CIBTech Journal of Pharmaceutical Sciences ISSN: 2319–3891 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/cjps.htm
2016 Vol.5 (4) October-December, pp.27-36/Jadhav et al.
Research Article

FORMULATION & EVALUATION OF ORALLY DISINTEGRATING TABLET OF IBUPROFEN FOR PAEDIATRIC USE

***Ashwini V.Jadhav, Vaishali R. Shinde, Sandip S. Kshirsagar and Swati. B. Suradakar**
Department of Pharmaceutics, Kasturi College of Pharmacy, Shikrapur, Pune, Maharashtra
**Author for Correspondence*

ABSTRACT
Ibuprofen is a non-steroidal anti-inflammatory drug, has extensive and commonly use in children in order to overcome pain, fever, and inflammation. As its serum concentrations and analgesic effect are correlated, rapid absorption of ibuprofen could be a prerequisite for the quick onset of its action. Approach used was use of super disintegrants to prepare tablets. Tablets were prepared by direct compression using super disintegrants such crospovidone, croscarmellose sodium, with incorporation of diluents like lactose; MCC. FTIR studies of formulations have shown no interactions between drug and excipients. In vitro disintegration and in vitro dissolution profiles were shown less time for disintegration and rapid dissolution respectively. Short term stability study indicated that Tablets were found to be Stable.

Keywords: *ODT, Pediatric, Ibuprofen*

INTRODUCTION
In an effort to develop drug products that are more convenient to use and to address potential issues of patient compliance for certain product indications and patient populations, pharmaceutical manufacturers have developed products that can be ingested simply by placing them on the tongue. The products are designed to disintegrate or dissolve rapidly in contact with saliva, thus, eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with liquids. This mode of administration was initially expected to be beneficial to paediatric and geriatric patients, to people with conditions related to impaired swallowing, and for treatment of patients when compliance may be difficult (e.g., for psychiatric disorders) (Biradar *et al.*, 2006).
The concept of orally disintegrating dosage forms has emerged from the desire to provide patients with more conventional means of taking their medication. US Food and Drug Administration Centre for Drug Evaluation and Research (CDER) defines, an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon tongue". Interestingly, the demand for Orally disintegrating tablets has enormously increased during the last decade, particularly for geriatric and paediatric patients who experience difficulty in swallowing conventional tablets and capsules (Kaushik *et al.*, 2004; Brown et *al.*, 2001). When orally disintegrating tablet place in the mouth, these dosage forms disintegrate instantly to release the drug, which dissolves or disperses in the saliva.
Thereafter, the drug may get absorbed from the pharynx and oesophagus or from other sections of GIT as the saliva travels down. In such cases, bioavailability is significantly greater than that observed from conventional tablet dosage form (*Saravanan et al.*, 2010).
Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems, mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In such cases swallowing conventional tablets may be difficult.
So, orally disintegrating tablets are beneficial to such paediatric patients (Gupta *et al.*, 2012).
25-40% of the world population is affected by acute and chronic diseases. Pediatric patients have unique physiology, drug PK/PD and safety features. Ease of administration to patient who refuses to swallow tablet basically pediatric patient so, Convenience of administration and accurate dosing as compared to liquid dosage forms.

Although, ODTs in general offer improved convenience and are frequently preferred over conventional solid oral-dosage forms, ODTs may lead to significant improvements over current treatment options for specific patient groups, for instance, paediatric patients.

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) described or dispersible dosage forms as having "great promise for children" (Chang *et al.*, 2000). A fast disintegration time will reduce any potential choking hazard and will also make it harder to spit out the dose.

Specific consideration needs to be given to the type and level of flavours and sweeteners used in paediatric formulations, especially where artificial ingredients are used. As solid-unit doses, ODTs generally offer improved dose accuracy, storage, and stability advantages over liquid preparations. ODT technologies that can offer low-dose accuracy will be of particular benefit to this group. Fast Dissolve, Quick Dissolve, Rapid Melt, Quick Disintegrating, Mouth Dissolving, Oro Dispersible, Melt-in-Mouth'etc. are terms that represent the same drug delivery systems (Konapure *et al.,* 2011).

