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Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF IBUPROFEN

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Abstract

The main objective of this study was to formulate and evaluate the Ibuprofen oro-dispersible tablets using different concentration of disintegrates i.e., Ac-Di-Sol, Polyplasdone, L-hydroxy propyl cellulose and sodium starch glycolate ranging from 3-7% were prepared by direct compression. The drug and exicpient compatibility study was performed by FT-IR & study revealed that there was no interaction between drug & exicpient. The blend of F01 to F07 formulations had prepared and they were evaluated for various precompression parameters like angle of repose, bulk density, tapped density, compressibility index, and hausner's ratio & were found to be satisfactory. The tablets were evaluated for various parameters like weight variation, thickness, hardness, friability, wetting time, water absorption ratio and the results were found to be within the limits. The wetting time, water absorption ratio disintegration time & *In vitro* drug release of optimized formulation F07 was found to be16.5 sec, 68.4sec, 13.5 sec and 98.33% of drug release at 60 min respectively. The optimized formulation F07 was compared with drug release characteristics of marketed formulation. The kinetic treatment showed that the optimized formulation F07 follow first order kinetics with diffusion mechanism and have good stability as per ICH guidelines. It can be concluded that the ODT was beneficial for delivering the drug which needs faster release to achieve the immediate action.

Key Words: Mouth dissolving tablets, water absorption ratio, wetting time, *in-vitro* dissolution studies, stability studies.

Introduction

In the recent past several novel technologies have emerged with improved performance, improved patient compliance and reduced adverse effects. One such approach is to formulate mouth-dissolving tablets or mouth-

disintegrating tablets which are dissolves rapidly in saliva without the need of water within few seconds due to the action of superdisintegrant in the formulations. The demand for mouth dissolving tablets has been growing over the other oral dosage forms (such as tablets, capsule, dry syrups, chewing gums/chewable tablets) among pediatric, geriatric, dysphasic, psychotic and non-cooperative patients and travelers. The basic approach used in development of mouth dissolving tablets is the use of superdisintegrant, which provide instantaneous disintegration of tablets after putting on tongue, thereby releasing the drug in saliva. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form [1].

To design rapidly disintegrating oral tablets of Ibuprofen for pediatric patients and elderly patients, in order to improve bioavailability, ease of administration and patient compliance.. Ibuprofen is Non-Steroidal anti-inflammatory drug and well absorbed orally with peak plasma levels usually occurring within 1 to 2 hours. Drug is highly protein bound. It has a biphasic plasma elimination time curve with a half-life of approximately 2 hrs [2]

Drug (and its salts) irritates the throat much more than the mouth, and that its quality in the throat is characterized primarily as sting/ prick, itch and tickle (often leading to cough).[3] It exhibits significant risks of gastrointestinal side effects, when chronically administered in the elderly. The present research endeavour was directed towards the development of taste masked orally disintegrating tablets and minimizes the gastro intestinal side effects of the drug that exhibits more patient compliance than that of the marketed product.

Materials and Methods

Ibuprofen was obtained as gift sample from Dr. Reddy's Laboratories, Hyderabad, Sodium lauryl sulfate, NF was obtained from Loba Chemie, Mumbai, Stearic acid NF was obtained from JT Baker. Polyplasdone-xl was obtained from Merck chemicals Ltd.,Mumbai, Titanium dioxide USP was obtained from Ranbaxy, Haryana. Sodium stearyl fumarate was obtained from JRS Pharma, Spain. Colloidal Silicon dioxide NF, Mannitol, Spray dried lactose and Talc were obtained from S.D. Fine Chemicals. Pvt Ltd, Mumbai, India. All chemicals and solvents used were of analytical grade.

Drug-Excipients compatibility study

The excipients weighed according to mentioned ratio and sifted through ASTM # 40 and blended together. The mixture placed in two vials. One set of vials is stored at 4^0C as control. The other set was stored at 40^0C/75% RH. The caps of the vials, which were kept at 40°C/75% RH, were punctured for the permeation of moisture. The vials

were observed after every week and compared with vials kept at 4^0C as control for any physical incompatibility like lump formation, color change. The results are shown in Table a & b and Figures a & b.

Table-a: Drug-Excipient compatibility studies for one month.

