Formulation development and evaluation of delayed release enteric coated Paracetamol tablets

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ABSTRACT

The aim of this study was to investigate and evaluation of delayed release enteric coated paracetamol tablets. Successful delivery of drugs specifically to the intestine requires the protection of drug from being released in stomach. PCM core tablets were prepared with and without superdisintigrant using wet granulation method. Dip coating method is used for coating were different concentration of Eudragit L100 is used as coating agent. Preformulation studies like angle of repose, bulk density, tapped density, porosity, Carr's index, Hausner's ratio were performed. The FDT2 batch shows the highest drug release at end of total 135 min of 94.13 % which are the satisfactorily promising results. So, we can conclude that the FDT2 is the optimized batch among all three batches. From the reproducible results obtained from the executed experiments it can be concluded that Eudragit L 100 can be used as enteric coated polymer. These results reflect that PCM can be successfully enteric coated in order to prevent its release in the stomach and facilitate rapid release of the drug in the duodenum, due to the presence of superdisintegrant. Formulating these enteric coated tablets could increase patient compliance by decreasing adverse drug reactions (ADR_s) associated with PCM therapy.

KEY WORDS: Eudragit L100; Drug release; wet granulation; superdisintigrant

INTRODUCTION

Sustained release dosage form is mainly designed for maintaining therapeutic blood or tissue levels of the drug for extended period of time with minimized local or systemic adverse effects. Sustained release dosage forms would be most applicable for drugs having short elimination half-lives.[1]An ideal drug delivery system should be able to deliver an adequate amount of drug for an extended period of time for its optimum therapeutic activity. Most drugs are inherently not long lasting in the body and require multiple daily dosing to achieve the desired blood concentration to produce therapeutic activity. To overcome such problems greater attention has been focused on sustained release drug delivery system.[2] Convenience of administration and patient compliance are the aim of the formulation of sustained release dosage form preparations. A number of enteric coating polymers are available and capable of protecting the drug core from the aggressive environments of the stomach.[3-5] Being soluble at higher pH values, these polymers dissolve in the intestine and release the core for ready action. These polymers include several synthetic polymers like polymethacrylates (Eudragits), cellulose acetate phthalate (CAP), hydroxy propyl methyl cellulose phthalate (HPMCP).[3-7]

The design of such system involves release of drugs only at a specific site in the gastrointestinal tract. The drugs contained in such a system are those that are:[8]

-Destroyed in the stomach or by intestinal enzymes
-Known to cause gastric distress
-Absorbed from a specific intestinal site or
-Meant to exert local effect at a specific gastrointestinal site

The two types of delayed release systems are:[9, 10]

1. Intestinal release systems: A drug may be enteric coated for intestinal release for several known reasons such as to prevent gastric irritation, prevent destabilization in gastric pH etc.

2. Colonic release systems: Drugs are poorly absorbed through colon but may be delivered to such a site for two reasons

a) Local action in the treatment of ulcerative colitis

b) Systemic absorption of protein and peptide drugs

Ideal enteric coating materials should have the following properties:[3, 5, 7, 9, 10]

1. Resistance to gastric fluids
2. Ready susceptibility to or permeability to intestinal fluids
3. Compatibility with most coating solution components and the drug substrates.
4. The film should not change on aging
5. Formation of continuous film.
6. Non-toxicity
7. Low cost
8. Ease of application.

MATERIALS AND METHODS

Materials

The ingredients were procured from following source: Paracetamol (Sehat Pharma, Himmatnagar), Eudragit L100 (Astron, Ahmedabad), Sodium starch glycol (SD fine chemical), Lactose (SD fine chemical), Magnesium Stearate and Talc were of analytical grade.

