.2	3.2	3.2	3.2
Total weight	**140.0**	**140.0**	**140.0**	**140.0**	**140.0**

Table 2: Evaluation of S (-) Pantoprazole Tablets

Formulation	F1	F2	F3	F4	F5
Weight in (mg)	140	140	140	140	140
Hardness (Kp)	6-7	4-5	4-5	3-4	3-4
Friability	0%	0%	0%	0%	0%
Thickness (mm)	3.2	3.2	3.2	3.2	3.2
In-vitro disintegration time (minute)	20 mins	20 mins	4 -5 mins	3-4 mins	19 mins

Table 3: Comparative % Drug Release of Formulation (F1to F5)

% Drug Release	F1	F2	F3	F4	F5
Min	32.44%	34.59%	75.68 %	85.75 %	16.91%
Max	38.97%	43.14%	103.55%	93.84%	24.73%
Average	36.17%	37.27%	84.31%	90.62%	21.00%

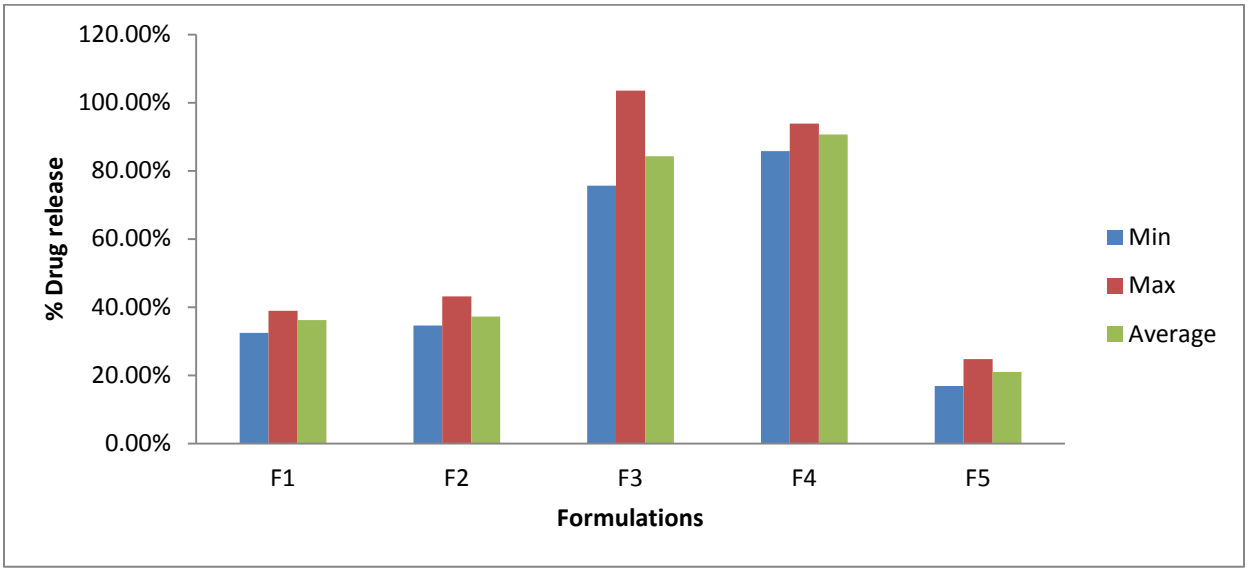

Figure: 1. Comparative % Drug Release of Formulation (F1to F5)

Table 4: Comparison of Different Batches of S (-) Pantoprazole Sodium Tablet (API from different batches)

Ingredients	F1	F2
S (-) Pantoprazole Sodium [Batch No. 1]	20.000	-
S (-) Pantoprazole Sodium [Batch No. 2]	-	20.000
Mannitol	69.800	69.800
Sodium Carbonate [Anhydrous]	20.000	20.000
Croscarmellose Sodium [FMC Biopolymer]	10.000	10.000
Povidone [PVP K- 90]	2.000	2.000
Purified Water	40.000	40.000
Crospovidone [Polyplasdone XL]	15.000	15.000
Calcium Stearate	3.200	3.200

Table 5: Evaluation of S (-) Pentaprazole Tablets of different API batches

Formulation	F1	F2
Weight in (mg)	140	140
Hardness (Kp)	5-6	6-7
Friability	0%	0%
Thickness (mm)	3.2	3.2
In-vitro disintegration time (minute)	>15mins	21 mins

Table 6: Comparative % Drug Release of Formulation F1and F2

% Drug Release	F1	F2
Min	32.44%	31.57%
Max	38.97%	34.49%
Average	36.17%	32.88%

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