Ingredients (g)	Ratio	**Initial**	**After 1 week**	**After 2 weeks**	**After 3 weeks**	**After 4 weeks**
			40^0C / 75% RH			
Drug + Sodium lauryl sulphate	1:0.1	White	NC	NC	NC	NC
Drug + Stearic acid	1:0.5	White	NC	NC	NC	NC
Drug + Talc	1:0.5	White	NC	NC	NC	NC
Drug + Titanium dioxide	1:0.5	White	NC	NC	NC	NC
Drug + Pearlitol SD 200	1:0.5	White	NC	NC	NC	NC
Drug + Crospovidone XL	1:0.25	White	NC	NC	NC	NC
Drug + Orange flavour	1:0.03	White	NC	NC	NC	NC
Drug + Aspartame	1:0.1	White	NC	NC	NC	NC
Drug + Sodium stearyl fumarate	1:0.03	White	NC	NC	NC	NC
Drug + Aerosil	1:0.02	White	NC	NC	NC	NC
Drug		White	NC	NC	NC	NC

NC – No color change.

Table-b: Infrared spectra of API and API, Opadry tm.

Material	**Wave number (cm^{-1})**	**Functional group**
Pure API	2955.55	C – H stretching
	1719.29	C = O stretching

	1229.59	C – O band
API : Opadry tm (1:1)	2955.89	C – H stretching
	1728.86	C = O stretching
	772.16	C – H stretching

Formulation of ibuprofen oro-dispersible tablets (Direct Compression)

Procedure:

API, disintegrant, diluent, and lubricant was sifted through ASTM #40separately. Glidant, flavor, sweetener were sifted through ASTM #60. All ingredients were weighed accurately. Ingredients were blended in a poly bag for 10 min. Compressed the material into biconvex, round shaped tablets using 11mm punch at 3.0 ± 0.5 kp. The composition of all formulations shown in Table-c. Taste masking by using fluidized bed processor was chosen, as it is the simplest and most feasible method.

Table-c: Composition of all formulations.

INGREDIENT	**F01**	**F02**	**F03**	**F04**	**F05**	**F06**	**F07**
Ibuprofen (20%)	100	100	100	100	100	100.0	-
20% Opadry coated Ibuprofen pellets (mg)	–	–	–	–	–	–	246.0
Pearlitol SD 200	358.75	358.75	358.75	358.75	368.75	348.75	212.75
Superdisintegrant	25.0	25.0	25.0	25.0	15.0	35.0	25.0
Sodium stearyl fumarate (0.5%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Aerosil (0.25%)	1.25	1.25	1.25	1.25	1.25	1.25	1.25

Orange flavor (0.5%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Acesulfame potassium (2%)	10.0	10.0	10.0	10.0	10.0	10.0	10.0
Total	500	500	500	500	500	500	500

F01 – 5% Ac-Di-Sol F02 – 5% Polyplasdone XL F03 – 5% Sodium starch glycolate

F04 – 5% L-Hydroxy propyl cellulose F05 – 3% Polyplasdone XL

F06 – 7% Polyplasdone XL F07 – 5% Polyplasdone XL

Coating of Ibuprofen with Opadry tm coating solution:

Drug was accurately weighed and passed through ASTM # 40.Opadry tm film coating material was accurately weighed and passed through ASTM # 40.Isopropyl alcohol was accurately weighed and transferred into a beaker. The Opadry tm coating system was added to isopropyl alcohol under stirring and stirring was continued for about 45min to make a 16% w/w solution. Ibuprofen was loaded in the product cone of the fluid bed processor with the cone in inclined position to avoid dust generation and powder blocking the spray gun. Bottom spray gun was fixed to the fluid bed processor and the process parameters of fluid bed processor were set as given in the Table e & f. Coating of drug particles with Opadry tm marketed system was carried out in Pam glatt 1.1 fluid bed processor. The drug particles were allowed to dry in the fluid bed processor after drying.

Table-e: Process parameters.

S.No	Parameters	Limits
1	Spray gun	Pam Glatt Top spray gun
2	Blower drive speed (%)	45 – 55
3	Inlet air temperature (°C)	30 – 35
4	Product temperature (°C)	35 – 40
5	Atomization air pressure (bar)	1.5
6	Spray pump speed (rpm)	1.0
7	Filter shaking mode	Asynchronous
8	Filter shaking interval (sec)	8

9	Filter shaking pause (sec)	60

Table-f: Coating of Ibuprofen using Opadry tm.

