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Formulation and evaluation of fast dissolving tablet of diclofenac sodium

Kanishk Katyan[1], Manish Kumar[2], Parag Bhushan Gautam[3], Aman Sharma[4*], Rohit Choudhary[5]
[1] Department of Pharmaceutics, Meerut Institute of Enginnering and Technology, Meerut, Uttar Pradesh, India
[2] Department of Pharmaceutics, Bharat Institute of Technology, Meerut, Uttar Pradesh, India
[3]The Central Drugs Standard Control Organisation, Ahmedabad, Gujarat, India
[4] Department of Pharmaceutics, Kalka Institute of Advanced Research & Studies, Meerut, Uttar Pradesh, India
[5] Department of Pharmaceutical Chemistry, Kalka Institute of Advanced Research & Studies, Meerut, Uttar Pradesh, India

Abstract
Fast dissolving tablets (FDTs) are novel drug delivery type of tablets that dissipate or disintegrate in saliva within a few seconds without water. Diclofenac Sodium was used as a main drug in this formulation. Diclofenac Sodium is widely prescribed analgesic drug and used to relieve pain, inflammation and joint stiffness. All the formulations were prepared by using direct compression method, which is a traditional method of preparation. Different parameters like pre and post-compressional parameters were tested and final formula was selected based on in-vitro disintegration time and in-vitro dissolution profile. Where, all the formulations were dissipated < 40 seconds and F6 formulations was showing 100% release at 30 minute and faster, compared to the marketed formulation and the formulation was found to be stable.

Keywords: fast dissolving tablet, direct compression method, diclofenac sodium

1. Introduction

1.1. Oral Route

Oral administration is denoted by the "PO" from "per os" which refers as "by mouth". Oral route/ingestion is the general and the first choice for the administration of any solid or liquid dosage form of the drugs. The drug travels from your mouth into the esophagus and then into the intestine i.e. oral route is the part of the enteral route with 'enteral' referring to the intestines these drugs eventually reach, since it is accessible, safer, noninvasive, often painless and medicament need not to be sterile. It does not need any special knowledge and special supplies (like syringes, needles, etc.) for its use only a basic set of instructions allow patients to take their medicament safely and it reducing visit to health centres. Both solid dosage forms (powders, tablets, capsules, dragees, spansules, moulded tablets, gastrointestinal therapeutic systems-GITs) and liquid dosage forms (syrups, elixirs, mixtures, emulsions) can be given orally [1, 2].

Advantages

- Can be self-administered, pain free, easy to take.
- Absorption takes place along the whole length of the GI tract.
- The drugs preparation needs no sterilization.
- Most suitable route for GIT infections and GI parasites.
- Cheap as compared to most other parenteral routes.[3]

1.2. Fast Dissolving Tablets (FDT)

A fast dissolving drug delivery system can be defined as a compressed dosage form for oral administration, when placed in mouth, rapidly disintegrates and can be swallowed in the form of liquid. Fast dissolving tablets disintegrates or breakdown swiftly in the saliva without the need of water. There are some tablets which are designed/delineated to diffuse in saliva remarkably rapid, within a few seconds and are accurate fast dissolving tablets. Fast dissolving tablets are also called as mouth dissolving tablet, orodispersible tablet, rapimelts, quick dissolving tablets, etc. The target populations for these new fast dissolving dosage forms have generally been pediatric, geriatric and bedridden or developmentally disabled patients [4, 5].

Advantages

1. Ease of administration for those patients who have difficulty in swallowing tablet.
2. No need of water to swallow the dosage form.
3. Have acceptable taste masking property.
4. Achieve increased bioavailability through absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
5. Have rapid dissolution and absorption of the drug which will produce quick onset of action.
6. Cost effective [6].

