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Formulation and evaluation of oral fast disintegrating tablet of ibuprofen

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Abstract
Fast disintegrating tablets are novel drug delivery type of tablets that dissipate in saliva within a few seconds without the need of water. The object of the present investigation was to design and evaluate oral disintegrating tablet (ODT) of Ibuprofen, a non-steroidal anti-inflammatory drug used for the treatment of arthritis with a view to ameliorating its oral bioavailability. The focus of the study was to develop ODT of ibuprofen using super disintegrating agents for ease of administration and its physiochemical characterization. All the formulations F1-F5 were prepared by using direct compression method. Different parameters like pre-compression parameters like angle of repose, bulk density, tapped density, carr's index, hausner's ratio and post compression parameters like friability, hardness, thickness, drug content were tested and the disintegration time was in the range of 45 to 55 seconds an in-vitro dispersion time was found to be 22 to 55 seconds. Where F3 formulation offered the relatively rapid release of ibuprofen when compared with other formulations.

Keywords: ibuprofen, direct compression method, nsaid, fast dissolving tablet

1. Introduction
Oral routes of drug administration have broad acceptance upto 50-60% of the total dosage forms. Solid dosage forms are popular because of the comfort in administration, accurate dosage, self- medication, pain avoidance and most importantly the patient compliance[1]. Fast dissolving drug delivery system first developed in the 1970s as a substitute to conventional dosage forms for the geriatric and pediatric patients. These tablets are created or designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds. Pharmaceutical technologist have developed a novel oral dosage forms known as fast disintegrating tablets (FDTs), orally disintegration tablets (ODTs), mouth melting tablets (MMTs) or mouth dissolving tablets (MDTs) which disintegrate or dissolve rapidly in saliva, usually in a matter of seconds without need to take water [2].

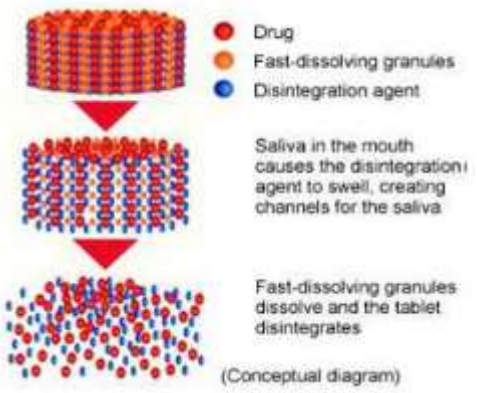

Fig 1: Conceptual diagram of FDT

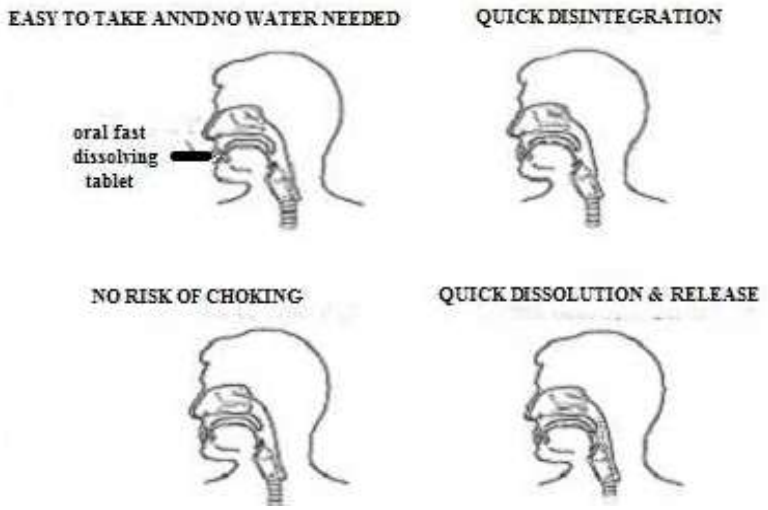

Fig 2: Advantages of FDTs

1.1. Profile of Ibuprofen

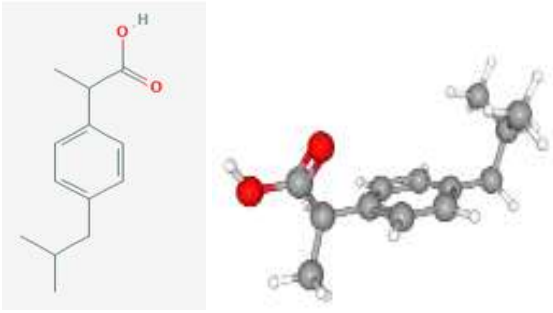

Fig 3: Structure of Ibuprofen

IUPAC Name: 2-[4-(2-methylpropyl) phenyl] propanoic acid
Formula: C_{13} H_{18} O_2
Molecular Mass: 206.28 g/mol
Bioavailability: 80-100%
Protein Bounding: 90-99%
Metabolism: Liver
Half Life: 2-4 Hrs
Excretion: Urine & Feces

