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Effect of superdisintegrants on formulation of taste masked fast disintegrating Ciprofloxacin tablets

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ABSTRACT

The present investigation deals with the formulation of taste masked fast disintegrating tablets of Ciprofloxacin that disintegrate in the oral cavity upon contact with saliva and thereby improve therapeutic efficacy. Ciprofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class. It is a second-generation fluoroquinolone antibacterial that kills bacteria by interfering with the enzymes that cause DNA to rewind after being copied, which stops synthesis of DNA and protein. It may also be used to prevent or slow anthrax after exposure. The influence of superdisintegrants, crospovidone and sodium starch glycolate on disintegration time, wetting time and water absorption ratio were studied. Tablets were evaluation for weight and thickness variation, disintegration time, drug content, in vitro dissolution, wetting time and water absorption ratio. The in vitro disintegration time of the best fast disintegration tablets was found to be within 36 seconds. Tablets containing crospovidone (40%) exhibits quick disintegration time than tablets containing sodium starch glycolate. The fast disintegrating tablets of ciprofloxacin with shorter disintegration time, acceptable taste and sufficient hardness could be prepared using crospovidone and other excipients at optimum concentration.

***Key Words*:** ciprofloxacin, sodium starch glycolate, crospovidone, superdisintegrants, taste mask, fast disintegrating tablet.

INTRODUCTION

Most pharmaceutical dosage forms for oral administration are formulated for direct ingestion, for chewing, for prior dispersion and/or dissolution in water; some of them are absorbed in mouth (sublingual or buccal tablets) (Birudaraj *et al.*, 2005). Elderly individuals have difficulty in swallowing when prescribed in conventional tablet and capsule form (Rajitha *et al.*, 2009, Chang *et al.*, 2000, Yeola *et al.*, 2000). The problem of swallowing is also evident in pediatrics, psychiatric as well as traveling patients who may not have ready access to water. The rapidly disintegrating tablet in mouth oro-dispersible tablets overcome all the above problems and thus offer an alternate form of oral medication, which provide patients with a more convenient means of taking their Addition of super disintegrating agent in the formulation is one of the approaches to formulate oral dispersible tablets. Orally disintegrating tablets contain wide variety of pharmaceutical active ingredients covering many therapeutic categories. The time for disintegration of orally disintegrating tablets are generally considered less than 1 minute (IP, 2007). Orally disintegrating tablets are characterized by high porosity, low density and low hardness. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and is subsequently swallowed. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly patient compliance (IP, 2007). Keeping in view the advantages of this delivery system, in the present study attempts were made to formulate taste masked orally disintegrating tablets of ciprofloxacin which is used as an antibiotic taste masking of ciprofloxacin was done by keeping it with sodium saccharin and different superdisintegrating agent.

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MATERIALS AND METHODS

Materials

Ciprofloxacin was gifted from Dr. Reddy's Laboratories (Hyderabad, India). Crospovidone, sodium starch glycolate were obtained from Merck LTD (Mumbai). Magnesium stearate and all other ingredients used were of analytical grade.

Super Disintigrants

Crospovidone

It is a white, free flowing, compressible powder; a synthetic homopolymer of cross-linked N-vinyl pyrrolidinone. It is completely insoluble in water, acids, alkalis and all organic solvents. Hygroscopic in nature, swells rapidly in water, rapidly disperse in water, but does not gel even after prolonged exposure (IP, 2007).

Sodium Starch Glycolate

It is sodium salt of carboxymethyl ether of starch. It is white to off white tasteless, odourless, relatively free flowing powder, insoluble in organic solvent (IP, 2007).

Preparation of fast disintegrating tablets of ciprofloxacin by Kneading technique

Required quantity of ciprofloxacin was weighed and sifted through # 40 ASTM SS sieve. Drug was mixed with the crospovidone and starch glycolate in different ration (Table 1) with the above powder base with sifted avicel, and other exicipients by tumbling. All the ingredients were mixed thoroughly for not less than 5 minutes and until to get uniform mixed powder. Finally, the lubricated granules were compressed on rotary tablet machine (Sastr *et al.*, 2000; Ito *et al.*, 1996; Dobetti, 2001).