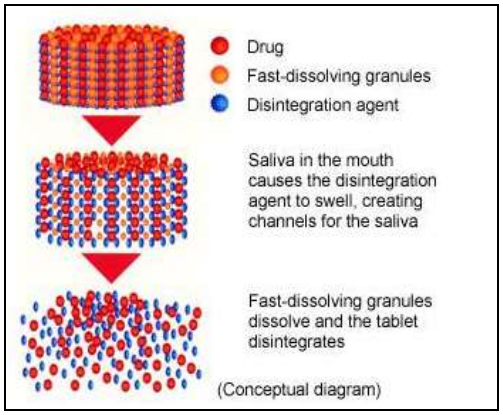

Fig 1: Concept of FDT

1.3. Profile of Diclofenac Sodium

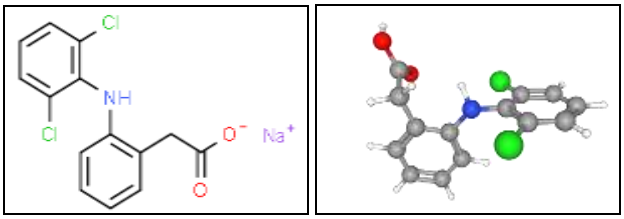

Fig 2: Diclofenac Sodium Structure

IUPAC Name Sodium 2-{2-[(2,6-Dichlorophenyl) amino] phenyl} acetate
Formula $C_{14}H_{10}Cl_2NNaO_2$
Molecular Mass 318.1 g/mol
Melting Point 284^{O}C [543.2^{O}F]
Bioavailability 49-73%
Protein Binding 99.5%
Metabolism Hepatic
Half Life 1.2-2 Hrs
Excretion Biliary
Diclofenac Sodium is the sodium salt form of the Diclofenac, a benzene acetic acid derivative and n on steroidal anti-inflammatory drug (NSAID) with analgesic, antipyretic and anti-inflammatory activity. Diclofenac sodium is a non-selective reversible and competitive inhibitor of cyclooxegenase (COX), subsequently blocking the conversion of arachidonic acid into prostaglandin precursors. This leads to an inhibition of the formation of prostaglandins that are involved in pain, inflammation and fever [7, 8, 9].

2. Material and Method

2.1. Material Used

Diclofenac Sodium was obtained as a gift sample from Central Drug House (CDH) Pvt. Ltd. In Delhi and Croscarmellose Sodium, PEG-400, Acacia, Talc, Lactose, and Magnesium Stearate were obtained as a gift sample from CDH.

2.2. Method

By Direct Compression Method

Direct compression is defined as the process by which tablets are compressed directly from the powder blends of the active pharmaceutical ingredients and with suitable excipients including diluent, disintegrant, lubricant and other additives. Direct compression technique/procedure does not require the use of heat or water during the formulation process and is the ideal technique for moisture and thermo-labile medications. This is the procedure of compressing mixed powders into tablets without the need of granulating step [10].

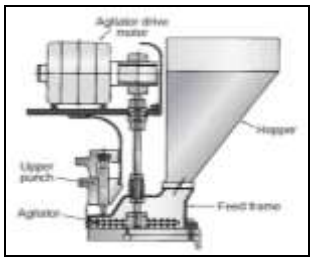

Fig 3: Direct Compression Machine

3. Evaluation of Fast Dissolving Tablets Of Diclofenac Sodium 125 mg.

3.1. Evaluation of Blends

The powder blend was evaluated for carr's index, tapped density, angle of repose, bulk density and hausner's ratio.

3.1.1. Bulk Density (D_b)

It is the ratio of total mass of the powder to bulk volume of powder, it was measured by pouring the weighed powder into a measuring cylinder and the initial volume was noted. The initial volume is called the bulk volume. From this the bulk density is calculated according to the formula given below. It is expressed in g/cc.

$$D_b = M/V_o$$

Where, M = the mass of powder
V_o = the bulk volume of powder

3.1.2. Tapped Density (D_t)

It is the ratio of total mass of powder to the tapped volume of the powder. The volume was measured by tapping the powder repeatedly, then the tapping was done after sometime, and the tapped volume was noted. Tapped density is calculated according to the formula given below. It is expressed in g/cc.

$$D_t = M/V_1$$

Where, M = the mass of powder
V_1 = the tapped volume of the powder

3.1.3. Carr's Index (%)

The carr's index is an indication of the compressibility of the powder. A volume is filled into a graduated glass cylinder and repeatedly tapped for a known duration. The volume of powder after tapping is measured. It can be calculated by the formula given below.

$$Carr's\ index = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density} X\ 100$$

3.1.4. Hausner's Ratio

It is the ratio of tapped density to bulk density. Lower the value of Hausner's ratio better is the flow property. It can be calculated by the formula given below.