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID), has extensive and commonly use in children in order to overcome pain, fever, and inflammation.

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 problem with drug is its 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 (Giri *et al.,* 2009; Jain *et al.,* 2010).

As more than 50% of pharmaceutical products are orally administered for several reasons, undesirable taste is one of the important formulation problems that can be encountered with certain drugs. Oral administration of bitter drugs with acceptable level of palatability is a key issue for health care providers especially with paediatric patient (Kimura *et al.,* 1992).

Thus, elimination or reduction of bitterness is an important issue during design of oral pharmaceutical formulations.

In order to eliminate or reduce bitter taste of orally administered pharmaceuticals various techniques and strategies are adopted by pharmaceutical scientist (Sunda *et a1*., 1996; Punit *et al*., 2007).

Ibuprofen is bitter in taste, so masking is necessary, sweetener gives Soothing effect on the membranes of the throat by using various sweeteners as sorbitol, sucrose, aspartame and American mint as flavours we mask the bitter taste of ibuprofen.

In order to improve the dissolution rate and thereby the absorption, orally disintegrating tablets of Ibuprofen were prepared using synthetic superdisintegrants by direct compression.

Orally disintegrating are prepared by various techniques. Direct compression one of the techniques requires the incorporation of a superdisintegrants into the formulation to achieve fast tablet disintegration The objective of the study was to formulate Oral Disintegrating Tablets using synthetic superdisintegrants.

In the present study Ibuprofen was used as a model drug, crosspovidone and crosecarmellose sodium as synthetic superdisintegrant. Addition of flavours and sweetener mask the taste of ibuprofen, precompression and post Compression parameter of tablets was evaluated.

MATERIALS AND METHODS

Ibuprofen was obtained as a gift sample from Cipla Pvt. ltd Kurkumbh. Crosspovidone, Croscarmellose sodium & sucrose were purchased from Ana lab fine chemicals Mumbai, Sorbitol, & lactose were purchased from Research lab fine chem. industries Mumbai. Talc was purchased from Vishal chem. Mumbai.

Magnesium stereate was purchased from pure chem. lab pune. Aspartame & Flavours were obtained as gift samples from Quepharma Pvt LTD Gujarat.

All other materials used were of analytical grade. Distilled water was used for formulation of orally disintegrating tablet and direct compression method.

Table 1: Formulation of Ibuprofen Orally Disintegrating Tablet

Ingredient Mg/Tablet	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8
Ibuprofen	100	100	100	100	100	100	100	100
Sorbitol	-	-	-	-	10	10	10	10
MCC	34	14	-	14	14	14	24	30
CP	4	4	4	4	4	4	4	4
CCS	4	4	4	4	4	4	4	4
Lactose	-	20	34	20	20	18	18	18
Sucrose	38	48	48	46	42	38	38	34
Aspartame	-	2	2	2	8	8	8	8
Aerosil	-	-	-	-	-	-	3	3
American mint	2	2	2	2	2	2	2	2
Magnesium Stereate	4	2	2	2	2	4	4	4
Talc	4	4	4	4	4	8	8	8
Citric acid	-	-	-	1	-	-	-	-
Tartaric acid	-	-	-	1	-	-	-	
In mg	200	200	200	200	200	210	220	225

Formulation of Orally Disintegrating Tablet

Ibuprofen is NSAIDs drug of choice for treating body pain, fever, cold, and headache disintegrant have major role in disintegration and dissolution of orally disintegrating tablets made by direct compression. Preparation involves the addition of superdisintegrants in optimum concentration to the formulation to achieve rapid disintegration/dissolution. For e.g. MCC and Crosspovidone, crosscarmellose sodium as synthetic superdisintegrant.

Preparation involves the addition of sweetener to optimum concentration to achieve better patient compliance and palatability of dosage form. For e.g. Sorbitol, sucrose, Aspartame, Flavour-mint. Talc, Magnesium stereate is an inert substance possessing good flow and compressibility property used as diluents and lubricants.

Direct Compression Method

The vast majority of medicinal agents are rarely so easy to tablet, however in addition, the compression of a single substance may produce that do not disintegrate. If disintegration is the problem, other component are needed, which in turn may interfere with the compressibility of the active ingredient and thus, minimize the usefulness of the method.

