INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN: 2320-2831

IJPAR |Vol.4 | Issue 4 | Oct - Dec - 2015

Journal Home page: www.ijpar.com

Research Article *Open Access*

Formulation development and *invitro* characterization of oro dispersible tablets of Celecoxib

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ABSTRACT

In this study was to prepare fast disintegrating tablets of Celecoxib by using super disintegrants in varying proportions. The tablets were prepared by using various super disintegrants like crospovidone, cros carmellose sodium, explotab, magnesium sterate, talc and microcrystalline cellulose. The tablets were evaluated for weight variation, hardness, friability, wetting time, water absorption ratio, and disintegration time (DT) and dissolution study. From the results obtained, it can be concluded that the prepared tablets were shown good pre & post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation containing crospovidone as super disintegrant, showed maximum % drug release i.e., 99.8 % in 6 min hence it is considered as optimized formulation.

Keywords: Celecoxib, Fast disintegrating tablets, Crospovidone, Direct compression, Dissolution rate & oral bioavailability.

INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance. Many patients especially children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. Almost 50% of the population is affected by such problem, resulting in the high incidence of noncompliance and ineffective therapy. Most pharmaceutical forms for oral administration are formulated for direct ingestion, or for chewing, or for prior dispersion and/or dissolution in water; some of them are absorbed in the mouth (sublingual or buccal tablets). To obviate the problems associated with conventional dosage forms, orally fast disintegrating tablets have been developed, which combine hardness,

dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and traveling patients. FDTs can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method. The aim of this study was to formulate FDTs with sufficient mechanical integrity and to achieve faster disintegration in the oral cavity without water within 10 sec to 6 min. Most of the FDTs include certain super disintegrants and taste masking agents. Fast disintegrating tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. When Faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form.

EXCIPIENTS COMMONLY USED FOR FDTs PREPARATION

Excipients used in FDTs contain at least one superdisintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavorings. The most important ingredients of a mouth dissolving tablets are:

Super disintegrants

The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrant. Sodium starch glycolate, Ac-di-sol (crosscaremellose sodium), crosspovidone, microcrystalline cellulose, pregelatinised starch are some of examples of disintegrants.

Sugar based excipients

So taste masking is necessary in most of the cases sorbitol, mannitol, xylitol, dextrose, fructose is mainly used.

MATERIALS & METHODOLOGY

MATERIALS

Celecoxib, crospovidone, croscarmellose sodium, explotab, magnesium sterate, talc and microcrystalline cellulose.

METHODOLOGY

Preparation of standard calibration curve of celecoxib

The absorbance was measured in UV spectrophotometer at 243 nm against 0.1 N HCl (pH 1.2) as blank.

Formulation of celecoxib dispersible tablets

Composition of preliminary trials for Celecoxib dispersible tablet by direct compression is shown in table 6.1. All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-8 station with 6mm flat punch, B tooling. Each tablet contains 50 mg Celecoxib and other pharmaceutical ingredients.

Table 1: Formulation of Celecoxib oro dispersible tablets

Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Celecoxib	100	100	100	100	100	100	100	100	100
CP	8	12	16	-	-	-	-	-	-
CCS	-	-	-	8	12	16	-	-	-
SSG	-	-	-	-	-	-	8	12	16
Talc	2	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2	2
MCC pH 102	88	84	80	88	84	80	88	84	80
Total weight	200	200	200	200	200	200	200	200	200

CP - Cros povidone, CCS - Cros Carmellose Sodium SSG - Sodium Starch Glycolate

All ingredients are expressed in mg only

RESULTS & DISCUSSION

Standard Calibration curve of Celecoxib

Concentration and absorbance obtained for calibration curve of Celecoxib in 0.1 N hydrochloric acid buffer (pH 1.2**).**

Table 2: Standard Calibration curve of Celecoxib

S. No.	Concentration (µg/ml)	Absorbance* (at 243nm)
1	2	0.113
2	4	0.220
3	6	0.337
4	8	0.445
5	10	0.566

It was found that the estimation of Celecoxib by UV spectrophotometric method at λ_{max} 243.0 nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2- 10µg/ml. The regression equation generated was y = 0.056x -0.003.

