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Design and Development of Fast Dissolving Tablets of Ibuprofen

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Research Article

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ABSTRACT

The aim of the present investigation was to develop fast dissolving tablets of Ibuprofen, an NSAID drug used for the treatment of arthritis. Due to its low solubility, gastric irritation and its short biological half-life of 2 hours, fast dissolving tablets of Ibuprofen were prepared using superdisintegrants in order to improve the dissolution rate, thereby the absorption and to reduce gastric irritation. The influence of concentration of the sodium starch glycolate was studied by a set of four formulations (F1, F2, F3, F4) with concentrations of sodium starch glycolate *viz,* 2%, 3%, 4% & 5%w/w respectively. Also the influence of various superdisintegrants was studied by a set of three formulations (F4, F5 and F6) with three superdisintegrants *viz*, Sodium starch glycolate(5%), Croscarmellose sodium(5%), Crospovidone (5%) respectively. The formulation prepared with 5%w/w of sodium starch glycolate was offered relatively rapid release of Ibuprofen when compared with other concentrations of Sodium Starch glycolate. The formulation prepared with Crospovidone was offered relatively rapid release of Ibuprofen when compared with other superdisintegrants. So, we can conclude that nature and concentration of the superdisintegrant showed influence on the rate of dissolution. The dissolution rate was found to follow first order kinetics.

INTRODUCTION

Fast dissolving tablets are defined as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue[1]". In case of conventional tablets, physical problems with swallowing (dysphagia) can occur at any age but are particularly prevalent in the elderly and those with dementia, whereas refusal to swallow is often encountered in geriatric, pediatric and psychiatric patients. Difficulties and resistance to tablet-taking are common in all patient groups. In recent years, fast dissolving tablets have been developed to overcome problems related to swallowing difficulties[2]. Fast Dissolve', 'Quick Dissolve', 'Rapid Melt', 'Quick Disintegrating', 'Mouth Dissolving, 'Orally Disintegrating', 'Oro Dispersible', 'Melt-in-Mouth' etc. are terms that represent the same drug delivery systems. The orally disintegrating property of tablet is attributed to a quick ingress of water into the tablet matrix, which creates porous structure and result in rapid disintegration. When put on tongue, these tablets disintegrates instantaneously, releasing the drug which dissolves or disperses in saliva. The drugs may be absorbed from mouth, pharynx or esophagus as the saliva passes down into the stomach. Advantages of the Fast dissolving tablets include ease of swallowing without the aid of water, rapid onset of action, enhanced dissolution rate, increased gastric absorption, improved oral bioavailability, minimized first pass metabolism and improved patient compliance[3,4,5].

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) used for relief of signs and symptoms of rheumatoid arthritis, osteoarthritis and is used in chronic and acute conditions of pain and inflammation[6]. As its serum concentrations and analgesic effect are correlated, rapid absorption of ibuprofen could be a prerequisite for the quick onset of its action. The major problems with drug is its very low solubility in biological fluids, gastric irritation and its short biological half-life of 2 h. It is practically insoluble in water and so possesses poor solubility and subsequent poor GI absorption and bioavailability [7]. In order to improve the dissolution rate and thereby the absorption, fast dissolving tablets of Ibuprofen were prepared using superdisintegrants by direct compression.The use of fast

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dissolving tablets could help to reduce the gastrointestinal side effects of ibuprofen, since the tablet is disintegrated within the mouth.

MATERIALS AND METHODS

Ibuprofen was obtained from Natco Pharma ,Hyderabad, India. Sodium starch glycolate, crosspovidone, Croscarmellose sodium, Mannitol, Micro crystalline cellulose, talc and magnesium stearate were purchased from SD fine Chemicals Ltd, Mumbai. All other materials used were of analytical grade.