Most material posses relatively weak intermolecular attraction or are covered with films of adsorbed gases that tend to hinder compaction.

Uses of compressible diluents with many moderate dose drugs make this process the most streamlined method of tablet manufacture.

A directly compressible diluents is an inert substance that may be compacted with little difficulty and may be compressed even when other tablet material necessary to flow, disintegration, and so forth are blend in direct compression materials, in addition to possessing good flow and compressibility, must be inert, able to disintegrate, and inexpensive.

Ibuprofen Orally disintegrating tablets were formulated by using direct compression method. The compositions of the tablets are given in Table 1.

All the ingredients as shown in Table 1 except talc and magnesium stereate were passed through mesh # 66 and then mixed thoroughly in poly bag for 10 min.

The above blend was pre lubricated with talc and magnesium stearate. The powder blend was compressed into tablets on a 12 station rotary tablet punching machine (Cip Machineries lab Press) using 8mm punch size.

RESULTS AND DISCUSSION

Standard Calibration Curve of Ibuprofen

Standard curve of Ibuprofen was prepared in Buffer pH 6.8; correlation coefficient R and calibration curve equation are as given below.

Using absorbance and concentration data Beer lamberts plots were prepared which are shown in figure 1. In all the standard curves, calibration curve equation has shown linear relationship and high degree of correlation in the range of 5-25 µg/ml. These curves were utilized in drug estimation as and when required.

Table 2: Standard Calibration Curve of Ibuprofen

Sr. No.	Concentration in µg/ml	Absorbance at 221 nm ± S.D*
1	0	0.0000±0.0000
2	5	0.206033±0.000306
3	10	0.361433±0.000265
4	15	0.5352±0.000289
5	20	0.696267±0.00099
6	25	0.874533±0.000839

*Standard deviation, mean n = 6

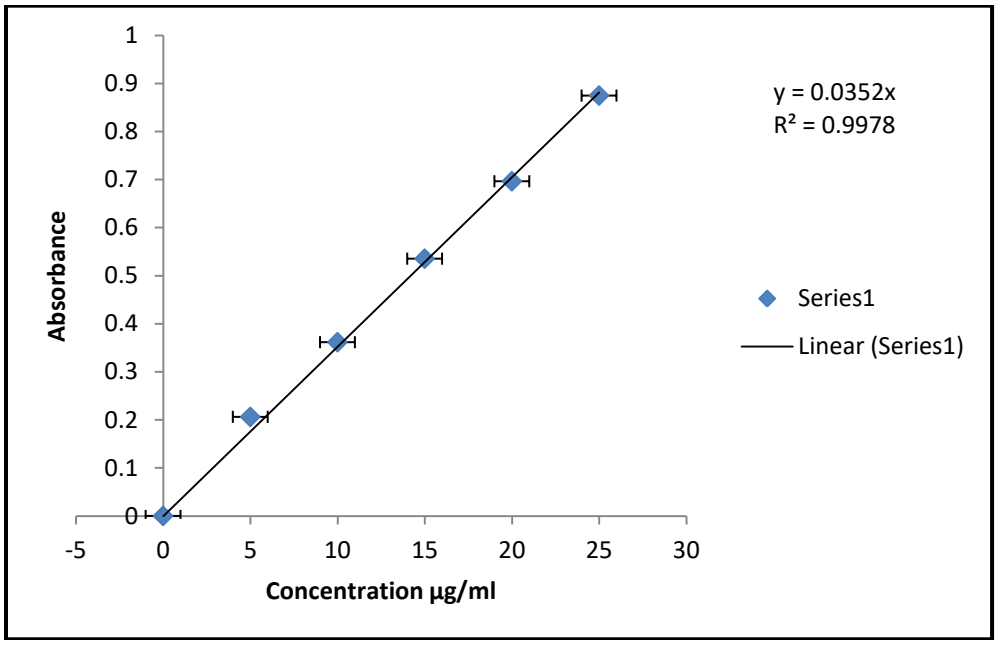

Figure 1: Calibration Curve of Ibuprofen

Evaluation of Orally Disintegrating Tablets

Pre-compression Parameter:

A. Angle of repose:

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, H was obtained. Diameter of heap, D, was measured.

