The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 02-03-2013
Accepted: 03-04-2013

Vol. 2 Issue 3 2013
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Formulation and Evaluation of Rapidly Disintegrating Tablet of Ibuprofen

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Objective: The aim of the proposed work was to formulate and characterize fast dissolving tablets of ibuprofen for rapid dissolution of drug and absorption, which may produce rapid onset of action. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for pediatric and geriatric patients. **Method:** The fast dissolving tablets of ibuprofen were prepared by two methods named melt technology and super disintegrant addition method. Comparatively evaluation parameters with respect to various physical parameters (weight variation, hardness, friability, etc.) were evaluated and drug release profile was analyzed. The concentration of sucrose and ac-di-sol were optimized for desired rapidly disintegrating formulations.

Result and conclusion: Both the methods of rapidly disintegrant tablets showed desirable results. The formulations prepared by super disintegrant addition were having lesser wetting time, disintegration time, invitro dispersion time and better drug release as compared to the formulations prepared by melt technology.

Keyword: Rapidly Disintegrating, Ibuprofen, Super Disintegrant Addition, Melt technology, ac-di-sol.

1. Introduction

Fast release tablets can disintegrate and dissolve rapidly once placed into the oral cavity. These tablets are prepared by using either of effervescent melt technology, addition of super disintegrant or melt technology[1]. All the technologies formulate rapidly disintegrate tablet and release desired drug concentration at the end of 10 minutes. There are various patented technologies such as Zydis, WOW TABS, FLASH DOSE, CEFORM and ORAQUICK[2]. In zydis technology tablets are prepared by lyophilization process that's why it becomes highly porous in nature which on contact with saliva get solublized and drug releases in suspension form in oral cavity. WOW TAB technology utilizes sugar or its substituent like mannitol which show smooth melt action and gets dissolve within 15 seconds[3]. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients[4]. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily

swallowable dosage forms[5]. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva[6]. In present study an attempt has been made to formulate it as fast dissolving tablets to increase its oral bioavailability[7].

Table 1: Composition of fast disintegrating formulations of ibuprofen prepared by addition of super disintegration (S1-S3) and melt technology method (M1-M3)

Ingredients	S1 (mg)	S2 (mg)	S3 (mg)	M1 (mg)	M2 (mg)	M3 (mg)
Ibuprofen	50	50	50	50	50	50
Mannitol	65	65	65	36	36.85	36.85
Microcrystalline cellulose	65	60	62	30	20	32
Ac- di- sol	15.5	20	18	-	-	-
Sucrose+glucose	-	-	-	45	55	40
Sorbitol	-	-	-	35	35	35
Talc	3.68	3.68	3.68	3.68	3.68	3.68
Magnesium stearate	1.8	1.8	1.8	1.8	1.8	1.8

2. Material and methods

Ibuprofen, Microcrystalline cellulose, Ac- di- sol and mannitol were obtained as gift sample from Ranbaxy fine chemical limited, New Delhi. Sucrose was gifted by Qualigens Fine Chemicals, Mumbai, talc and magnesium stearate were obtained from S.D. fine chemical, limited Mumbai.

2.1 Super Disintegrate Method:

Ibuprofen (50 mg) was mixed with mannitol and microcrystalline cellulose in a glass mortar with slight triturating [Table 1]. Super disintegrate Ac-di-sol was added and granules were prepared followed by addition of magnesium stearate and talc[8].

Table 1: Composition of fast disintegrating formulations of ibuprofen prepared by addition of super disintegration (S1-S3) and melt technology method (M1-M3)

2.2 Melt Technology:

In this method Ibuprofen (50 mg) was mixed with low mould ability sugar like mannitol, sucrose and granulated using high mould ability sachharides which worked as binder. Low moldable sugars used for rapid dissolution and high mould sachharides showed for good binding property [Table 1]. Granules prepared were lubricated and compressed into tablets. Prepared tablets were dried in hot air oven to evaporate the water and to form pores in the sugar melt[9].

2.3 Pre-formulation study

Standardization of the drug was carried out using phosphate buffer pH 6.4 by UV spectrophotometer (UV-160A, SHIMADZU). Solubility analysis of drug in various solvents including water, phosphate buffer pH 6.4 and organic solvents like ethanol, methanol[10,11].

