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Formulation and Evaluation of Fast Disintegrating Tablets of Antiinflamatory Drug Flurbiprofen

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ABSTRACT

Flurbiprofen, a propionic acid derivative, is a non-steroidal anti-inflammatory agent (NSAID) with antipyretic and analgesic activity. Poor water solubility is its constraint for its oral bioavailability. The rationale of the present study is to enhance the solubility and bioavailability of the drug by using superdisintegrants like crosspovidone, sodium starch glycolate and β cyclodextrin. In the present study attempt has been made to prepare fast dissolving tablets of flurbiprofen using superdisintegrants, β-cyclodextrin inclusion complex with drug. The inclusion complex was prepared by physical mixture method and was further formulated as tablets by using direct compression method. The pure drug was evaluated by flow properties. The pure drug and drug excipient complex was characterized by FTIR and tablets were evaluated for hardness, %friability, wetting time, water absorption ratio, disintegration, drug content and in vitro dissolution studies. From F1 to F12 formulations it was concluded that F8 formulation was best and the best formulation was compared with the marketed tablet flurbiprofen uncoated tablet of 50 mg, and the drug release from marketed tablet was less compared with the F8 formulation.

Keywords: Flurbiprofen, Crosspovidone, Sodium starch glycolate, β-cyclodextrin, Inclusion complex, Direct compression

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INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. Oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, noninvasive method and ease of administration leading to high level of patient compliance. FDT are novel types of tablets that dissolve, disintegrate, and disperse in saliva within few seconds without water. These dosage forms dissolve in oral cavity within a minute without need of water or chewing. The FDT is also known as fast melting, fast dispersing, rapid dissolving tablets. These dosage forms are also used to attain instantaneously a high concentration of drug in body for immediate actions. Higher drug loading as well as pleasant feeling to the mouth are other advantages offered by the FDT. Most commonly used methods of preparation include Lyophilisation, tablet molding, direct –compression methods. Fast disintegrating tablets are prepared by using superdisintegrants such as crosspovidone, crosscarmellose sodium, Sodium starch glycolate, and by using cyclodextrins [1].

Superdisintegrants: Superdisintegrants are substances which disintegrates the drug within seconds. The disintegrants major function is to oppose the efficacy of the tablet binder and the physical forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on [2]

i. By capillary action
ii. High swell ability of disintegrants
iii. Capillary action and high swell ability
iv. Chemical reaction (release of gases).

Cyclodextrins: Cyclodextrins are cyclic oligosaccharides containing at least six D-(þ)-glucopyranose units attached by a glucoside bonds. The three natural cyclodextrins, a, b, and g, differ in their ring size and solubility. β-Cyclodextrin is the most commonly used cyclodextrin, although it is the least soluble. It is the least expensive cyclodextrin and commercially available from a number of sources and is able to form inclusion complexes with a number of molecules of pharmaceutical interest. Cyclodextrin form inclusion complex with poor soluble drug to improve solubility and bioavailability. The inclusion complexes are prepared by kneading method, physical mixture, Co- precipitate method [3].

MATERIAL AND METHODS

Flurbiprofen drug was gifted by Hygro chemicals pharmatec Pvt limited, Bollaram. Sodium starch glycolate, Crosspovidone, Microcrystalline cellulose, Mannitol, Talc, Magnesium stearate and β – cyclodexrtin.

Method

Preformulation testing is the first step in the rational development of dosage forms of a drug. It can be defined as an investigation of physical and chemical properties of drug substance like tapped density, bulk density, hausner's ratio, compressibility index, solubility [4].

Melting point

Melting point of drug was determined by capillary method. Fine powder of flurbiprofen was filled in a glass capillary tube which is placed in melting point apparatus, the powder at what temperature it will melt was noticed, which complied with IP standards, indicating purity of the drug sample [5].

Solubility studies

The solubility of flurbiprofen was analyzed by using different chemicals such as dimethyl sulphoxide, ethanol, water, methanol, dimethyl formamide. Each chemical of 5 ml was taken in to a measuring cylinder and excess amount of drug was added and the solubility of the drug was analyzed. It was observed that the solubility of flurbiprofen was more in ethanol [6].