B. Bulk density:

Bulk density is of great importance when considers the size of high-dose product or the homogeneity of low dose formulation in which there is large differences in drug and excipients densities. Bulk density has been calculated as per official guidelines.

C. Tapped density:

It is determined by placing a graduated cylinder containing a known mass of drug or formulation on mechanical tapping apparatus, which is operated for a fixed number of taps (1000) until the powder bed volume has reached a minimum. Using the weight of drug in cylinder and this minimum volume, the tapped density may be computed

D. Powder flow properties:

One of the ways of measurement of free flowing ability of powder is compressibility.

% Compressibility = $(\rho_1 - \rho_2)/ \rho_1$ x 100

Where ρ1 = tapped density,

ρ_2 = initial bulk density

Post-Compression Parameter:

A. Thickness of tablets

Thickness is measured by using instrument called digital "vernier callipers" (Index). Randomly 10 tablets were taken and thickness was measured for each tablet by placing between two anvils and rotating sliding knob until the tablet was tightly fitted and the reading was noted on the digital scale.

B. Weight variation

With a tablet designed to contain a specific amount of drug in a specific amount of formula, the weight of a tablet being made is routinely measured to ensure that a tablet contains proper amount of drug. First weight of 20 tablets was determined.

From that average weight was calculated. Then, individual tablets were weighed and the individual weight was compared with an average weight as per I.P.

C. Hardness

The strength of tablet is expressed as tensile strength (Kg/cm2). 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).

D. Friability

Ten tablets were accurately weighed and placed in the friability apparatus, and operated for 100 revolutions. The tablets were de dusted and reweighed. Percentage friability was calculated.

E. Content uniformity

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 by spectrophotometer at 221 nm.

F. Fineness of dispersion

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.

G. In vitro dissolution studies

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 OC 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.

H. In-Vitro Dispersion time

In vitro dispersion time was measured by dropping a tablet in spoonful of water or in 20ml of water in a beaker. The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and *in vitro* dispersion time was performed.

I. Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed.

Stability Studies

In any rational drug design or evaluation of dosage forms for drugs, the stability of the active component must be major criteria in determining their acceptance and rejection.

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions and shelf lives to be established.

ICH specifies the length of study and storage conditions.

Long term testing: $25^{c}\pm 2^{0}$C/60%RH± 5% for 12months

Short term testing: $40^{c} \pm 2^{0}$C/75%RH± 5% for 6months

Accelerated stability study

In the present study, the accelerated stability studies were carried out as per ICH guidelines 40^{0}C ± 2^{0}C / 75% ± 5% RH and 25^{0}c± 2^{0}C/60%RH± 5% for the following selected formulation batch number 8 for 1and 2 month.

After specified time intervals, parameters like physical appearance, disintegration time, drug content, hardness, friability and dissolution were evaluated according to the procedure described as earlier.

The present study was carried out to develop orally disintegrating tablets of Ibuprofen for paediatric use by direct compression method. Hence, it was necessary to find suitable excipients with good compatibility and disintegrating ability. Eight formulations of Ibuprofen were prepared with different concentration of superdisintegrants namely, Crospovidone, Cross carmellose, sodium Microcrystalline cellulose as a synthetic superdisintegrant.

For formulation F1, F2, F3, blend characteristics were not done because they were prepared to optimise the taste, good mouth feel and rapid dispersion of tablet so blend were prepared for 20 tablets only. For formulation F4 to F8 blend of drug and excipients were prepared and evaluated for various parameters like angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index results were shown in Table 3.

The bulk density and tapped density for all formulations were found to be 0.47 gm/cm^2- 0.53 gm/cm^2 and 0.55 gm/cm^2-0.58 gm/cm^2 respectively. The Hausner's ratio, compressibility index and angle of repose were found to be in the range of 1.13-1.17, 12.92%-15.19% and 228.92^{0}-29.66 ^{0}respectively. All formulations shows good flow property for direct compression and hence tablets were prepared by using direct compression technique.