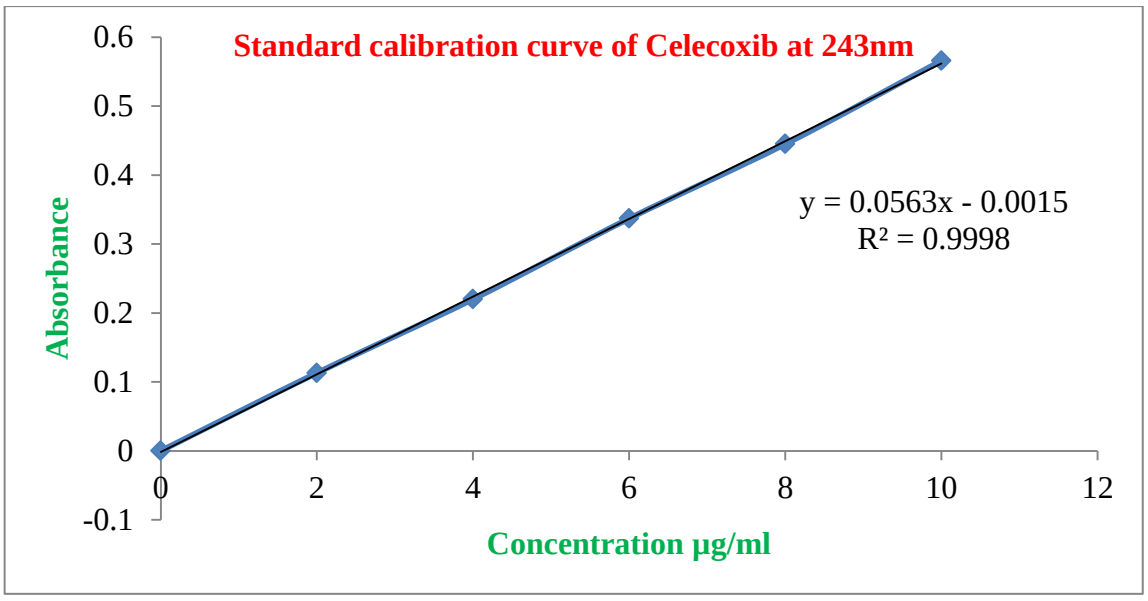

Figure 1: Standard graph of Celecoxib in 0.1 N HCl

EVALUATION PARAMETERS FOR FAST DISSOLVING TABLETS

Pre-compression parameters

The data's were shown in Table 7.2.The values for angle of repose were found in the range of 25°-30°. Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.50 (gm/cc) and 0.50 to 0.58 (gm/cc) respectively. Carr's index of the prepared blends fall in the range of 13.06% to 18.18%. The Hausner ration fall in range of 1.14 to 1.22. From the result it was concluded that the powder blends had good flow properties and these can be used for tablet manufacture.

Table 3: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle Of Repose(θ)
F_1	0.40	0.54	17.18	1.20	26.91
F_2	0.50	0.56	15.54	1.18	28.23
F_3	0.50	0.58	13.79	1.19	29.34
F_4	0.46	0.56	16.36	1.19	26.71
F_5	0.44	0.58	13.79	1.16	29.34
F_6	0.48	0.56	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.42	0.50	18	1.20	26.78
F_9	0.49	0.50	18	1.20	26.78

POST COMPRESSION PARAMETERS

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 7.3. The average weight of the tablet is approximately in range of 107 to 98.5, so the permissible limit is ±10% (110-90mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 7.3. The results showed that the hardness of the tablets is in range of 2.5 to 3.00 kg/cm^2, which was within IP limits.

Thickness

Thickness of three tablets of each batch was checked by using Vernier Caliper and data shown in Table-7.3 The result showed that thickness of the tablet is raging from 3.56 to 3.64.

Friability

The average friability of all the formulations lies in the range of 0.30 to 0.51% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Invitro disintegration time

Tablets of each batch were evaluated for *Invitro* disintegration time and the time was found to be in the range of 19.33 to 27 seconds.

Invitro Dissolution studies

Invitro dissolution studies were carried out by using 500ml of 0.1 N HCl in USP II dissolution apparatus by using paddle method. The dissolution studies were carried out for about 30 min. The dissolution data for all the formulations were given in the Table.