S.No.	Ingredients	Batch Quantity (gm)
1	Ibuprofen	300
2	Opadry tm	16
3	Isopropyl alcohol	84

Granulation of Ibuprofen with Povidone K–30 binder in planetary mixer and coating of the granules with Opadry tm

Ibuprofen, Povidone K - 30 were accurately weighed and passed through ASTM # 40 separately. Purified water was accurately weighed and transferred into a beaker. Weighed amount of PVP K-30 binder was added into the water under stirring and stirring was continued for about 20min.The drug was loaded in a planetary mixer and binder solution was gradually added into the dry mix. Mixing was done until granules were achieved. The granules were dried in a retch rapid dryer for about 30 – 45 min and were checked for their loss of drying. The dried granules were taken and processed for further coating. A 16% w/w solution of opadry tm coating system was prepared by adding weighed amount of opadry coating system into isopropyl alcohol under stirring for about 45min.Top spray gun was fixed to the fluid bed processor. The process parameters of fluid bed processor were set as given in the Table g. The granules were loaded in the glatt 1.1 fluid bed processor and coated with the marketed opadry tm solution. The product was dried after completion of the granulation.

Table-g: Granulation of Ibuprofen using PVP K - 30 as binder.

S.No.	Ingredients	Quantity (gm)
1	Ibuprofen (95.23%)	300
2	Povidone K – 30 (4.77%)	15
3	Purified water	q.s

Extrusion - Spheronization of Ibuprofen and MCC with PVP K – 30 and coating of pellets with Opadry tm coating solution:

Ibuprofen, MCC PH 101, Povidone K – 30, Opadry tm were passed through ASTM # 40 separately and weighed accurately. Drug and MCC were blended in a poly bag for 5–10 min. Purified water was accurately weighed and transferred into a beaker. Weighed quantity of PVP K-30 was added slowly into purified water under stirring. Stirring was continued for about 20min.The drug, MCC blend was loaded in a planetary mixer and dry mixing was done up to 5 min. Then the Povidone binder solution was gradually added into the dry mix. Purified water was added until the wet mix showed extrusion property. The wet mass was loaded into an extruder that has a 0.5mm (500μ) extrusion screen to get the cylindrical extrudates that were then passed through an Spheronizer to get spherical pellets of 0.5mm.The pellets obtained were then dried in a rapid dryer until they get the dry blend LOD. The dried pellets were then sifted through #35 (500μ), #40, #60 sieves. The pellets retained on #40 were taken for further processing. Opadry tm coating solution was prepared by adding the sifted opadry coating material in a weighed quantity of isopropyl alcohol under stirring. Stirring was done for 45 min to get a 16%w/w solution. Bottom spray gun was fixed to the fluid bed processor and the process parameters were set as given in the Table h & i. The dried pellets were loaded in the product cone with the cone in inclined position to avoid dust generation and pellet blocking the spray gun. Stirring was continued throughout the process to avoid settling of the talc and titanium dioxide in the prepared Opadry tm dispersion. The pellets were dried after completion of the coating process.

Table-h: Pellet composition

S.No.	Ingredients	Quantity (gm)
1	Ibuprofen (47.62%)	476.2
2	Microcrystalline Cellulose PH 101 (47.62%)	476.2
3	PVP K – 30 (4.76%)	47.6
4	Purified Water	q.s (679gm)

Table-i: Formulation of ODT using Opadry coated pellets.

Ingredients	F07
	Quantity (mg/tab)
20% Opadry coated Ibuprofen pellets (49.2%) (mg)	246.0
Pearlitol SD 200 (42.55%) (mg)	212.75
Polyplasdone XL (5%) (mg)	25.0
Orange flavor (0.5%) (ml)	2.5
Acesulfame potassium (2%) (mg)	10.0
Sodium stearyl fumarate (0.5%)	2.5
Aerosil 200 (0.25%) (mg)	1.25
Total Weight (mg)	500.00

Preformulation studies

Physico-Chemical Characterization of the Drug.

Flow properties.

Angle of Repose

A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm over the platform. About 2gm of drug was slowly passed along the wall of funnel until the tip of the pile formed touches the stem of the funnel. A rough circle was drawn around the pile base and the radius of powder cone was measured. Angle of repose was calculated from three averages using following formula. The results are presented in Table d.

Table-d: Evaluation of pre compression parameters.