For post Compression evaluation

The percentage weight variation was found to be within the limit of ± 7.5% as per Indian pharmacopoeia. Hence all the tablet formulations were within the pharmacopeia limits. Hardness was maintained to be within 2.3 kg/cm2 to 54.7 kg/cm2.

Orally disintegrating tablets are less hard then conventional ones, due to lower compression force. These tablets can therefore, be fragile and need individual packaging. Thickness was found in the range from 3.39 mm to 3.58mm.

Formulation F-1 to F-6 posses' poor mechanical strength. Formulation F7 & F 8 possesses good mechanical strength (Less than 1%). The most important parameter that needs to be optimized in the development of oral disintegrating tablet is the disintegration time of the tablet. In the present study all the formulations except (F1, F2, and F3) disintegrated within 1 minute. The drug content of tablets was found between 98.18±0.85% to 99.66±0.33. The results indicated that, in all the formulation drug content was uniform.

The dispersion time for the formulation prepared with Crosspovidone + Crosscarmelose in the range of range of 0.29 to 1.26sec. For prepared formulation batches water absorption ratio in the range of 62% to 98.66%. All batches passes through a sieve screen with a nominal mesh aperture of 710 μm without leaving a residue on the mesh.

Table 3: Pre Compression Parameter of Ibuprofen IP ODT 4 to IBU ODT 8

Formulation	Bulk Density (gm/cm3) ± SD	Tapped Density (gm/cm3) ± SD	Carr's Index (%)± SD	Hausner's Ratio ± SD	Angle of Repose (°)± SD
F-4	0.48 ±0.008	0.56 ±0.008	15.19± 0.012	1.17 ±0.008	28.92 ±0.124
F-5	0.50±0.015	0.55±0.0219	13.32±1.231	1.13±0.001	29.66±1.527
F-6	0.53±0.0360	0.58±0.01	14.20±0.575	1.17±0.01	29.52±1.529
F-7	0.47±0.015	0.55±0.020	14.30±0.900	1.17±0.01	29.57±0.576
F-8	0.49±0.064	0.55±0.025	12.92±1.050	1.13±0.002	29±1

Table 4: Post Compression Parameter of Ibuprofen IP ODT 1 to IBU ODT 8

Formulation	Weight Variation ± SD	Hardness kg/cm2± SD	Thickness (mm) ± SD	Friability (%)± SD	Disintegration Time (sec) ± SD
F-1	209±2.941	3±0.408	3.44±0.016	1.90±0.020	92±2.054
F-2	204±2.867	3.9±0.169	3.41±0.008	1.47±0.024	85±4.082
F-3	199±1.699	3.6±0.402	3.41±0.012	1.50±0.049	72±2.058
F-4	202±2.160	4.7±0.124	3.40±0.008	0.72±0.020	60±2.942
F-5	199±2.624	2.3±0.249	3.39±0.008	1.60±0.032	57±2.0548
F-6	214±1.699	3.3±0.286	3.47±0.02	1.40±0.163	42±0.548
F-7	221±1.632	3.9±0.163	3.52±0.02	0.94±0.016	33±2.624
F-8	225±1.632	3.5±0.124	3.58±0.012	0.83±0.012	27±2.0548

Table 5: Post Compression Parameter of Ibuprofen IP ODT 1 to IBU ODT 8

Formulation	*In vitro* Dispersion Time (min) ± SD	Wetting Time (sec) ± SD	Water Absorption Ratio ± SD	Drug Content (%)± SD	Fineness of Dispersion
F-1	1.26±0.02	65±0.81	62±1.63	-	Pass
F-2	1.5±0.04	63±2.16	63±1.63	-	Pass
F-3	1.03±0.03	60±1.41	73±1.63	-	Pass
F-4	0.65±0.02	53±1.69	83.66±1.88	98.27±0.82	Pass
F-5	0.35±0.01	53±2.16	89.33±0.94	98.18±0.85	Pass
F-6	0.31±0.01	42±1.63	94.33±1.69	97.85±0.49	Pass
F-7	0.31±0.01	35±0.81	98±0.81	99.66±0.33	Pass
F-8	0.29±0.01	38±0.81	98.66±1.24	99.62±1.17	Pass