Evaluation of granules

The angle of repose was measured by using funnel method (Kuchekar *et al.*, 2003) which indicates the flow ability of the granules. Loose bulk density (LBD) and tapped bulk density (TBD) (Liberman and Lachman, 2006) were measured using the formula-

$$\text{LBD} = \frac{weig\,ht\ of\ the\ powder}{volume\ \ of\ the\ packing}$$

$$\text{TBD} = \frac{weig\,ht\ of\ the\ powder}{tapped\ \ volume\ \ of\ the\ packing}$$

Compressibility index (Shah and Rampadhan, 1997) of the granules was determined by using the formula-CI (%) $= \left[\left(\text{TBD-}\frac{\text{LBD}}{\text{TBD}}\right)\right] \times 100$

Table 1: Composition of Different Batches of Fast Disintegrating Cipro Tablets.

Ingredients	Amount (mg)					
	F-1	F-2	F-3	F-4	F-5	F-6
Ciprofloxacin	150	150	150	150	150	150
Avicel	60	60	60	60	60	60
Lactose	18	18	18	18	18	18
Starch powder	50	50	50	50	50	50
Crospovidone	40	50	60	-	-	-
Sodium Starch Glycolate	-	-	-	40	50	60
Sodium Saccharin	20	20	20	20	20	20
Vanillin	20	20	20	20	20	20
Magnesium Stearate	25	25	25	25	25	25
Coloring agent	25	25	25	25	25	25

Evaluation of the tablets

All prepared matrix tablets were evaluated for its uniformity of weight, hardness, friability and thickness according to official methods (Aulton and Well, 2000).

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability

Ten tablets were weighed and placed in a Roche friabilator (Electrolab USP friabilator) and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was calculated as per the following formula-

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight Variation

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5% (USP XX).

Drug content

Twenty tablets were weighed and powdered by using mortar and pestle. An amount of the powder equivalent to 150 mg of ciprofloxacin was dissolved in 100ml of phosphate buffer pH 6.8, filtered, diluted suitably and analyzed for drug content at

Table 2: Data for Blend Evaluation of Formulation F-1 to F-6.

Parameter	Formulation code					
	F-1	F-2	F-3	F-4	F-5	F-6
Angle of repose (°)	24.33±0.91	28.99±0.33	23.33±0.11	24.13±0.23	24.30±0.49	25.38±0.19
Loose bulk density (LBD) (g/ml)	0.278±0.20	0.521±0.3	0.321±0.72	0.342±0.21	0.376±0.69	0.421±0.64
Taped bulk density(TBD) (g/ml)	0.346±0.17	0.589±0.24	0.434±0.90	0.463±0.88	0.572±0.22	0.482±0.83
Compressibility index (%)	14.66±0.33	13.23±38	15.21±19	14.56v0.22	13.28±0.39	13,98±0.52

**Results are presented as Mean ± S.D*

257nm using UV-Visible spectrophotometer (UV 160 Shimadzu, Japan).

Wetting time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 9ml of buffer solution simulating saliva pH 7.4, which had the following composition, NaCl (0.126g), KCl (0.964g), KSCN (0.189g), KH_2PO_4 (0.655g) and urea (0.200g) in 1Litre of distilled water. A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.

Water absorption ratio (R)

The weight of the tablet prior to placement in the petri dish was noted (*wb*) utilizing a Shimadzu digital balance. The wetted tablet was removed and reweighed (*wa*). Water absorption ratio, *R*, was then determined according to the following equation.

$$R = \frac{wa - wb}{\text{wawb}} \times 100$$

Here *wb* and *wa* were tablet weights before and after water absorption, respectively.

In Vitro dispersion time

In vitro Dispersion time was measured by dropping a tablet in 10ml measuring cylinder containing 6ml of 0.1N hydrochloric acid.

In Vitro disintegration time

10 ml of water at 25°C was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted.

In Vitro drug release studies

In vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP XXII type II Labindia, Mumbai, India) at 50 rpm. Phosphate buffer pH 6.8 was used as the dissolution media with temperature maintained at 37±1°C. Samples were withdrawn at different intervals, diluted suitably and analyzed at 257 nm for cumulative drug release using an ultraviolet visible spectrophotometer (Shimadzu 1700 series). The study was performed in triplicate.