2.4 Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 50 mg of ibuprofen was dissolved in 100 ml of pH 6.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 264.5 nm using UV-Visible spectrophotometer (UV 160- Shimadzu, Japan)[10, 11].

Table 2: Comparative characteristic parameters of fast disintegrating formulations of ibuprofen (S1-S3) and (M1-M3)

Parameters	Hardness (kg/cm2)	Friability (%)	Drug content	% Weight Variation	Disintegration time (sec)	Wetting time (sec)
S 1	4.41 ± 0.16	0.62 ± 0.05	99.7 ± 0.4	0.82 ± 0.15	55	34±0.89
S2	4.22 ± 0.17	0.82 ± 0.05	99.3 ± 0.7	0.75 ± 0.21	48	22.69±0.23
S3	3.41 ± 0.24	0.81 ± 0.06	99.9 ± 0.5	0.89 ± 0.17	46	29.23±0.15
M1	4.12 ± 0.19	0.72 ± 0.03	100.4 ± 0.6	0.69 ± 0.11	52	33.93±0.12
M2	3.90 ± 0.25	0.79 ± 0.02	99.3 ± 0.4	0.71 ± 0.09	50	28.68±0.21
M3	3.95 ± 0.30	0.82 ± 0.05	100.7 ± 0.8	0.78 ± 0.20	50	25.65±0.19

2.5 Disintegration time

Three tablets per batch were evaluated for disintegration time by employing a modified dissolution apparatus. Instead of the disintegration apparatus described in JP XII, a modified dissolution apparatus (JP XII paddle method) was employed. Water (900 ml), maintained at 37±0.5 ℃ was stirred with a paddle at 100 rpm. Disintegration time was recorded when all the fragments of the disintegrated tablet passed through the screen of the basket. [10, 11]

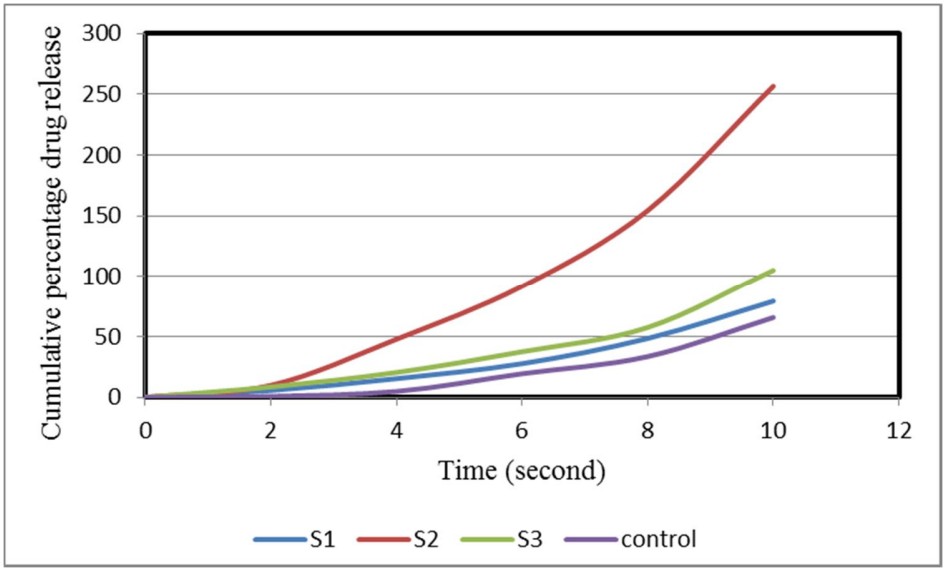

Fig 1: Comparative drug release profile of fast disintegrating formulations of ibuprofen prepared by addition of super disintegrant

2.6 Tablet Hardness

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 halves by compression. It was measured using a tablet hardness tester (Monsanto Hardness Tester)[10,11].

2.6.1 Friability: Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured[10,11].

2.6.2 Wetting Time: A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of pH6.2 (simulated saliva fluid). A tablet was put on the paper and the time for complete wetting was measured6. Three trials for each were performed[10,11].