S.no	Formulations	Angle of repose(^{0})	Bulk density g/ml	Tapped density g/ml	Compressibility index	Hausner's ratio
1	F01	32.13	0.495±0.01	0.562±0.05	25.610±0.08	1.34±0.12

2	F02	25.51	0.389±0.02	0.445±0.03	18.13±0.03	1.20±0.18
3	F03	27.12	0.390±0.02	0.450±0.04	19.25±0.04	1.12±0.03
4	F04	26.34	0.330±0.05	0.465±0.06	21.05±001	1.09±0.09
5	F05	28.13	0.445±0.09	0.587±0.11	26.75±0.06	1.36±0.24
6	F06	*29.23*	*0.379±0.11*	0.440±0.08	20.08±0.07	1.14±0.18
7	F07	*25.13*	*0.374±0.10*	*0.410±0.03*	17.31±0.03	1.15+0.07

All the values are expressed as mean ± S.D; n=6

$\theta = \tan^{-1} h/r$

Where, θ = angle of repose

h = height of powder cone

r = radius of the powder cone

Density Measurement

Different types of density calculations were done to characterize the drug. Generally two types of densities are determined i.e. bulk density and tapped density.

Bulk Density: Bulk density of the drug was determined by pouring gently 2gm of drug sample through a glass funnel into a 10 ml clean dry graduated measuring cylinder. The volumes occupied by the sample were recorded. Bulk density was calculated. The results are presented in Table d.

$$\text{Bulk density (g/ml)} = \frac{\text{weight of sample in gms}}{\text{volume occupied by the smaple}}$$

Tapped density

Tapped density of the drug was determined by pouring gently 5gm of sample through a glass funnel into a 10ml clean dry graduated measuring cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated. The results are presented in Table d.

$$\text{Tapped density (g/ml)} = \frac{\text{weight of sample in gms}}{\text{volume occupied by the smaple}}$$

Percentage Compressibility: It is also one of the simple methods to evaluate flow property of a powder by comparing the bulk density and tapped density. An useful empirical guide is given by Carr's compressibility. The results are presented in Table d.

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Evaluation of Ibuprofen Oro-Dispersible Tablets

The evaluations of physico-chemical parameters of Ibuprofen mouth dissolving tablets were done as per standard procedures. The following parameters were evaluated.

Hardness [3]

The test was done as per the standard methods. The hardness of three randomly selected tablets from each formulation (F1 to F7) was determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale was noted down in Kg/cm^2. The results are presented in Table j.

Table-j: Evaluation of post compression parameters.

	F01	**F02**	**F03**	**F04**	**F05**	**F06**	**F07**
Color	White	White	White	White	White	White	Off white
Surface	Smoo t h	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth

Thickness (mm)	4.48± 0.2	4.45±0.3	4.43±0.3	4.42±0.3	4.48±0.3	4.43 ± 0.3	4.49 ± 0.3
Hardness (kP)	3.0±0.5	3.0±0.5	3.0±0.5	3.0±0.5	3.0±0.5	3.0±0.5	3.0 ± 0.5
Weight (mg)	500± 1.0	500±1.2	500±1.3	500±1.6	500±1.0	500±1.5	500 ± 1.0
Assay (%w/w)	99.98	101.6±1.1	98.86±0.9	99.76±2.0	98.5±1.3	100.2±1.7	98.79 ± 2.1
D.T. (sec)	27.5± 1.45	18.1±1.1	42.2±2.3	35.8±1.6	17±0.9	15±1.7	13.5± 1.67
Friability (%)	0.79± 0.01	0.78± 0.02	0.81±0.01	0.82±0.03	0.85±0.03	0.76±0.05	0.88± 0.01
Wetting time(sec)	29.58	19	44	38	21	18	16.5
Water absorption ratio	41.6	70.56	29.56	35.36	66.8	62.4	68.4

Thickness [3]

The thickness of three randomly selected tablets from each formulation was determined in mm using a vernier caliper (Pico India). The average values were calculated. The results are presented in Table j.

Uniformity of Weight [3]

Weight variation test was done as per standard procedure. Ten tablets from each formulation (F1 to F7) were weighed using an electronic balance and the average weight was calculated. The results are shown in Table j.

Friability [3]

The friability of tablets using 10 tablets as a sample was measured using a Roche Friabilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were taken out, dedusted and reweighted. The

percentage friability was calculated from the loss in weight as given in equation below. The weight loss should not more than 1%.The results are shown in Table j.

%Friability = (initial weight- final weight) x 100

(initial weight)

Drug Content [3]

Ten randomly selected tablets from each formulation (F1 to F7) were finely powdered and powder equivalent to 4 mg of Ibuprofen was accurately weighed and transferred to 100 ml volumetric flasks containing 50 ml of phosphate buffer(pH 6.8). The flasks were shaken to mix the contents thoroughly. The volume was made up to the mark with phosphate buffer pH 6.8 and filtered. One ml of the filtrate was suitably diluted and Ibuprofen content was estimated at 235 nm using a double beam UV-visible spectrophotometer. This procedure was repeated thrice and the average value was calculated. The results are presented in Table j.