Preparation of fast dissolving tablets

The compositions of the tablets are given in Table 1. All the ingredients as shown in Table 1 were passed through mess80, co-ground in a motor and pestle. Then talc and magnesium stearate were added and mixed for 10 minutes. To study the influence of concentration of the sodium starch glycolate on the performance of Ibuprofen, a set of four formulations (F_1, F_2, F_3, F_4) were prepared using four different concentrations of sodium starch glycolate *viz,* 2%, 3%, 4% & 5%w/w respectively. To study the influence of various superdisintegrants on the performance of Ibuprofen, a set of three formulations (F_4, F_5 and F_6) were prepared using three different superdisintegrants *viz*, Sodium starch glycolate(5%), Croscarmellose sodium(5%), Crospovidone (5%) respectively. The powder blend was compressed into tablets on a rotary multi-station tabletting machine (Cadmach Machinery Co. Pvt. Ltd., Mumbai) using 7 mm round and flat punches. Tablets were stored in airtight container and used for further study.

Table 1: Composition of ingredients for Ibuprofen fast dissolving tablets:

S.No	Ingredients	F_1	F_2	F_3	F_4	F_5	F_6
1	Ibuprofen	100	100	100	100	100	100
2	Sodium starch glycolate	4	6	8	10	-	-
3	Croscarmellose sodium		-	-	-	10	-
4	Crospovidone	-	-	-	-	-	10
5	Mannitol	50	48	46	44	44	44
6	Micro crystalline cellulose	40	40	40	40	40	40
6	Talc	3	3	3	3	3	3
7	Magnesium stearate	3	3	3	3	3	3
8	Total weight	200	200	200	200	200	200

Evaluation of formulated tablets

The prepared tablets were evaluated for the following parameters.

Hardness test[8]

The compression force required to break the tablet in to two halves was measured by using Monsanto hardness tester.

Weight variation[9]

Weight variation test is done with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets.

Friability [10]

Roche friabilator was used to determine the friability. Pre weighed tablets were placed in friabilator and rotated at a speed of 25 rpm for 4 minutes or up to 100 revolutions. The tablets are dropped from a distance of 6 inches in each revolution. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

Content uniformity [11]

Twenty tablets were powdered, and powder equivalent to 100 mg of Ibuprofen was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 5 ml methanol was added and shaken for 10 min. Then, the volume was made up to 100 ml with 6.8 phosphate buffer. The solution was filtered, diluted suitably and analyzed spectrophotometrically at 221 nm.

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Wetting time and water absorption ratio [12,13]

A piece of paper folded twice was kept in a Petri dish containing 6 ml of purified water containing amaranth dye. A tablet was placed on the tissue paper. The time required to develop a colour on the upper surface of the tablet was recorded as the wetting time. The same procedure was followed for determining the water absorption ratio(R) and was determined according to the following equation.

$$R = [(Wa - Wb)/Wb] \times 100$$

Where, Wb and Wa were the weights of the tablet before and after water absorption.

In vitro dispersion time[14]

Tablet was added to 10 ml of phosphate buffer solution pH 6.8 (pH of saliva) at 37± 0.5°C. Time required for complete dispersion of tablet was measured.

Disintegration test [15]

The disintegration time for all formulations was carried out using tablet disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus. The water was maintained at a temperature of 37°±2°C and time taken for the entire tablet to disintegrate completely was noted.

Fineness of dispersion [16]

This test is performed by placing two tablets in 100 ml of water and stirring it gently, till the tablets get completely disintegrated. The formulation is considered to form a smooth dispersion if the complete dispersion passes through a sieve screen with a nominal mesh aperture of 710 µm without leaving a residue on the mesh.

In vitro dissolution studies [17]

In vitro dissolution studies are performed by using USP dissolution test apparatus using 6.8 phosphate buffer as dissolution medium. The paddles are allowed to rotate at speed of 100 rpm. The dissolution medium was maintained at a temperature of 37+0.5 ^{o}C and samples are withdrawn at an interval of every 5 min. The volume of the withdrawn samples is replaced by fresh dissolution medium in order to keep the volume of the dissolution medium as constant. The withdrawn samples were filtered and absorbance was measured at absorption maxima of 221nm using UV-visible spectrophotometer.