Partition coefficient

10 mg of the drug was accurately weighed and transferred into a separating funnel. Take 20 ml of chloroform and 20 ml of water and transfer in to a separating funnel containing drug. The separating funnel was shaked for 30 minutes up to the dissolved. After that the separating funnel was kept aside until the chloroform and water separates. The water portion was collected and the absorbance was observed by using UV-Visible spectrophotometer at 247 nm [7].

Construction of calibration curve

100 mg of drug was accurately weighed and ethanol was added to dissolve the drug and then it was make up to the mark with 7.2 phosphate buffer to give 1000 ug/ml. from the stock solution 10 ml of sample was taken in to a 100 ml volumetric flask and was made up to the mark with 7.2 phosphate buffer to give 100 ug/ml. From that solution different concentrations of (2, 4, 6, 8, 10 µg/ml) was made and make up to the mark with phosphate buffer and absorbance was seen at 247 nm by using UV- visible spectrophotomer. The calibration curve was plotted by using absorbance vs. concentration [8].

Preparation of 7.2 phosphate buffer

Dissolve 245 g of monobasic potassium phosphate and 50 g of sodium hydroxide in water to make 2000 ml of solution. Dilute 333 ml of this stock solution to 6000 ml with water.

FT-IR Spectroscopy

FT-IR Spectroscopy can be used to investigate and predict any physiochemical interaction between different components in a formulation and therefore it can be applied to the selection of suitable chemical compatible excipients while selecting the ingredients [9].

Preparation of fast disintegrating tablets by drug and cyclodexrtin complex

The drug cyclodexrtin complex was prepared by using drug and β- cyclodexrtin of 1:0.1, and 1:0.2 ratios. The complex mixture was sieved by using sieve no. 60 and remaining excipients like mannitol, microcrystalline cellulose, talc, magnesium stearate were added to the above mixture and was compressed by direct compression technique [10].

Preparation of fast disintegrating tablets by using Superdisintegrants

The superdisintegrants are taken in 2%, 3%, 4%, 5% and was passed through sieve no.80. The superdisintegrants were added to the drug and remaining excipients like mannitol, microcrystalline cellulose, talc, magnesium stearate were added to drug and was compressed by using direct compression method (Tables 1-10) (Figures 1-6).

Table 1: Formula for preparation of fast disintegrating tablets.

S. No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Flurbiprofen	50	50	50	50	50	50	50	50	50	50	50	50
2	Sodium starch glycolate	10	15	20	25	-	-	-	-	30	40	-	-
3	crosspovidone	-	-	-	-	10	15	20	25	25	25	-	-
4	Microcrystalline cellulose	75	75	75	75	75	75	75	75	-	-	73.47	96.47
5	Mannitol	355	350	345	340	355	350	345	340	310	300	341.53	318.53
6	Magnesium stearate	5	5	5	5	5	5	5	5	75	75	75	75
7	Talc	5	5	5	5	5	5	5	5	5	5	5	5
8	Total (mg)	500	500	500	500	500	500	500	500	5	5	5	5
										500	500	500	500

Table 2: Melting point.

S. No	Reported melting point	Observed melting point
1	111°C	110°C

Table 3: Partition coefficient of flurbiprofen.

S. No	Drug	Partition coefficient log p
1	Flurbiprofen	1.91

Table 4: Calibration curve of flurbiprofen in 7.2 phosphate buffer.

S. No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.243
3	4	0.428
4	6	0.589
5	8	0.778
6	10	0.956

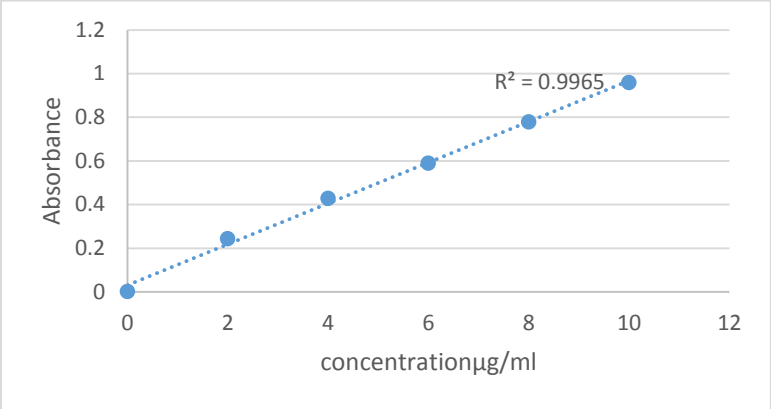

Figure 1: Flow characteristics of API (Flurbiprofen and excipients).