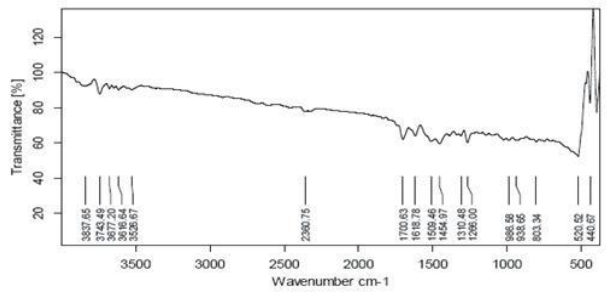
Stability studies

Short term stability studies on the optimum formu-

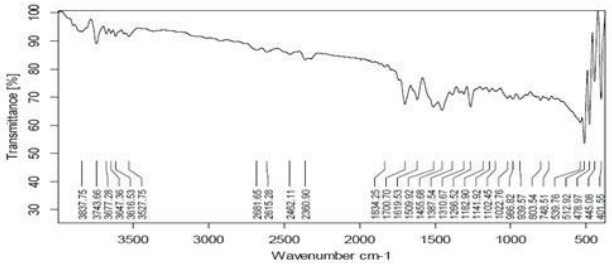
Table 3: Thickness, Hardness, Friability, Drug Content, Weight Variation, Wetting Time, Water Absorption Ratio, *in-vitro* Dispersion Time, *in-vitro* Disintegration Time of Ciprofloxacin Fast Disintegrating Tablets.

Parameter	Formulation code					
	F-1	F-2	F-3	F-4	F-5	F-6
Hardness*	3.42±0.36	3. 8 ± 1.4	3.03±1.19	3.2±1.33	3.81 ± 1.8	3.38±1.23
Thickness*	2.01±0.18	2.10 ± 0.49	2.11±0.22	2.51±1.72	2.24 ± 0.17	2.43±1.21
Friability	0.398	0.430	0.532	0.521	0.562	0..432
Drug content*	96.66±0.33	99.1±0.08	97.21±19	96.56±0.22	97.1 ± 0.71	96.98±0.52
Weight variation	201.34	200.48	203.42	202.54	203.45	204.32
Wetting time	47	30	43	41	31	45
Water absorption ratio	92	94	91	92	95	93
In-vitro* dispersion time (sec)	63	67	66	64	65	63
In-vitro* disintegrating time (sec)	39	36	40	41	38	40

**Results are presented as Mean ± S.D*



(A)



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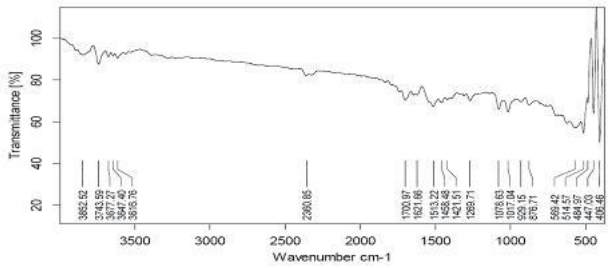

(C)

Figure 1: Fourier transform infra red (FTIR) spectra of (A) Ciprofloxacin (B) Ciprofloxacin + Crospovidone (C) Ciprofloxacin +SSG.

lation (F-2, F-5) were carried out by storing the tablets (in amber colored rubber stoppered vials) at 40°C/75% RH for 3 weeks. At every 1 week intervals, the tablets were examined for physical changes, properties, drug content and *in vitro* release studies (Chang and Robinson, 2006, Marshall *et al.*, 2000).

RESULTS AND DISCUSSION

The supplied drug passed the various tests of identification and analysis. The pure drug ciprofloxacin and the solid admixture of drug and various excipients used in the preparation of fast dispersible tablet formulations were characterized by FT-IR spectroscopy to know the compatibility (Figure 1).

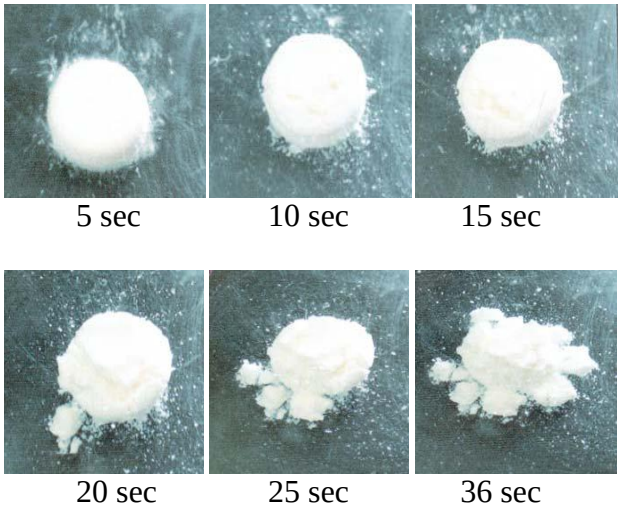

Figure 2: Disintegration process of tablet (F-2).