Table 4: *Invitro* Dissolution studies of F1-F9

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	28.4	39.5	82.9	24.3	31.7	48.3	18.4	35.2	62.4
4	35.2	76.3	99.4	31.6	34.5	82.9	25.2	48.9	79.1
6	48.9	96.2	99.8	49.3	41.9	88.7	48.7	66.8	89.5
8	66.8	99.7		58.3	62.4	95.8	58.3	79.3	
10	78.1			74.3	89.1		74.3	88.9	
15	86.4			88.1	99.5		87.4	93.5	
20	100.3			94.6			98.77		
25				99.8					

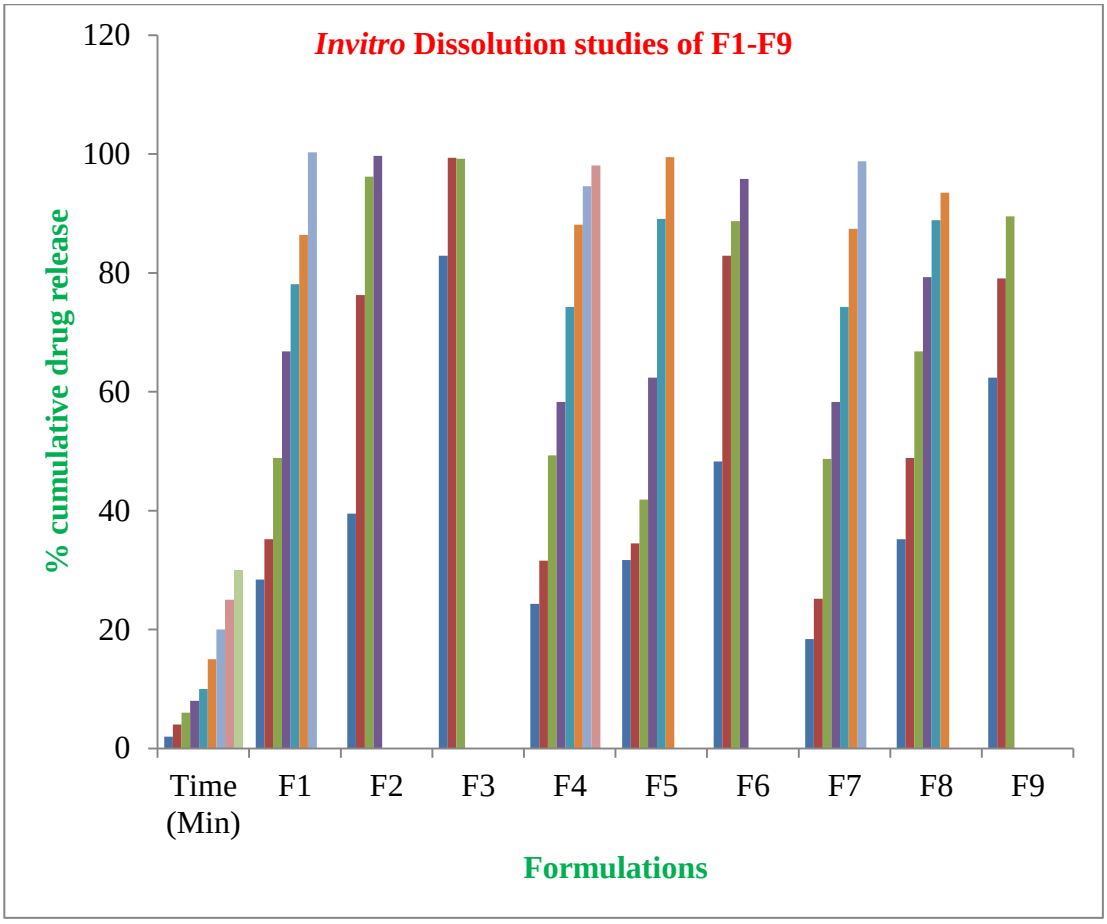

Figure 2: *Invitro* Dissolution studies of F1-F9

From the results it was evident that the formulation F3, prepared with super disintegrant crospovidone showed maximum % drug release in 6 min (99.8 %).