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ Density}$$

Hausner ratio	Flow character
1.00-1.11	Excellent
1.12-1.18	Good
1.19-1.25	Fair
1.26-1.34	Passable
1.35-1.45	Poor
1.46-1.59	Very poor
>1.60	Very, very poor

Fig 4: Hausner's Ratio

3.1.5. Angle of Repose (ɵ)

It is defined as the maximum angle possible between the surface of a pile of a powder and the horizontal plane.

Tan ɵ = h/r

Then, **ɵ = $\tan^{-1}$ (h/r)**

Where, ɵ = the angle of repose

h = height in cm

r = radius in cm

The powdered mixture was allowed to flow through the funnel with its tip fixed to stand at a definite height (h) from a paper placed on a horizontal surface. The angle of repose was then calculated by measuring the height and radius of the heap of powder formed.

Flow Property	Angle of Repose (degrees)
Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	> 66

Fig 5: Angle of Repose

3.2. Evaluation of Tablets

3.2.1. Friability Test

The friability of tablets was measured in a Roche Friabilator. Tablets of known weight (W_o) or sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1%.

% Friability = 100 (W_o – W) / W_o

3.2.2. Weight Variation Test

The weight variation test would be a satisfactory method for determining drug content uniformity of drug distribution. In practice this test is performed by taking 20 tablets, from a batch. 20 tablets are weighed at a time and the average weight is taken. Then the tablet is weighed individually.

Average weight (U.S.P)	Average Weight (I.P)	Percentage Difference
130mg or less	Less than 80 mg	10
More than 130 mg through 324 mg	More than 80 mg through 250 mg	7.5
More than 324 mg	More than 250 mg	5

3.2.3. Content Uniformity Time

Ten (10) tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of diclofenac sodium was transferred to a 100 ml of volumetric flask and 10 ml of methanol was added. The drug was extracted in methanol by vigorously shaking the stoppered flask for 15 minutes. Then the volume was adjusted to the mark with 0.1 N HCl. The diclofenac sodium content was determined by measuring the absorbance after appropriate dilution in UV spectrophotometer.

3.2.4. In-Vitro 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 37ºC 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.

3.2.5. In-Vitro Dissolution Studies

In-vitro dissolution studies of the tablets were carried out in USP dissolution apparatus Type II by employing a paddle stirrer at 50 rpm using 900 mL of pH 6.8 phosphate buffer at 37 ± 0.5ºC 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.

3.2.6. Tablet Thickness

The thickness of tablet was determined by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the filled material and the force applied during compression. Tablet thickness may be measured by Vernier Calipers or by automated equipment or by hand gauge during the production of the tablet.

3.2.7. Hardness Test

Tablet hardness testing is a laboratory procedure used by the pharmaceutical industry to test the breaking point and structural integrity of a tablet. Placed the diclofenac sodium tablet in the Monsanto hardness tester and then rotated the screw till break point of the tester. The procedure was repeated 8 to 10 times for average reading. The force of fracture ease record and the zero-force reading was deducted from it. It is expressed in kg/cm2.

4. Result & Discussion

The formulation of various batches is described in Table No. 1. The pre-compression study and evaluation parameters like carr's index, hausner's ratio, bulk density, tapped density, angle of repose and weight variation, hardness, thickness, friability, disintegration and in-vitro dissolution rate and assay for drug content were found to be acceptable and result were presented in Table No. 2, 3 and 4.