RESULTS AND DISCUSSIONS

Micromeritic properties of the blends were studied and results were shown in Table 2. All the blends exhibited good flow properties and suited for direct compression. To study the influence of concentration of the sodium starch glycolate on the performance of ibuprofen, a set of four formulations (F_1, F_2, F_3, F_4) were prepared using four different concentrations of sodium starch glycolate (2%, 3%, 4% & 5%w/w) respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table 3. All the tablets complied with the pharmacopeial standards, but F_1 and F_2 failed to meet the fineness of dispersion requirements. The dissolution data was presented in Table 4 and Figure 1. The dissolution kinetics was presented in Table 5. The dissolution rate followed first-order kinetics (Figure 2) as the graphs drawn between log % drug unreleased vs time were found to be linear. The dissolution rate of ibuprofen was found to be effected by the concentration of the superdisintegrant (sodium starch glycolate) used in the preparation of tablets. Based on the dissolution rate, the order of drug release from the four formulations was $F_4 > F_3 > F_2 > F_1$. The formulation prepared with 5%w/w of sodium starch glycolate was offered relatively rapid release of Ibuprofen when compared with other concentrations employed in this investigation.

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Table 2: Micrometric properties for formulation blends

Formulation	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Carr's index (%)	Hausner's ratio	Angle of repose (°)
F_1	0.442	0.516	14.34	1.16	29.81
F_2	0.447	0.525	14.85	1.17	26.01
F_3	0.459	0.530	13.39	1.15	25.54
F_4	0.480	0.566	15.19	1.17	28.92
F_5	0.448	0.532	15.78	1.18	26.43
F_6	0.439	0.521	15.73	1.18	27.97

Table 3: Physical parameters of Ibuprofen fast dissolving tablets

S.No.	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
1	Average weight (mg)	198±0.2	198±0.1	198±0.2	200±0.2	199±0.1	200±0.1
2	Drug content(%)	98.3	99.8	97.9	99.46	99.33	100.1
3	Disintegration time (sec)	90	85	78	65	46	39
4	Friability(%)	0.82	0.87	0.73	0.86	0.6	0.78
5	Hardness(kg/cm²)	3.5	3	4	4	3.5	4
6	Wetting time (sec)	46	54	58	50	41	33
7	Water absorption Ratio	53	68	70	89	95	103
8	*In-vitro* dispersion time (min)	6.9 ± 0.12	5.2 ± 0.15	3.4 ± 0.18	2.3 ± 0.11	1.9 ± 0.08	1.4 ± 0.13
9	Fineness of dispersion	Fail	Fail	Pass	Pass	Pass	Pass

Table 4: *In-vitro* dissolution data of Ibuprofen fast dissolving tablets

S.No.	Sampling time (min)	Percentage of drug released					
		F_1	F_2	F_3	F_4	F_5	F_6
1	0	0.00	0.00	0.00	0.00	0.00	0.00
2	5	25.152±0.08	38.02±0.07	50.32±0.05	63.19±0.07	64.33±0.04	78.47±0.06
3	10	28.686±0.06	43.46±0.09	57.37±0.02	72.17±0.05	76.0±0.06	90.22±0.03
4	15	31.956±0.04	48.37±0.02	64.07±0.04	80.35±0.06	84.90±0.04	99.49 49±0.08
5	20	35.668±0.05	53.73±0.04	71.36±0.03	89.42±0.09	97.68±0.07	-
6	25	38.117±0.07	58.97±0.07	78.25±0.05	97.97±0.03	-	-

Table 5: *In-vitro* dissolution kinetics of Ibuprofen fast dissolving tablets

S.No.	Formulation	T_{50} (min)	T_{90} (min)	DE_{15} (%)	K (min^{-1})	Correlation coefficient values	
						Zero Order	First order
1	F_1	29.87	99.26	35.70	0.0232	0.7524	0.8197
2	F_2	17.11	56.86	44.43	0.0405	0.7486	0.8643
3	F_3	10.51	34.94	49.09	0.0659	0.7513	0.9261
4	F_4	5.16	17.14	61.31	0.1343	0.7490	0.9560
5	F_5	4.22	14.01	70.44	0.1641	0.8193	0.9569
6	F_6	2.20	7.33	75.13	0.314	0.8237	0.9658