Table 5: Flow chart of Flurbiprofen.

Drug/Excipient	Bulk density(g/cc)	Tapped density (g/cc)	Angle of repose
Flurbiprofen	0.4	0.416	19.3
Sodium starch glycolate	0.2	0.28	20.9
crosspovidone	0.2	0.22	28.15
β −cyclodextrin	0.25	0.285	37.5

Table 6: Flow chart of excipients.

Drug/ excipient	% compressibility index	Hausner's ratio
Flurbiprofen	3.84	1.04
Sodium starch glycolate	28.5	1.4
crosspovidone	9	1.1
β −cyclodextrin	12.2	1.14

RESULTS AND DISCUSSION

FTIR Images of pure drug and drug and polymer complex

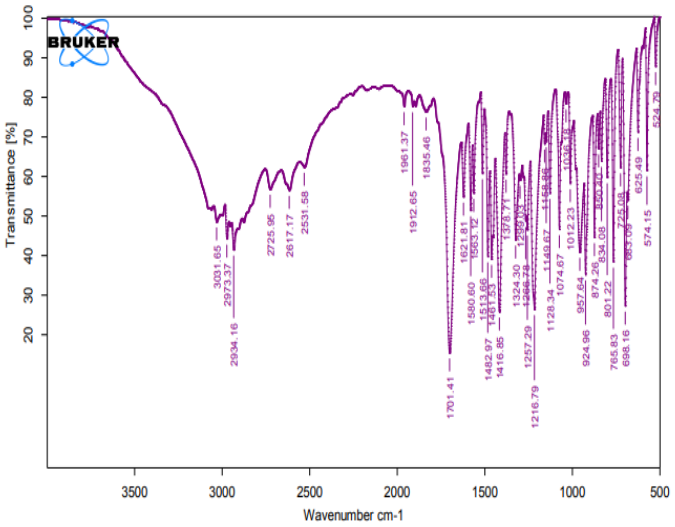

Figure 2: Spectra of Flurbiprofen.

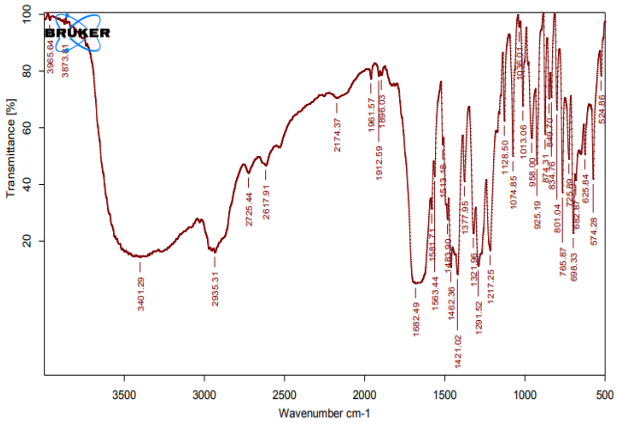

Figure 3: Spectra of flurbiprofen and crosspovidone mixture.

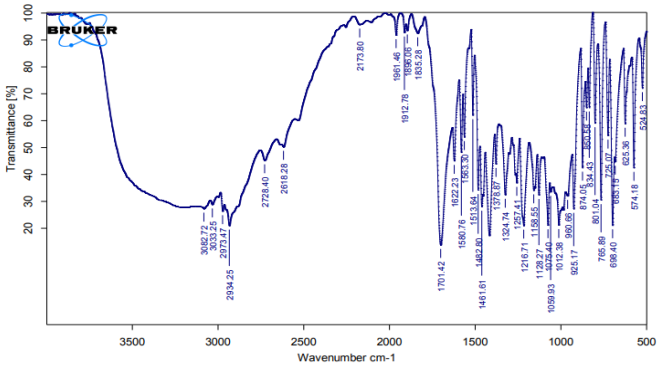

Figure 4: Spectra of flurbiprofen and sodium starch glycolate mixture.

