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Formulation and Evaluation of Diclofenac Sodium Oro Dispersible tablets using superdisintegrant by direct compression technique

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ABSTRACT
The present study was aimed to formulate, evaluate and optimized a tablet which disintegrates and dissolves rapidly to show a rapid onset of action. Diclofenac sodium, a non-steroidalanti-inflammatory drug with analgesic and anti-inflammatory properties was selected as a model drug. In the present study, attempt has been made to prepare fast dissolving tablets of Diclofenac sodium using superdisintegrants like sodium starch glycolate and starch by direct compression technique using 3 different concentration of superdisintegrant. The precompression parameters of prepared tablet blend like angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio and the post compression parameters of the tablet like hardness, friability, weight variation, disintegration time, invitro dissolution release rate were evaluated. It was concluded that formulation F9 showed better release characteristics of the drug.

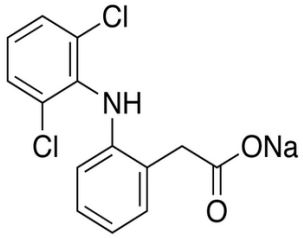
Keywords: Oro dispersible tablets, Diclofenac sodium, Sodium starch glycolate

INTRODUCTION

For decade, oral drug delivery has been known as the most widely used route of drug administration when compared to all the other routes that have been explored for delivery of different dosage forms to systemic circulation.

The reason for such popularity of oral route may be attributed to its ease of administration. Recent advances in novel drug delivery systems (NDDS) aim at formulating a convenient dosage form for administration and to achieve better patient compliance to enhance safety and efficacy of drug molecules. One such approach is oro-dispersible tablet. An oral fast dissolving drug delivery system is a novel tablet dosage form which dissolves or disintegrates in the oral cavity with a good taste and flavor increasing the acceptability of bitter drugs without the need of water or chewing and hence called melt in mouth tablets or oro-dispersible or rapid disintegrating or quick dissolving tablets. The drugs may be absorbed from mouth, pharynx or esophagus while the saliva passes down into stomach. Advantages of the fast dissolving tablets include rapid onset of action, ease of swallowing without the aid of water, enhanced dissolution rate, increased gastric absorption, minimized first pass metabolism, improved oral bioavailability and improved patient compliance. ODT formulation combines the advantages of both conventional tablets and liquid formulations.

In the present study it was proposed to formulate fast dissolving tablets of Diclofenac sodium by using direct compression technique, with the aim of reaching high serum concentration of the drug in a short time period. In this study, effort has been made to formulate the fast dissolving tablets using super dis-integrant like Sodium Starch Glycolate.



METHODOLOGY

Materials

All the materials used in this present work were commercial samples. Diclofenac sodium was received from Sahyadri scientific research, Islampur, Sodium starch glycolate received from Sahyadri scientific research, Islampur, Lactose purchased from Sahyadri scientific research, Islampur, Magnesium stearate, Talc. All the reagents used were of analytical grade. Freshly prepared distilled water was used in the work.

Method

Oro dispersible Tablets of Diclofenac Sodium using Direct Compression Technique

Direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredients and suitable excipients. No pre-treatment of the powder blends by wet or dry granulation is involved. Direct compression technique does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications. This is a process of compressing mixed powders into tablets without the need of intermediate granulating step. This technique involves conventional equipment, commonly available excipients and a limited number of processing steps. High doses can be accommodated and the final weight of tablet can easily exceed than that of other production methods.

Fast dissolving tablets of Diclofenac sodium were prepared by direct compression method. All the ingredients were passed through # 60mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 200mg by using 10-station rotary mini press tablet machine.

EVALUATION

Pre Compression Parameter

1. Angle of Repose

Angle of repose was determined by using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap was measured and angle of repose was calculated using the formula,

$$\theta = \tan^{-1} h/r$$

Where, θ is the angle of repose, h is the height of pile
r is the radius of the base of pile

Table 1- Formulation Table

Sr. no.	Ingredient	Formulation Code (mg)								
		F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
1	Diclofenac Sodium	50	50	50	50	50	50	50	50	50
2	Lactose	131	130	133	132	131	134	133	134	135
3	Starch	6	6	6	5	5	5	4	4	4
4	Sodium Starch glycolate	6	5	4	6	5	4	6	5	4
5	Talc	4	4	4	4	4	4	4	4	4
6	Magnesium Stearate	3	3	3	3	3	3	3	3	3
7	Total weight	200	200	200	200	200	200	200	200	200

Table 2: Limits of angle of repose

Angle of repose (ɵ)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

2. Bulk density

Bulk density of a powder is defined as the ratio of the mass of the powder and its bulk volume. It is used to describe packing of particles. For bulk determination, a weighed quantity of the powder material was introduced into a graduated measuring cylinder and volume of powder was determined.