FOURIER TRANSFORM-INFRARED SPECTROSCOPY

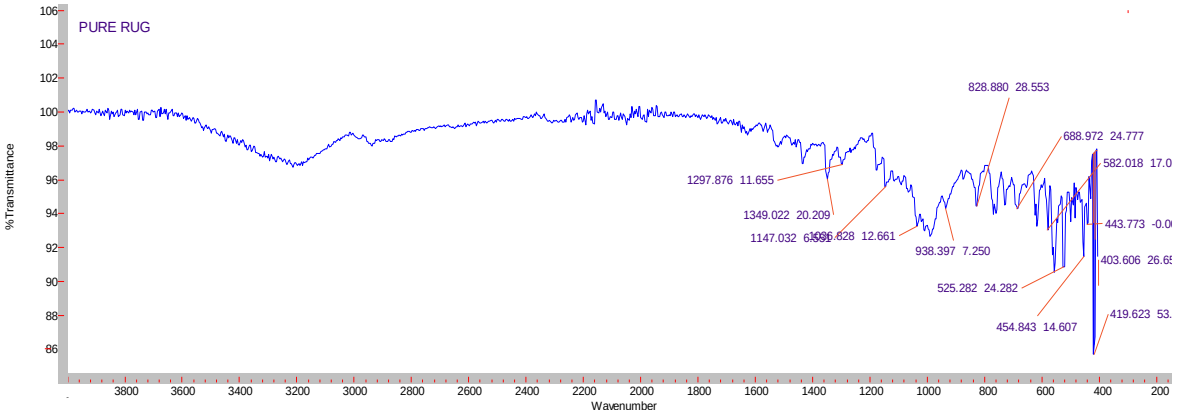

Figure 3: FT-IR Spectrum of Celecoxib pure drug

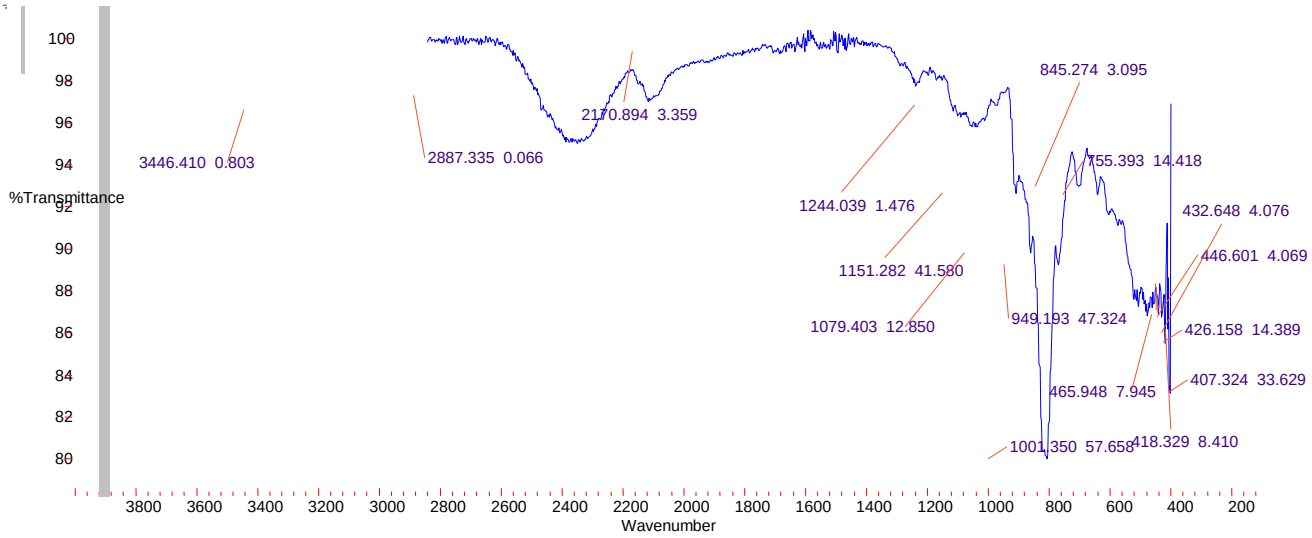

Figure 4: FT-IR Spectrum of optimized Formulation

From the FTIR data it was evident that the drug and super disintegrates, other excipients doses not have any interactions hence they were compatible.

CONCLUSION

In the present work, an attempt has been made to develop fast disintegrating tablets of Celecoxib. New generation super disintegrants crosspovidone, Cros carmellose Sodium, Sodium Starch Glycolate were selected as super disintegrates. All the formulations were prepared by direct compression method using 8mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation showed maximum % drug release i.e., 99.8 % in 6 min, hence it is considered as optimized formulation. The F3 formulation contains crospovidone as super disintegrant. F3 formulation was considered as optimized formulation.

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