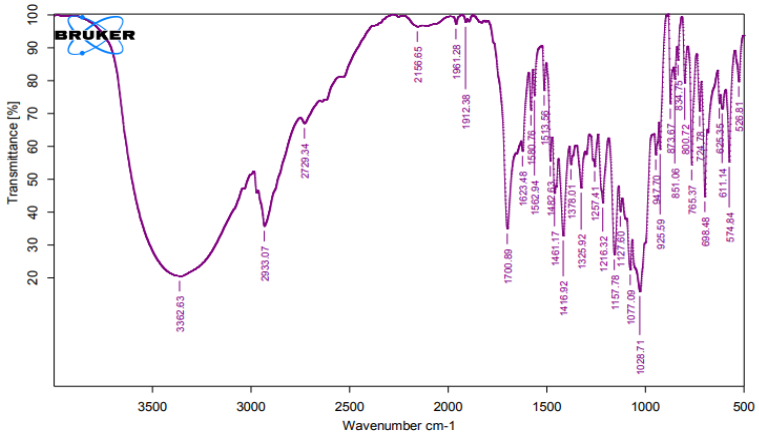

Figure 5: Spectra of flurbiprofen and β −cyclodexrtin.

Table 7: Evaluation of fast disntegrating tablets.

S. No	Formulation	%weight variation	%Friability	Hardness (kg/cm^2)	Wetting time(sec)
1	F1	2.35	0.4	2.4	38
2	F2	2.35	0.6	3	36
3	F3	2.78	0.4	3	30
4	F4	2.65	0.4	2.3	28
5	F5	3.12	0.5	2.1	43
6	F6	3.26	0.3	2.3	39
7	F7	3.12	0.5	2.3	28
8	F8	4.5	0.4	3.1	26
9	F9	3.12	0.6	3	26
10	F10	3.12	0.3	2.5	24

11	F11	2.65	0.8	3	46
12	F12	2.65	0.8	2.5	42

Table 8: Evaluation of fast disntegrating tablets.

S. No	Formulation	Disintegration time (sec)	Water absorption ratio	% drug content
1	F1	50	98	93.34
2	F2	47	94	93.75
3	F3	44	92	94.36
4	F4	39	82	95.38
5	F5	45	74	96.8
6	F6	40	66	97.21
7	F7	34	58	92.03
8	F8	31	52	98.25
9	F9	35	96	97.03
10	F10	30	88	97.45

Table 9: Cumulative % drug release of fast disintegrating tablet flurbiprofen.

S. No	Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	Marketed formulation
1	5	25.48	27.50	29.15	30.25	24.38	24.93	26.03	27.50	23.83	28.05	29.15	30.00	18.88
2	10	32.08	33.00	33.00	33.26	31.35	33.10	35.02	36.30	36.48	37.77	30.00	31.35	26.77
3	15	47.12	49.14	50.42	52.80	46.39	48.04	49.50	51.34	44.74	47.85	47.12	53.90	32.45
4	20	52.07	53.17	54.09	55.00	51.15	51.52	54.27	54.82	51.15	53.17	55.19	58.85	35.38
5	25	59.22	60.14	62.15	63.07	63.99	64.17	66.19	67.84	55.19	64.35	57.20	60.87	39.60
6	30	65.09	66.19	67.11	69.12	68.76	69.67	72.06	73.34	63.44	73.16	63.44	69.86	44.37
7	35	79.02	80.0	81.04	83.06	75.17	75.36	77.37	78.84	73.71	79.02	69.67	73.52	47.85
8	40	86.17	87.09	87.09	87.88	85.99	86.36	88.01	90.39	88.56	90.94	73.71	78.29	54.45
9	45	92.04	96.26	97.36	99	91.68	93.51	93.88	99.36	97.18	98.09	97.91	98.64	60.14