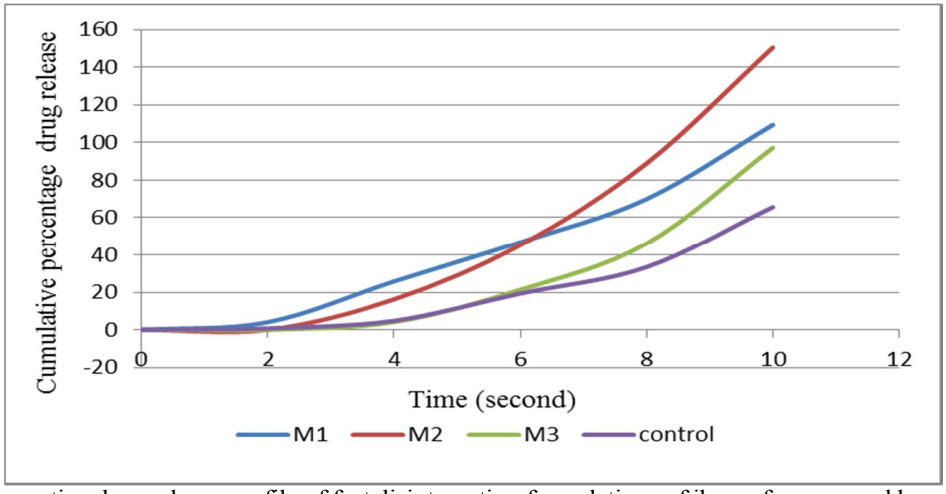

Fig 2: Comparative drug release profile of fast disintegrating formulations of ibuprofen prepared by melt technology method

2.6.3 *In vitro* dispersion time: *In vitro* dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6ml of buffer solution simulating saliva fluid (pH 6.4). Dissolution test was carried out in 900 ml of pH 6.4 phosphate buffer in dissolution apparatus USP II at 50 rpm. An aliquot of dissolution medium was withdrawn at regular interval and absorbance was measured at 264.5 nm. An equal volume of phosphate buffer was added to maintain the sink condition. Dissolution was carried out for all the formulations. Absorbance of these solutions was measured at 264.5 nm using a Thermospectronic-1 UV/Vis double beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve[10,11].

3. Results and discussion

Several Technologies are available to manufacture orally distintegrating tablets. The most common preparation methods are molding, lyophilization or freeze drying, direct compression, spray drying and sublimation. In the present investigation fast release tablets of ibuprofen were formulated by addition of super disintegrant and melt technology. All the tablets were prepared under similar conditions. All the formulations exhibited white color, odorless, convex shape with smooth surface.

The characteristics of prepared FDTs of Ibuprofen are shown in Table 2. The average weight of the FDTs prepared by addition of super disintegrating method was 195.89- 202.65 mg. Weight variation of FDTs was within 0.89%. Hardness and friability of all formulations (S1-

S3) were within acceptable limits. Hardness of tablets prepared by direct compression was 3.95 to 4.22 kg/cm^2. The friability of all formulations was found to be less than 1% indicating good mechanical resistance. Disintegration time play a important role for FDTs which is desired to be less than 60 seconds for orally disintegrating tablets. This rapid disintegration assists swallowing and also plays a role in drug absorption in buccal cavity, thus promoting bioavailability. Disintegration time of prepared FDTs was in the range of 45 to 55 seconds. Wetting time is used as an indicator from the ease of the tablet disintegration in buccal cavity. The wetting time of the formulations was in the range 22±1.2 to 64±1.2. The wetting time was decreased on increasing the concentration of Ac-di- sol in formulations (S1 – S3). This may be due to the formation of pores in formulations on increasing concentration of super disintegrant. *In vitro* dispersion time was found to be 22 to 52 seconds. Which may be attributed to faster uptake of water due to the porous structure formed (S1 – S3). Fast release tablets of ibuprofen showed different pattern of drug release. Tablet S2 prepared by super disintegrate method showed maximum % drug release profile as compared to S1 and S3 [Figure 1]. Similarly tablet formulated by melt technology showed hardness within a range of 3.44 kg/cm^2 to 4.41 kg/cm^2. M2 tablet showed maximum drug release as compared to remaining M1 and M3 tablets [Figure 2]. The *invitro* drug release after 10 minutes was between 96.03 to 100.10 % indicating better drug release and improved bioavailability. The formulations (F1-F3) prepared by super disintegrant addition were having lesser wetting time, disintegration time, *invitro* dispersion time and better drug release as compared to the formulations prepared by melt technology (M1-M3). So it was concluded that super disintegrant addition method was excellent as compared to melt technology in formulation of mouth dissolving tablets.

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