Method

Method for formulation of core paracetamol (PCM) tablets: Wet granulation method

The core tablets were prepared by wet granulation method. The weighed quantity of paracetamol, lactose and half quantity of intra granular super disintegrator sodium starch glycolate passed through 60# sieve. The above shifted materials were mixed using mortar & pastle. This powder mixture made as damp mass using starch paste (10%) as binder which after that passed through 10# & allow to dry in hot air oven. After completion of drying the granules passed through the upper 22# and at lower 40#. The granules which retained in between these collected granules lubricated with magnesium stearate and talc as glidant and 15% fines. These granules were ready for compression. The tablets were evaluated for thickness, weight variation, friability, hardness. Tablets were compressed on 16-station rotary tableting machine (Cadmach Machinery, Ahmedabad)

Preparation of coating solution (Coating method: Dip coating)

Enteric coating of the compressed tablets is achieved by deep coating technique. Coating solutions of Eudragit L100 polymers prepared separately with plasticizers (castor oil), opacifier(CaCO3), lake(bromo thymol blue) in three different concentrations using isopropyl alcohol and dichloromethylene as solvent system.

Table 1: Formulation batch of the research work- core tablet

No.	Ingredients	Quantity per 1 tablet (mg)
1	Paracetamol (Drug)	100
2	Starch paste (10%)	q.s.
3	Sodium starch glycol(10%) (Super disintegrant)	20
4	Lactose (Diluent)	74
5	Talc(2%)(glidant)	4
6	Magnesium stearate(1%)(lubricant)	2
	Total	200

Table 2: Different coating solution

No.	Ingredients	FDT1(gm)	FDT2(gm)	FDT3(gm)
1	Eudragit L100 (enteric coating polymer)	25	35	45
2	Isopropyl alcohol	225	225	225
3	Dichloromethylene	225	225	225
4	CaCO3 (opacifier)	2.55	2.55	2.55
5	Castor oil (plastisizer)	0.83	0.83	0.83
6	Bromo thymol blue (lake)	1%	1%	1%

EVALUATION:

Hardness:[9] Pfizer hardness tester was used for the determination of hardness of tablets.

Friability:[5] Six tablets were accurately weighed and placed in the friabilator and operated for 100 revolutions. The tablets were dedusted and reweighed. The tablets that loose less than 1% weight were considered to be compliant.

Weight variation:[9] 10 tablets were selected randomly from the lot and weighed individually to check for weight variation.

Drug content:[4] Powder of PCM tablets taken equivalent to100mg of paracetamol and dissolved in7.4 pH phosphate buffer and analyzed spectrophotometrically (UV- 1601 Shimadzu Corporation, Japan) at 257 nm.

Dissolution:[11] In vitro dissolution studies were performed for paracetamol enteric coated tablets using USP dissolution apparatus II (paddle method) at 100 rpm, 37◦C ± 0.5◦C, and 900 mL of dissolution medium. The variation in the pH of the gastrointestinal tract (GIT) was mimicked by 2 hour dissolution study in 0.1 N HCL and 1 hour in pH7.4 phosphate buffer. Samples were withdrawn at regular time intervals, filtered and were estimated using ultraviolet-visible (UV/VIS) spectrophotometer (Shimadzu UV 1601, double beam UV/VIS Spectrophotometer).

RESULTS & DISCUSSION

At first, the conventional PCM tablets made and enteric coated by eudragit L100 polymer using dip coating technique. The results of evaluation parameters for core tablets and enteric coated tablets of three different coating polymer concentrations are:

Table 3: Post compression parameters

No.	Parameter	Results
1	Average weight	195.8 mg
2	Hardness(kg/cm^2)	4.08 kg/cm^2
3	Friability(%)	1.2 %
4	Weight variation(mg)	176.75-205.41 mg

Table 4 Dissolution profile comparison for conventional enteric coated PCM tablets

Dissolution media	**0.1 N HCL**	**Phosphate buffer pH 7.4**					
Time (min)	120	130	140	150	160	170	180
Batch no.	**% cumulative drug release**						
F1	9.63	21.84	30.09	56.67	82.24	89.67	95.73
F2	7.13	15.30	24.20	39.39	70.08	79.60	92.64
F3	6.35	12.94	20.83	39.20	63.56	83.84	92.71

From above results of drug release profile it was found that as the concentration of enteric coated material increases from F1 to F3 the drug release at end of the 120 min in 0.1 N HCL dissolution media decreases due to increase in the thickness of the coating film. The F3 batch shows the most delayed release as compare to others and at the end of 180 min. The total cumulative percentage drug release for F1, F2 and F3 were 95.73%, 92.64%, 92.71% respectively.