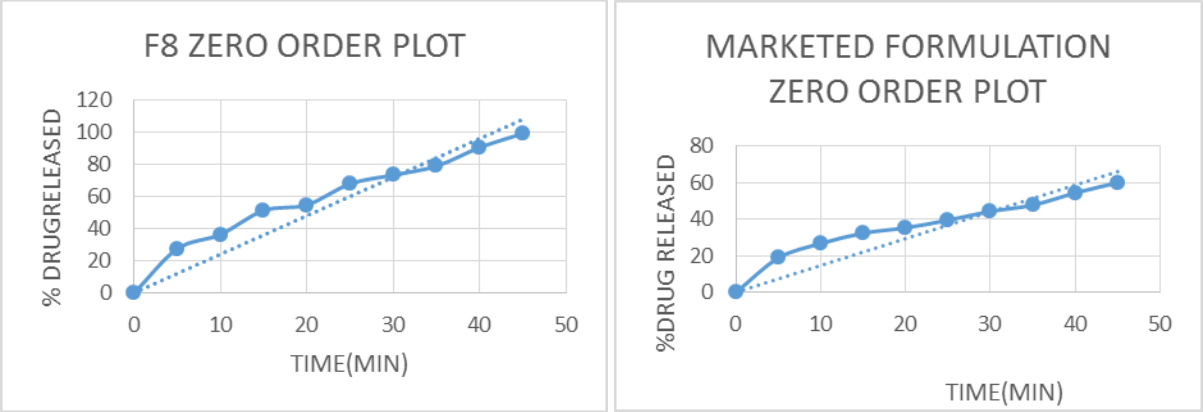

Figure 6: % Cumulative drug release of optimized f8 formulation and marketed formulation.

Table 10: Dissolution efficiency and time taken to release 50% and 90% of drug release profile.

S. No	Formulation	Dissolution Efficiency DE_{30}	T50% (Min)	T90% (Min)
1	F1	52.295%	18.17	43.04
2	F2	53.644%	17.17	40.44
3	F3	54.51%	15.42	41.36
4	F4	55.589%	14.0	41.02
5	F5	52.35%	19.15	44.00
6	F6	53.09%	19.52	42.51
7	F7	54.66%	16.27	42.88
8	F8	56.287%	14.44	40.39
9	F9	51.8%	19.15	41.18
10	F10	55.60%	17.17	40.94
11	F11	50.70%	17.19	44.91
12	F12	53.884%	14.80	40.64
13	Marketed tablet	34.98%	38.14	3.45(hrs)

CONCLUSION

By studying all the experimental results of the prepared fast disintegrating tablets it can concluded that anti-inflammatory drug like flurbiprofen can be successfully formulated by using superdisintegrants crosspovidone, sodium starch glycolate, β −cyclodexrtin, micro crystalline cellulose. The IR spectrum of pure drug and drug-polymer mixture revealed that the characteristic peaks of pure drug cannot be affected with the polymer in drug and polymer mixture. So there was no interaction between polymer and drug. The drug release rate was found to be increased upon increase in the concentration of the polymer. The *in vitro* drug release of fast dissolving tablets exhibited quickly release pattern for all the formulations. On the basis of

percentage yield of formulations F1 to F12, IR study, *in vitro* release studies and its kinetic data it was concluded that formulation F8 was optimized formulation. Hence, a finally it was concluded that the prepared fast dissolving tablets of flurbiprofen can be considered as one of the promising formulation technique for fast disintegrating drug delivery system and hence can be effectively used in the therapeutic management of anti-inflammatory.

REFERENCES

[1]. Lindgren, S., and Janson, L., Dysphagia: Prevalence of swallowing complaints and clinical finding. *Med Clin North Am*, **1993.** 77: 3-5.

[2]. Sastry, S.V., et al. Recent technological advances in oral drug delivery: A review. *Pharm Sci Technol Today*, **2003.** 3:138-45.

[3]. Fu, Y., et al. Orally fast disintegrating tablets: Development, technologies, taste-masking and clinical studies. *Crit Rev Ther Drug Carrier Sys*, **2004.** 21: 433-476.

[4]. Seager, H., Drug- delivery products and the zydis fast dissolving dosage form *J. Pharm Pharmacol*, **1998.** 50: 375-382.

[5]. Habib, W., and Khankari RK., Hontz J. Fast dissolving drug delivery systems**.** . *Crit Rev Ther Drug Carrier Sys*, **2000.** 17: 61-72.

[6]. Dobetti, L., Fast dissolving tablets. *US Patent*, **2003.** 596: 311.

[7]. Brown, D., Orally disintegrating tablets –taste over speed. *Drug Del Tech*, **2003.** 3: 58-61.

[8]. Behne, K., et al. Mitrazepine orally disintegrating tablet vs. sertraline: A prospective onset of action study**.** *J. clin Psychopharmacol*, **2003.** 23: 358-364.

[9]. Jaccard, T.T., and Leyder, J., Une nouvelle formegalenigueIeIyoc. *Ann Pharm Fr*, **1985.** 43: 123-131.

[10]. Doll, G., et al. Bioavaliability of phloroglucinol in man. J. *Pharm Belg*, **1999.** 54: 75-82