Bulk Density= Mass of the powder/ bulk volume

3. Tapped density

For determination of the tapped density, a weighed quantity of the powder was introduced into a graduated measuring cylinder and was tapped mechanically either manually or using a taping device till a constant volume was obtained

Tapped Density= Mass of the powder/ tapped volume

4. Carr's compressibility index

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow. The compressibility index is determined by Carr's index, which is calculated by using the following formula,

$C = 100(1-B/T)$

Where, B is bulk density, T is tapped density

5. Hausner's Ratio Hausner's ratio is an index of ease of powder flow. It is calculated by the following formula,

Hausner's Ratio= Tapped density/ Bulk density

Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (>1.25)

Table 3: Flow Characteristics

Carr's Index	Flow Character	Hausner's Ratio
<10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very very poor	>1.60

Post Compression Parameter

1. Hardness

The hardness of the tablet indicates its tensile strength and is measured in terms of load/pressure required to crush it when placed on its edge. Hardness has influence on disintegration and dissolution times and may affect bioavailability. Monsanto hardness tester was used to measure hardness of the formulated tablet. The tester consists of a barrel containing a compressed spring held between two plungers. The lower plunger was then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring was compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture ease record and the zero force reading was deducted from it. It is expressed in kg/cm^2.

2. Friability

This test evaluates ability of tablet to withstand abrasion and edge damage during packing, handling and shipping. Friability generally reflects poor cohesion of tablet ingredients. Friability was measured by the help of Roche friabilator. 10 tablets were weighed and placed in plastic chamber that revolves at 25 rpm for 4 minutes. Tablets were re-weighed after removal of fines. The friability was calculated by the formula

$F = w(initial) - w(final)/w(initial)$

3. Weight variation

Tablets are designed to contain a specific amount of drug in a specific amount of tablet formulation. The weight of the tablet is measured to help ensure that a tablet contain the proper amount of drug. 20 tablets were selected randomly from each formulation were individually weighed using an electronic balance. Average weight of the tablets was calculated. The individual weight of the tablet was compared with average weight. The tablets meet the USP specification if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

$Weight\ variation = w_{avg} - w_{initial} / w_{avg} \times 100$

Where, W_{avg}= Average weight of tablet, $W_{initial}$= Individual weight of tablet

Table 4: Weight Variation

Average weight of tablets(IP)	Average weight of tablets(USP)	Maximum % Difference allowed
Less than 80mg	Less than 130mg	10
80mg-250mg	130mg-324mg	7.5
More than 250mg	More than 324mg	5

4. Disintegration time

The process of breakdown of a tablet into smaller particles is known as disintegration. One tablet was placed in each of 6 tubes of the basket. A disc was added to each tube and the apparatus was run using 6.8pH phosphate buffer maintained at 37^0C as the immersion liquid. The assembly was raised and lowered between 30 cycles per minute in the 6.8pH phosphate buffer. The time in second taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured and recorded. The tablet must be disintegrated **within 3 minutes.**

5. In vitro dissolution studies

In-vitro dissolution studies of the tablets were carried out in USP dissolution apparatus type IIby employing a paddle stirrer at 50 rpm using 900 mL of pH 6.8 phosphate buffer sat 37± 0.5^0C as a dissolution medium. One tablet was used in each test. Aliquots of 5 mL each were withdrawn at specified time intervals (0, 2, 6, 8, 10, and 12) and replaced with equal volume of fresh medium. The withdrawn aliquots were analyzed for drug content spectrophotometrically at λ_{max} 275nm. Drug concentration was calculated and expressed as cumulative percent of the drug released.

RESULTS AND DISCUSSION

Diclofenac Sodium Oro dispersible tablet were prepared by direct compression method. Sodium Starch Glycolate and Starch were used as super disintegrant which help in rapid and drug dissolution.

Weight Variation:

All tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopeia limits.

Friability:

The friability of the formulations was found to be between 0.33-0.75% and was within the official requirement (i.e. less than 1%).

Hardness:

The hardness was maintained to be within 2.8-3.2 kg/cm^2, no variation in the hardness was found which clearly indicates that the blending was uniform.

Disintegration time

In vitro disintegration time for all the formulations varied from 22.6 to 39.3 seconds. The formulation F_9 shows better disintegration time of 22.6seconds.