In this formulation containing microcrystalline cellulose and sodium starch glycolate show adequately decrease in disintegration time (average time 30 to 35 seconds) among all the formulations. In-vitro dissolution rate study show that after 15 minutes formulation F4-F6 % drug release 72%, 82% and 92% respectively. Pre- compression studies such as angle of repose of this formulation blends of F4-F6 was found to be 31.35, 32.05 and 24.20 respectively. Thus the formulation of batch F6 was prepared by direct compression method has shown better profile.

Table 1: Formulation table for Diclofenac Sodium (125 mg) Fast Dissolving Tablet

Ingredients	F1	F2	F3	F4	F5	F6
Diclofenac Sodium	125	125	125	125	125	125
Microcrystalline Cellulose	51	52	53	54	55	56
Starch	5	5	5	5	5	5
Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Lactose	39	38	37	36	35	34
Sodium Starch	25	25	25	25	25	25
Total	250	250	250	250	250	250

Table 2: Pre-Compression Parameters for Fast Dissolving Tablets of Diclofenac Sodium (125 mg)

Formulation Code	Angle of Repose (ɵ)	Bulk Density (g/cc)	Tapped Density (g/cc)	Carr's index (%)	Hausner's Ratio
F1	29.10	0.40	0.48	16	1.20
F2	26.20	0.41	0.50	13	1.15
F3	25.83	0.50	0.58	13	1.16
F4	31.35	0.39	0.47	17	1.16
F5	32.05	0.37	0.41	9.75	1.10
F6	24.20	0.43	0.52	17.3	1.14

Table 3: Post Compression Parameters for Fast Dissolving Tablets of Diclofenac Sodium (125 mg)

Formulation Code	Avg. Wt. (mg) n=20	Thickness (mm) n = 3	Hardness (Kg/cm^2) n=3	% Friability	% Drug Content	Disintegration Time (sec.)
F1	250.5	3.74	3.5	0.50	100.87	32.5
F2	251.3	3.62	3.2	0.42	101.25	38.2
F3	248.2	3.65	3.6	0.65	98.85	39.5
F4	250	3.95	3.6	0.55	100.20	28
F5	248.5	3.55	3.4	0.40	99.65	34.6
F6	251.2	3.58	3.1	0.45	100.55	26.5

Table 4: In vitro Dissolution studies for Diclofenac Sodium Tablets in 0.1 N HCl solution

Time	Marketed	F1	F2	F3	F4	F5	F6
5	15	15	13	17	18	20	20
10	28	25	27	31	32	35	46
15	45	37	42	38	51	56	69
20	60	47	60	62	72	82	92
25	85	65	82	86	89	96	99
30	95	79	90	95	98	100	100

The weight variation of tablets was within the range of ±7.5 % complying with pharmacopoeia specification of IP. The thickness of tablets was to be between 3.58 to 3.95 mm. the hardness of various formulations was found to be between 3.1 to 3.6 kg/cm^2, indicating acceptable mechanical strength. The friability was < 1.0 % w/w for all the formulations, which is a sign of good mechanical resistance of the tablets. The drug content found to be within limits 99 to 102 %.

5. Conclusion

The aim of this investigation has been achieved by preparing fast dissolving tablet of Diclofenac Sodium with the pharmaceutical additives of super disintegrating agent (sodium starch glycolate and microcrystalline cellulose). All six batches i.e. F1, F2, F3, F4, F5 and F6 were prepared by direct compression method. The evaluation parameters of tablet like hardness, weight variation, friability and drug content indicates that the value were within allowable limit for all formulations. Disintegration time for all the formulation were <40 seconds which is less than marketed formulations. In-vitro drug release study was carried out in 0.1 N HCl solution using USP II for 30 minutes. F6 formulation was differentiated as the best formulation among all the formulations and selected on the basis of in-vitro dissolution data. Diclofenac sodium formulation F6 was prepared by direct compression method and showed better drug release profile. Thus we are able to attain our aim of preparing fast dissolving tablets of diclofenac sodium with pharmaceutical additives and method of manufacturing to enhance the dissolution of the drug.

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