Wetting Time [4]

The tablets wetting time was measured by a procedure modified from that reported by Bi et al. The tablet was placed at the centre of two layers of absorbent paper fitted into a dish .After the paper was thoroughly wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch. The results are presented in Table j & Figure c.

Water absorption ratio [4]

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 weighted. Water absorption ratio, R was determined using following equation.

$R = 100 \times Wa - Wb/Wa$

Where, Wa = Weight of tablets after water absorption

Wb = Weight of tablets before water absorption.

The results are presented in Table j),& Figure d).

***In-vitro* Dissolution study**[5]: *In-vitro* drug release rate of Ibuprofen mouth dissolving tablets were carried out using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus (Paddle method). The dissolution test was

carried out using 900 ml of 6.8 pH phosphate buffer, at 37± .5^{0}C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 05, 10, 15, 20, 30, 40, 50 and 60 min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through Whatman filter paper No 40 and analyzed for Ibuprofen after appropriate dilution by UV spectrophotometer at 235 nm. The percentage drug release was calculated using an equation obtained from the calibration curve. The results are presented in Figure e.The dissolution testing was carried out in triplicate.

Drug release kinetics (dependent model method)

The mathematical models are used to evaluate the kinetics and mechanism of drug release from the tablets. The results are shown in Table-l. The model that best fits the release data is selected based on the correlation coefficient (r) value in various models. The model that gives high 'r' value is considered as the best fit of the release data.

Table-l: Drug release kinetics.

Formulation Code	Drug release kinetics (R^2)			
	Zero order	First order	Higuchi	Peppas
F01	0.386	0.809	0.949	0.930
F02	0.390	0.812	0.954	0.936
F03	0.374	0.857	0.957	0.924
F04	0.384	0.834	0.970	0.944
F05	0.379	0.852	0.966	0.963
F06	0.408	0.812	0.991	0.981
F07	0.630	0.988	0.998	0.973

Mathematical models are: Zero order release model[6], First order release model[7], Higuchi release model[8], Korsmeyer – peppas release model [9]

To analyse the mechanism of the drug release rate kinetics of the dosage form, the data were plotted as:

Zero order release rate kinetics:-

To study the Zero order release kinetics the release rate data were fitted to the following equation.

$$F = K t$$

Where,'F' is the fraction of drug release,

'K' is the release rate constant, and

't' is the release time.

When the data is plotted as Cumulative percent drug released Versus time, if the plot is linear then the data obeys Zero order release kinetics,with slope equal to K. The results are given in table.

First order kinetics:

A First order release would be predicated by the following equation.

$$\text{Log } C = \text{Log } Co - \frac{K\,t}{2.30\,3}$$

Where, C = Amount of drug remained at time 't'

Co = initial amount of drug

K = First order rate constant (hr^{-1})

When the data is plotted as Cumulative percent drug remaining versus time yields a straight line,Indicating that the release follows First order kinetics .The constant 'K' can be obtained by multiplying 2.303 with slope values.

Higuchi release model: **-**

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = K \cdot t_{1/t}$$

Where,'F' is the amount of drug release

'K' is the release rate constant, and

't' is the release time.

When the data is plotted as Cumulative drug released Versus Square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism .The slope is equal to 'K'.

Korsmeyer and peppas release model : The release rate data were fitted to the following equation.

$$M_t / M_\infty = K.\, t^n$$

Where, Mt / M_∞ is the fraction of the drug release,

'K' is the release rate constant,

't' is the release time, and

'n' is the diffusion exponent for the drug release that is dependent on the shape of the matrix dosage form. When the data is plotted as Log of drug released Versus log time, yields a straight line with a slope equal to 'n' and the 'K' can be obtained from Y-intercept.

Stability studies:

The design of the formal stability studies for the drug product was based on the knowledge of the behavior and properties of the drug substance and formal stability studies on the drug substance. Specification which is list of tests, reference to the analytical procedures and proposed acceptance criteria, including the concept of different acceptable criteria for release and shelf life specifications, is addressed in ICH. The selected batch was kept at 40°C with 75% RH and the samples were withdrawn at 30, 60 and 90 days for physical and *in vitro* evaluation of drug release. The results are shown in Table m.