Table 6: *In Vitro* Dissolution Studies

Sr.no.	Time	F-4	F-5	F-6	F-7	F-8
1	0	0	0	0	0	0
2	5	81.47	84.81	86.11	81.18	88.59
3	10	83.63	90.20	89.19	86.87	92.07
4	15	94.46	93.52	93.27	92.63	95.88
5	20	96.93	95.50	96.51	95.71	97.11
6	30	99.31	97.95	97.79	98.08	98.85

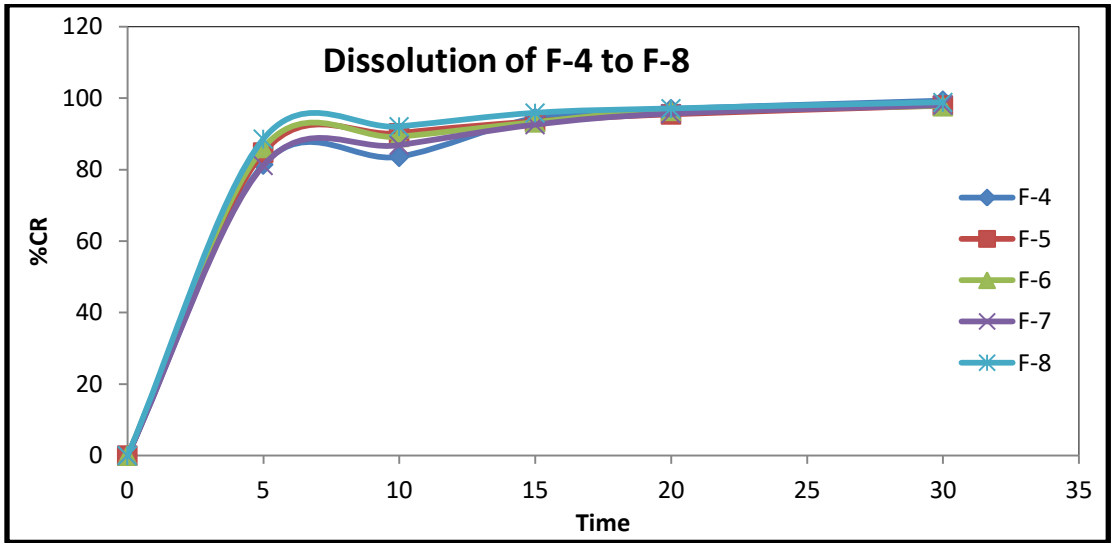

Figure 2: Dissolution of Formulation F: 4-F: 8

Stability Study

The formulation F8 were subjected to short term study by storing the formulation at 25°C/60% RH and 40°C/75% RH. After study tablet again analysed for the hardness friability, drug content uniformity, dispersion time, disintegration time and dissolution time.

Table 7: Result at 25^0C/60% RH

Formulation	Month	Hardness Kg/cm^2	Friability (%)	Dispersion Time (Sec)	Disintegration Time (sec)	Drug Content (%)
F-8	Initial	3.50±0.124	0.83±0.012	0.29±0.01	27±2.054	99.62±1.24
	1 month	3.51±0.124	0.83±0.014	0.28±0.01	29±1.51	100±0.21
	3 Month	3.52±0.008	0.84±0.008	0.30±0.01	28±0.816	99.80±0.16

Table 8: Result at 40^0C/75% RH

Formulation	Month	Hardness Kg/cm^2	Friability (%)	Dispersion Time (Sec)	Disintegration Time (sec)	Drug Content (%)
F-8	Initial	3.50±0.124	0.83±0.012	0.29±0.01	27±2.054	99.62±1.24
	1 month	3.53±0.152	0.84±0.015	0.30±0.01	28±1.52	99.87±0.22
	3 month	3.53±0.004	0.84±0.012	0.31±0.00	29±0.816	99.40±0.84