Ibuprofen is a propionic acid derivative and non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic effects. Ibuprofen inhibits the activity of cyclo-oxygenase I and II, resulting in a decreased formation of precursors of prostaglandins and thromboxanes. This leads to decreased prostaglandin synthesis by prostaglandin synthase, the main physiologic effect of ibuprofen.
Ibuprofen also cause a decrease in the formation of thromboxane A2 synthesis by thromboxane synthase thereby inhibiting platelet aggregation. Ibuprofen is a drug which is used for symptomatic treatment of rheumatoid arthritis, juvenile rheumatoid arthritis and osteoarthritis. It also used to treat mild to moderate pain and for the management of dysmenorrhea [3].

2. Materials and Methods

2.1 Materials

Ibuprofen purchased from Natco Pharma, Hyderabad, Sodium starch glycolate, Crospovidone, Croscarmellose sodium, Mannitol, Microcrystalline cellulose, Talc and Magnesium stearate were purchased from Prachin Chemicals, Gujarat.

2.2 Methods

The parameters to formulate or develop a fast dissolving tablet is depend upon the choice of super disintegrating agent. The main objective for fast dissolving tablets is to dissolve or disintegrate rapidly in the oral cavity in 15-60 seconds without the need of water and should have idyllic mouth feel.
Fast dissolving tablets of Ibuprofen were prepared using direct compression method incorporating super disintegrating agents Microcrystalline Cellulose and Croscarmellose Sodium. The Ibuprofen is equivalent to 100 mg, Mannitol and Microcrystalline cellulose were mixed uniformly in glass mortar by using pestle. Now other excipients Aspartame, Talc, and Magnesium stearate was added in the powder mixture. The whole mixture was passed through Sieve No. 80 twice.

Table 1: Formulation of Ibuprofen Fast Dissolving Tablets

Ingredients	F1	F2	F3	F4	F5
Ibuprofen	100	100	100	100	100
Sodium starch glycolate	-	2	4	6	8
Croscarmellose sodium	-	2	4	6	8
Mannitol	52	48	44	40	36
Microcrystalline cellulose	40	40	40	40	40
Talc	3	3	3	3	3
Magnesium stearate	3	3	3	3	3
Aspartame	2	2	2	2	2
Total	200	200	200	200	200

3. Evaluation of Fast Dissolving Tablet

3.1 Pre-compression Parameters

3.1.1 Angle of Repose

The angle of repose of the material is the angle of dip relative to the horizontal plane to which a material can be piled without depression. Angle of repose was determined by using fixed funnel method. The material was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured and it was calculated using formula [4, 5, 6].

$\tan \theta = h/r$

Then, $\theta = \tan^{-1} (h/r)$

Where, θ = the angle of repose
h = height in cm
r = radius in cm

3.1.2 Bulk Density

It is defined as the weight of many particles of the material divided by the total volume they occupy. The total volume includes particle volume, inter-particle void volume, and internal pore volume. It is the ratio of the bulk mass of powder to the bulk volume. It is expressed in g/cc [4, 6, 7].

$$D_b = M/V_o$$

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

3.1.3 Tapped Density

It is the ratio of the weight of powder to the minimum volume occupied in measuring cylinder. Tapped density is determined by placing a graduated cylinder containing known mass of drug or formulation on a mechanical tapper apparatus which is operated at fixed no. of taps. It is

expressed in g/cc [4, 8, 9].

$$D_t = M/V_1$$

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

3.1.4 Carr's Index
Carr's index is an indication of the ease with which a material can be induced to flow is given by compressibility of the granules was determined by Carr's compressibility index (C) which is calculated by using the formula [4, 8, 9].

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

3.1.5 Hausner's Ratio
It is the ratio of tapped density to bulk density and is an indirect index of ease of powder flow. Lower hausner ratio (<1.25) indicate better flow properties. It can be calculated by the following formula [4, 9, 10].

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

3.2 Post-compression Parameter
All the batches of tablet were evaluated for various parameters and these are as follows

3.2.1 Uniformity of Weight
This test is done by sampling and weighing 20 tablets at random and average weight is calculated. IP limit for weight variation in case of tablets weighing up to 120 mg ±10%, 120 mg to 300 mg is ±7.5% and more than 300 mg is ± 5%.

3.2.2 Tablet Thickness
The thickness and diameter of the tablets was determined using a Vernier calipers or by hand gauge. Tablet thickness should be controlled within 5% or less of a standard value.

3.2.3 Hardness Test
The strength of tablet is expressed as tensile strength kg/cm^2. The tablet crushing load which is the force required to break a tablet into pieces by compression. It was determined using Monsanto Hardness Tester.