Table 5: Percentage weight gain of enteric coated fast dissolving PCM tablets

No.	**Batch**	**% weight gain**
1	FDT1	3.642 %
2	FDT2	4.988 %
3	FDT3	5.835 %

Table 6 Percentage drug content of enteric coated fast dissolving PCM tablets

Absorbance	Amount per 100 ml	Drug content (%)
0.513	0.717 mg/100ml	95.6 %

Table 7 Dissolution profile comparison for fast dissolving enteric coated PCM tablets

Dissolution media	0.1 N HCL	Phosphate buffer pH 7.4		
Time (min)	120	125	130	135
Batch no.	% cumulative drug release			
FDT1	4.99	12.53	92.32	93.99
FDT2	2.49	5.60	91.88	94.13
FDT3	2.41	5.40	89.82	93.60

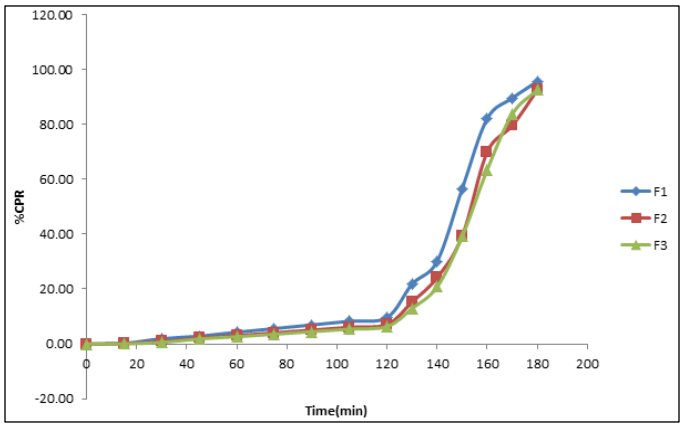

Figure 1: Drug release profile for conventional enteric coated PCM tablets

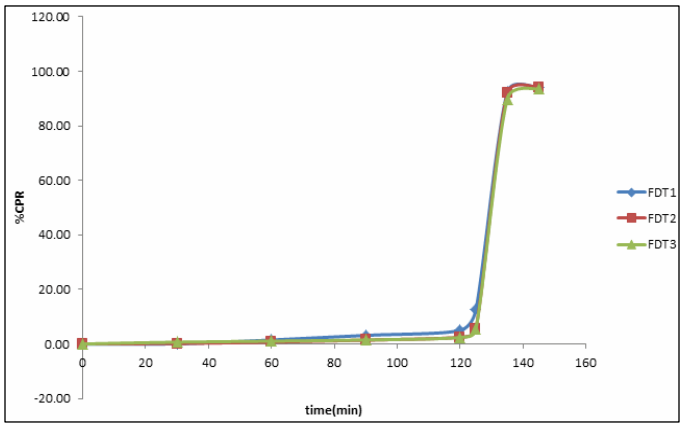

Figure 2: Dissolution profile comparison of fast dissolving enteric coated PCM tablets

From above results of drug release profile it was found that by making the fast dissolving enteric coated tablets of PCM we are able to release all the drugs at specific site in small intestine upto 95% of total drug content within the 15 min. after passage of tablet from gastric media (120 min), till that the drug remains intact in the tablet form. The use of super disintegrants and making it at fast dissolving tablet restrict the hindrance due to other excipients to release the drug within 15 min to the promising level. The total cumulative percentage drug release for FDT1, FDT2 and FDT3 were 93.99%, 94.13%, 93.60% respectively.

CONCLUSION

The aim of this study was to investigate coating behaviors of PCM tablets using Eudragit L100 as coating agent and its impact on drug release. The FDT2 batch shows the highest drug release at end of total 135 min of 94.13 % which are the satisfactorily promising results. So, we can conclude that the FDT2 is the optimized batch among all three batches. From the reproducible results obtained from the executed experiments it can be concluded that Eudragit L 100 can be used as enteric coated polymer.

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