Table 9: *In vitro* dissolution at 25^0C/60% RH

Sr. No.	Time (min)	In vitro release (% CR) IBU ODT-8 For Initial	In vitro release(%CR) IBU ODT-8 For 1 Month	In vitro release (% CR) IBU ODTF-8 For 3 month
1		0	0	0
2	5	88.59	89.12	87.95
3	10	92.07	90.08	90.52
4	15	95.88	96.12	96.56
5	20	97.11	98.23	98.64
6	30	98.85	99.01	99.21

Table 10: Accelerated Stability Study for *in Vitro* Dissolution at 40^0C/75% RH

Sr. No.	Time (min)	In vitro release (%CR) IBU ODT-8 For Initial	In vitro release (%CR) IBU ODT-8 For 1 Month	In vitro release (%CR) IBU ODTF-8 For 3 Month
1	0	0	0	0
2	5	88.59	85.21	86.54
3	10	92.07	88.36	87.89
4	15	95.88	92.33	93.65
5	20	97.11	96.25	97.01
6	30	98.85	98.66	98.57

Conclusion

Orally, disintegrating tablet of Ibuprofen IP for pediatric use was successfully prepared with different Superdisintegrants by direct compression. The present studies were helped in understanding the effect of formulation process variables especially the concentration of different super disintegrants on the dispersion time and drug release profile.

An overall result indicates that formulation F8 containing 2% Crosspovidone, crosscarmellose with FDA approved American mint flavor exhibited least disintegration time and faster drug dissolution will lead to enhance the patience compliance. Optimized F8 formulation has good physical appearance, *in vitro* dispersion time and drug release. All pre formulation parameters were within range indicates that powder has good flow properties. Non Pharmacopeia & pharmacopeia tests were complied within respective limits.

FTIR studies proved that no chemical interaction between Ibuprofen and Superdisintegrants of the developed disintegrating tablets. Hence, it is concluded from this work done that ODT of Ibuprofen can made and it is a good choice for pediatric use.

REFERENCES

Biradar SS, Bhagvati ST and Kuppasad IJ (2006). Fast dissolving drug delivery system, A brief overview. *The Internet Journal of Pharmacology* **4**(2) 23-24.

Brown D (2001). Orally disintegrating tablets: Taste over speed. *Drug Delivery Technology* **3** 58-61.

Chang RK, Burnside BA and Couch RA (2000). Fast dissolving tablets. *Pharmaceutical Technology Europe* **12** 52-58.

Giri TK, Badwaik H, Alexander A and Tripathi DK (2009). Solubility enhancement of ibuprofen in the presence of hydrophilic polymer and surfactant. *International Journal of Applied Biology and Pharmaceutical Technology* **2** 119-130.

Gupta VRM and Shree giri Prasad B (2012). Formulation and evaluation of oro dispersible tablets of stavudine by direct compression technique. *Asian Journal of Pharmaceutical and Clinical Research* **5**(4) 219-224.

Jain SK, Shukla M and Shrivastava V (2010). Development and in Vitro Evaluation of Ibuprofen Mouth Dissolving Tablets Using Solid Dispersion Technique. *Chemical and Pharmaceutical Bulletin* **58**(8) 1037-1042.

Kaushik D, Dureja H and Saini TR (2004). Mouth dissolving tablet: A review. *Indian Drugs* **41**(4) 187-188.

Kimura S, Imai T and Otagiri M (1992). Pharmaceutical evaluation of Ibuprofen syrup containing low molecular weight gelatine. *Journal of Pharmaceutical Sci*ence **81**(2) 141-144.

Konapure SA, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV and Chorage TV (2011). "Mouth dissolving tablets" an innovative technology. *International Journal of Applied Biology and Pharmaceutical Technology* **2**(1) 496-503.

Punit S, Rajshree M and Yogesh R (2007). Stability testing of pharmaceuticals: A global perspective. *Journal of Pharmaceutical Research* **6** 1-9.
Saravanan R and Dhachinamoorthi D (2010). Rapidly Dissolving Tablet: A Review. *Research Journal of Pharmacy and Technology* **3**(4) 1011-1017.
Sunda H, Bi YX, Yonezawa Y, Danjo K, Otsuka A and Iida K (1996). *International Journal of Chem Tech Research* **14**(11**)** 2121-2127.