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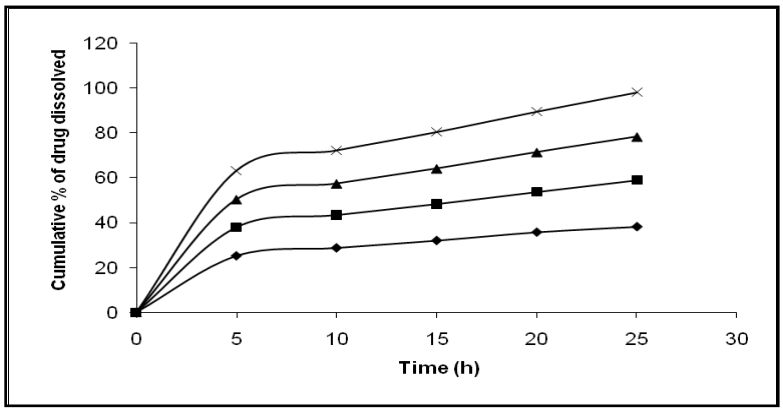
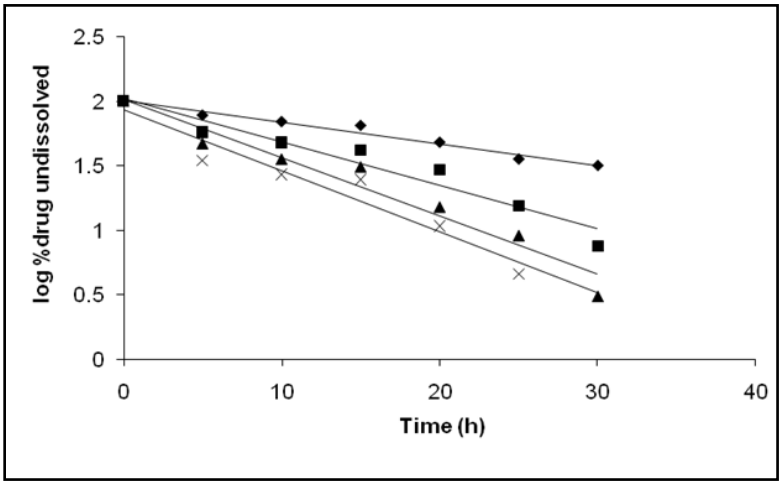
Figure 1: *In-vitro* dissolution profile of Ibuprofen fast dissolving tablets formulated with different concentrations of sodium starch glycolate



(◆) F_1 - Tablets prepared with 2% sodium starch glycolate
(■) F_2 - Tablets prepared with 3% sodium starch glycolate
(▲) F_3 - Tablets prepared with 4% sodium starch glycolate
(×) F_4 - Tablets prepared with 5% sodium starch glycolate

Figure 2: First order plots of Ibuprofen tablets formulated with different concentrations of sodium starch glycolate



(◆) F_1 - Tablets prepared with 2% sodium starch glycolate
(■) F_2 - Tablets prepared with 3% sodium starch glycolate
(▲) F_3 - Tablets prepared with 4% sodium starch glycolate
(×) F_4 - Tablets prepared with 5% sodium starch glycolate

A statistically significant difference between dissolution efficiencies (DE) of Ibuprofen tablets formulated with different concentrations of SSG was calculated using a one-way analysis of variance (ANOVA). The P value was found to be less than 0.05, which indicates that there was a significant difference between F_1, F_2, F_3, F_4 with respect to dissolution efficiencies.

To study the influence of superdisintegrants on the performance of Ibuprofen, a set of three formulations (F_4, F_5 and F_6) were prepared using three different superdisintegrants *viz*, sodium starch glycolate(5%),Crosscarmellose sodium (5%), Crospovidone (5%) respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table 3. All the tablets complied with the pharmacopoeial standards. The dissolution data was presented in Table 4 and Figure 3. The *In-vitro* dissolution kinetics was presented in Table 5. The dissolution rate followed first-order kinetics (Figure 4) as the graphs drawn between log % drug unreleased vs time were found to be linear. The dissolution rate of Ibuprofen was found to be effected by nature of the superdisintegrant used in the preparation of tablets. Based on the dissolution rate, superdisintegrants can be rated as SSG <Crosscarmellose sodium < Crospovidone. The formulation prepared with Crospovidone was offered relatively rapid release of Ibuprofen when compared with other superdisintegrants used in this investigation.