3.2.4 Friability Test
Roche friabilator was used to determine the friability. Pre weighed tablets were placed in friabilator and rotated at speed of 25 rpm for 4 minute or up to 100 revolutions. The percentage of weight loss was calculated by the formula.

% Friability = initial weight – final weight / initial weight X 100

3.2.5 Water Absorption Ratio
A piece of tissue paper folded twice was kept in a Petri dish containing 6 ml of purified water the tablet was placed on the tissue paper and allowed to wet completely. The wetted tablet was removed and reweighted.

$$R = (W_a - W_b) / W_b\ X\ 100$$

Where W_b = the weight before water absorption & W_a the weight after water absorption

3.2.6 Content Uniformity
20 tablets were powdered and equivalent to 100 mg of Ibuprofen was weighed and transferred into 100 ml of volumetric flask. 5 ml of methanol was added and shaken for 10 minutes. Then the volume make up to 100 ml with 6.8 pH phosphate buffer. The solution was filtered, diluted suitably and analyzed spetrophotometrically at 221 nm.

3.2.7 In- vitro Dispersion Time
Tablet was added to 10 ml of phosphate buffer solution of pH 6.8 at 37^0C ± 0.5^0C. the time required for complete dispersion of tablet was measured.

3.2.8 Disintegration Test
6 tablets were placed individually in each test tube of disintegration test apparatus. The water was maintained at a temperature of 37^0 ± 0.5^0 C and time taken for entire tablet to disintegrate completely was noted.

3.2.9 *In – vitro* Dissolution Studies
In vitro dissolutions studies performed by using USP dissolution test apparatus using 6.8 phosphate buffer as dissolution medium. The paddle are allowed to rotate at speed of 100 rpm.
The dissolution medium was maintained at a temperature of 37^0C and samples are withdrawn at an interval of every 5 minutes. The withdrawn samples were filtered and absorbance were measured at λ_{max} 221 nm using UV spectrophotometer.

4. Result and Discussion
Ibuprofen orally fast dissolving tablet were prepared by using direct compression method and carried out by using super disintegrating agents and other additives as mentioned in formulation Table 1.
A total number of 5 formulations were prepared by direct compression method. The pre-formulation studies such as bulk density, hausner's ratio, etc. were evaluated and mention in Table 2. The data obtained from the post-compression parameters such as hardness, % weight variation, Friability, dug content, average weight, disintegration time, water absorption ratio, in-vitro dispersion time and in-vitro dissolution studies are mentioned in Table 3 and Table 4. Out of all 5 formulations, F3 was found satisfactory.

Table 2: Pre- Compression Parameters of the Formulation

Formulation Code	Angle of Repose (ɵ)	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's Index	Hausner's Ratio
F1	26.1	0.40	0.45	12.10	1.10
F2	26.5	0.43	0.50	14.15	1.15
F3	27.5	0.45	0.54	13.50	1.19
F4	26.7	0.48	0.52	14.50	1.16
F5	27.9	0.42	0.55	14.5	1.18

Table 3: Post- Compression Parameters of the Formulation

Formulation Code	Hardness Kg/cm^2	Thickness (mm)	Friabilty (%)	Average Weight (mg)	Drug Content (%)	Disintegration Time (sec)	Water Absorption Ratio	In-vitro dispersion Time
F1	3.2	3.5	0.5	198.2	98.5	70	50	8.1
F2	3.6	3.8	0.2	199.1	99.7	75	65	6.8
F3	3.8	3.5	0.4	200	100	60	70	4.5
F4	3.5	3.1	0.6	201	101.2	68	85	3.8
F5	3.9	3.4	0.4	197.5	98.9	79	90	2.5

Table 4: Dissolution Profile of the Formulation

Time	F1	F2	F3	F4	F5
5	14.30	14.75	16.20	15.25	14.50
10	25.15	26.20	29.55	27.15	28.85
15	39.50	38.25	45.30	42.65	42.25
20	53.05	53.85	55.20	46.25	48.20
25	66.20	65.10	32.75	65.85	62.25
30	68.50	71.15	68.90	71.45	70.85
35	70.15	72.25	74.50	75.85	74.45
40	76.25	77.25	80.25	73.20	77.55
45	81.30	83.45	88.85	86.65	84.25
50	87.40	88.29	92.25	88.25	86.35
55	91.15	90.75	94.50	93.45	90.16
60	93.25	94.30	98.75	94.50	93.45

5. Conclusion

The aim of this investigation has been achieved by preparing orally fast disintegrating tablet of Ibuprofen with the super disintegrating agent. Therefore conclude that F3 offered the relatively rapid release of Ibuprofen when compared with other formulations. The formulation was prepared with croscarmellose sodium which offered the relatively rapid release of Ibuprofen. Thus we are able to attain our aim of preparing orally fast disintegrating tablet of Ibuprofen with pharmaceutical excipients and method of manufacturing to enhance the dissolution of the drug.

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