The FT-IR study did not show any possibility of interaction between ciprofloxacin and superdisintegrants used in the fast dispersible tablets.

Since the flow properties of the powder mixture are important for the uniformity of the mass of the tablets, the flow of the powder mixture was analyzed before compression of the tablets. The results of angle of repose and compressibility index (%) ranged from (23.33±0.11 to 28.99±0.33) and (13.23±38 to 15.21±19), respectively. The loose bulk density and tapped bulk density were ranged from (0.278±0.20 to 0.521±0.3) and (0.346±0.17 to 0.589±0.24), respectively. The lowest compressibility index is 5-15 % which indicates excellent flow properties (Table 2).

The physical properties of different batches of fast dissolving tablets are given in table 3. Tablet mean thickness was almost uniform in all the formulations. The thickness varies between 2.01±0.18 to 2.51±1.72 mm. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.03±1.19 to 3.81±1.8 kg/sq.cm. Friability values below 1% were an indication of good mechanical resistance of the tablets. The weight variation in all the six formulations was found to be 199.71 to 202.19 mg, thus the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The percentage drug content of all the tablets was found to be between 96.56±0.22 to 99.1±0.08 % of Ciprofloxacin which was within the acceptable limits.

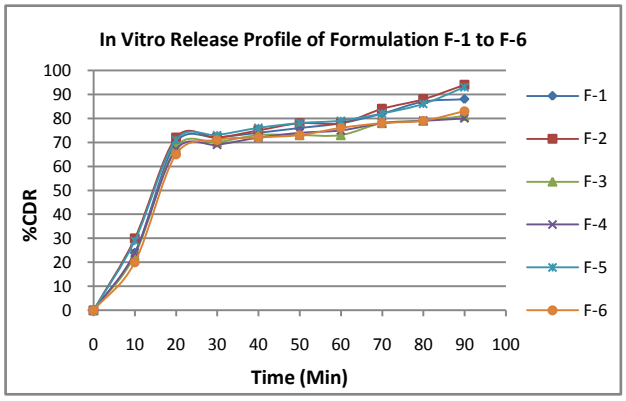

Figure 3: Comparison of *in-vitro* release profile of ciprofloxacin from formulations.

The wetting time for all the six formulations was performed in triplicate. The values lie between 23 to52 sec. *In vitro* dispersion is a special parameter in which the time taken by the tablet to produce complete dispersion is measured. The time for all the six formulations varied between 30 to 45 sec. Tablets were prepared with crospovidone F-1 to F-3 and with SSG F-4 to F-6. The wetting time, *in vitro* dispersion time of the tablets were also considerably reduced in tablets containing crospovidone which may be attributed due to the wicking type of disintegrants (crospovidone) formed thus facilitating the disintegrants to bring about faster disintegration. The water absorption ratio (%) and *in vitro* disintegrating time (sec) were ranged from (91 to 97) and (36 to 41), respectively. The *in vitro* dissolution profile indicated faster and maximum drug release from formulation F-2 & F-5 (Figure 2). *In vitro* drug release results of all the formulations were satisfactory (Figure 3).

Stability studies showed no significant change when compared with zero day of formulation (F-2 & F-5). The disintegration times of tablets prepared with crospovidone were comparatively lower than that with sodium starch glycolate (Figure 3). The faster disintegration of these tablets may be attributed to the rapid capillary activity and pronounced hydration of crospovidone with little tendency to gel formation. Thus, these results suggest that the disintegration time can be decreased by using wicking type of disintegrants (crospovidone).

CONCLUSION

The oral disintegrating tablets of ciprofloxacin with sufficient mechanical strength, acceptable taste and smaller disintegration time were achieved employing suitable superdisintegrants and other excipients at optimum concentration. Stability studies revealed that there was no significant change in drug content and dissolution profile of oral disintegrating tablets. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between ciprofloxacin and other ingredients used. Among two superdisintegrants used, crospovidone showed better performance in disintegration time when compared to sodium starch glycolate. So the formulation of F-2 was found to be best among all other formulations, because it has exhibited faster wetting time, good taste and faster disintegration time when compared to all other formulations.

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