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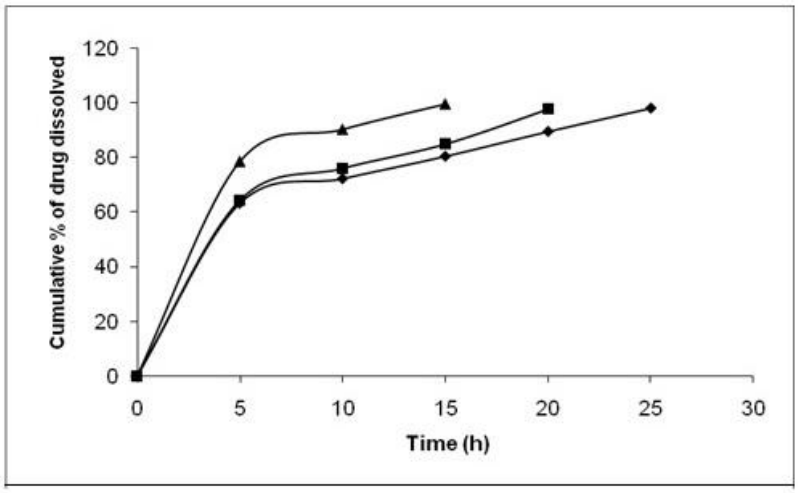
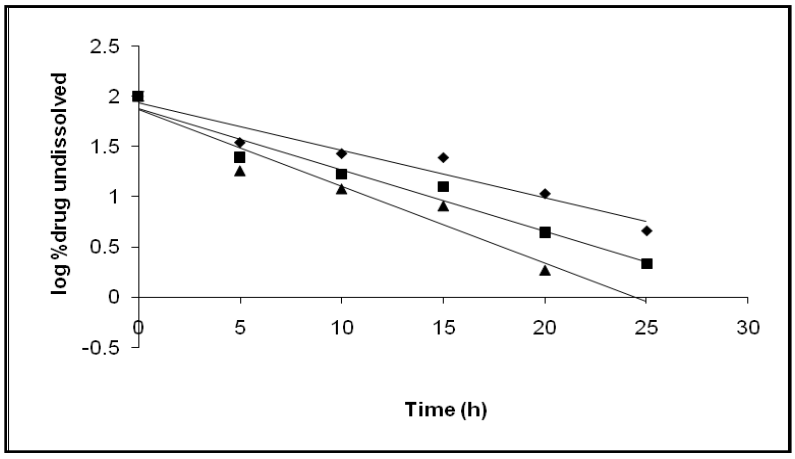
Figure 3: *In-vitro* dissolution profile of Ibuprofen fast dissolving tablets formulated with different superdisintegrants



(◆) F_4 - Tablets prepared with 5% sodium starch glycolate
(■) F_5 - Tablets prepared with 5% Croscarmellose sodium
(▲) F_6 - Tablets prepared with 5% crospovidone

Figure 4: First order plots of Ibuprofen tablets formulated with different superdisintegrants



(◆) F_4 - Tablets prepared with 5% sodium starch glycolate
(■) F_5 - Tablets prepared with 5% crosscarmellose sodium
(▲) F_6 - Tablets prepared with 5% crospovidone.

A statistically significant difference between dissolution efficiencies (DE) of Ibuprofen tablets formulated with different superdisintegrants was calculated using a one-way analysis of variance (ANOVA). The P value was found to be less than 0.05, which indicates that there was a significant difference between F_4, F_5, F_6,with respect to dissolution efficiencies.

CONCLUSION

From the results it was found that all the blends exhibited good flow properties and suited for direct compression. The formulation prepared with 5%w/w of sodium starch glycolate was offered relatively rapid release of Ibuprofen when compared with other concentrations employed in this investigation. Statistically significant difference between dissolution efficiencies (DE) of Ibuprofen tablets formulated with different concentrations of SSG was observed. The formulation prepared with Crospovidone was offered relatively rapid release of Ibuprofen when compared with other superdisintegrants used in this investigation. Statistically significant difference between dissolution efficiencies (DE) of Ibuprofen tablets formulated with different superdisintegrants was observed. So, we can conclude that nature and concentration of the superdisintegrant showed influence on the rate of dissolution. The rate of drug release was found to be increased by increasing the concentration of the superdisintegrant and found to be highest for tablets formulated with 5%w/w of crosspovidone. The dissolution rate was found to follow first order kinetics.

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