Table no 5- Evaluation of pre compression parameter

Formulations	Angle of repose (Mean ±SD)	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index compressibility index	Hausner's ratio
F_1	30.24±0.52	0.52±0.02	0.63±0.04	16.42	1.21
F_2	25.42±1.20	0.38±0.04	0.46±0.34	15.42	1.16
F_3	22.74±1.02	0.46±0.12	0.50±0.06	14.78	1.13
F_4	26.32±1.22	0.43±0.03	0.62±0.12	11.67	1.15
F_5	26.22±0.65	0.45±0.12	0.52±0.01	12.01	1.15
F_6	27.42±0.66	0.41±0.02	0.62±0.16	14.87	1.20
F_7	28.60±0.74	0.43±0.25	0.56±0.08	14.64	1.22
F_8	26.62±0.42	0.46±0.14	0.62±0.05	15.44	1.17
F_9	**25.72±0.82**	**o.42±0.03**	**0.62±0.06**	**13.45**	**1.28**

Table 6: Evaluation of Post compression parameter

Formulation Code	Hardness (kg/cm²)	Friability (%)	Weight variation (mg)
F_1	2.8±0.22	0.642±0.30	198.6±0.04
F_2	2.6±0.12	0.546±0.38	196.1±0.12
F_3	3.1±0.14	0.32±0.24	197.5±0.07
F_4	2.1±0.03	0.542±0.12	196.3±0.18
F_5	2.8±0.16	0.539±0.20	198.1±0.17
F_6	2.7±0.02	0.356±0.20	199.4±0.04
F_7	2.8±0.02	0.484±0.31	199.5±0.12
F_8	2.9±0.04	0.743±0.30	198.5±0.04
F_9	**2.8±0.05**	**0.688±0.40**	**198.7±0.07**

Table no 7- Disintegration Time

Formulation code	In vitro Disintegration time (sec)
F_1	38.2
F_2	36.8
F_3	32.4
F_4	28.6
F_5	29.5
F_6	32.6
F_7	28.1
F_8	29.4
F_9	**22.6**

In vitro Dissolution Study

The result of In vitro dissolution study indicates that process used to prepare the orodispersible tablet to enhance the rate and extent of dissolution of Diclofenac. From the In vitro dissolution data it was found that as the concentration of superdisintegrants increased, the drug release also increased. Among the different batches of formulation F_9 shows highest dissolution rate were around 84.6

Table 8:

Sr. no	Time in min	Formulation code (% drug release)								
		F_1	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**
1	0	0	0	0	0	0	0	0	0	0
2	2	8.77	14.48	15.70	21.79	7.24	12.74	19.39	13.74	**23.84**
3	4	10.24	20.55	22.06	27.64	11.20	17.00	24.50	17.72	**25.90**
4	6	14.53	27.52	26.42	32.36	13.56	23.20	28.34	23.82	**29.84**
5	8	16.11	28.95	32.69	35.54	19.23	27.24	34.50	25.97	**33.40**
6	10	20.54	33.05	35.52	38.50	23.06	32.84	38.93	32.72	**38.62**
7	12	22.83	35.85	37.81	41.60	26.88	41.65	39.56	37.24	**42.07**
8	14	25.65	37.86	42.84	49.74	29.85	43.12	44.17	47.76	**54.87**
9	16	28.63	40.65	45.67	58.67	32.77	48.26	57.62	47.44	**63.08**
10	18	32.0.5	42.82	50.22	67.22	44.65	61.15	86.21	64.52	**84.65**

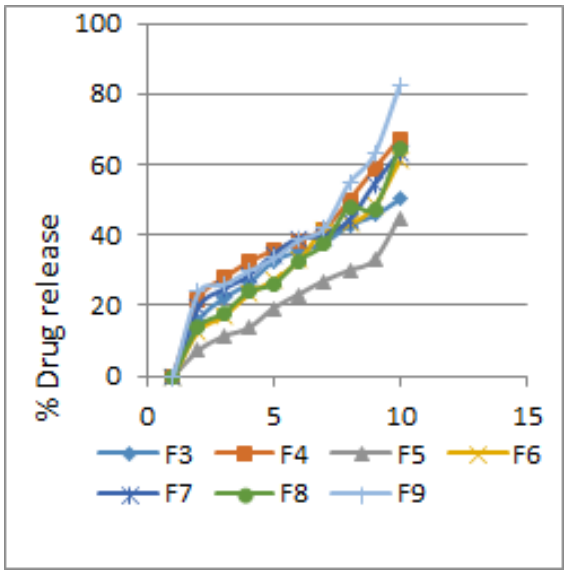


Fig: % drug release

CONCLUSION

Diclofenac Sodium is widely used Non-Steroidal Anti-inflammatory drug for rheumatoid arthritis, inflammation and pain relief. Fast dissolving tablets of Diclofenac Sodium are a useful approach for pain management and a feasible alternative to the available conventional immediate release dosage form. From the results, optimized F_9 formulation showed improved drug release characteristics.

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