Table-m: Stability studies.

Parameters	**Conditions**			
	Initial	**Time**		
	0 Day	**1month (40°c & 75% RH)**	**2month (30°c & 60% RH)**	**3month (25°c & 60% RH)**
Assay	98.79	98.72	98.50	98.30
In vitro Drug release	97.33	97.25	97.10	96.85

Results and Discussions

Drug-Excipients compatibility study: The IR spectrum of Ibuprofen and other excipients were determined and it was found that there were no any extra peaks were observed, which indicating that there was no interaction between drug and excipients. The results are shown in Figures a & b.

Figure-a: The infrared spectrum of pure API.

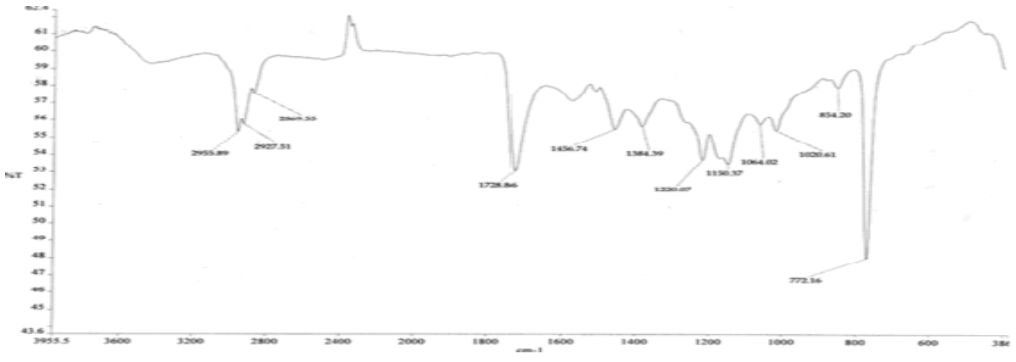

Figure-b: Infrared spectra of Opadry tm and API.

Preformulation studies

Preformulation parameters of all formulatios F01 to F07 are satisfactory, Bulk density, Tapped density, Angle repose, %compressibilty (or) cars index, Hausner ratio are within the limits. The results are shown in Table d.

Bulk density (gm/ml)	:	0.3302 to 0.495
Tapped density (gm/ml)	:	0.410 to 0.587
Angle of repose	:	25.13 to 38.23
%compressibility	:	17.31 to 26.79
Huasner ratio	:	1.09 to 1.36

The results obtained confirm that the batches which exhibit good flow properties have good packing characteristics

Selection of formulation method:

ODT tablets of Ibuprofen were formulated using Ac-Di–Sol as disintegrant by direct compression method (F001). The D.T. observed for this formulation was 27.5 sec. To decrease the D.T. of the formulation further, a study was performed using different disintegrants.

Selection of disintegrants in the formulation:

Ibuprofen was fabricated using four different disintegrants namely Ac–Di-Sol (F01), Polyplasdone XL (F02), Primojel (F03) and L–Hydroxy propyl cellulose (F04) out of which Polyplasdone XL showed lesser D.T. Different concentrations of Polyplasdone XL (3, 5, 7%) were evaluated from which 5% Polyplasdone XL was selected as it showed lesser D.T. of 12.1 sec when compared to other formulations.

Physical barrier – Fluidized Bed Coating:

The drug being a propionic acid derivative gives bitter or burning acid taste of the free acid. An attempt was made to mask the disagreeable acid taste of the drug by coating process.

Coating of Ibuprofen with Opadry tm coating solution:

The drug has poor flow property, so the drug did not get fluidized in the fluidized bed processor. Agglomerates were formed during the process. So, drug coating with Opadry tm coating solution was not successful.

Granulation of Ibuprofen with Povidone K-30 as binder and coating with Opadry tm in Fluid Bed Processor:

Granules were prepared and dried. The dried granules were sifted through #20 and were further used for coating in FBP using Opadry tm coating solution. The fluidization was better in this trial but even on 20% coating the taste masking was not attained due to irregular shape of the granules. As the objective of the work was to attain good coating efficiency (i.e., good taste masking for minimum coating) the process was stopped at 20% coating level keeping in mind of the weight build up in the formulation. The weight of an ODT should not be more than 500mg as per US FDA guidelines to the industry. So, the weight also played an important role in the formulation. By considering an increase in weight on further coating of the process this trial was stopped.

Extrusion– Spheronization of Ibuprofen and MCC with PVP K – 30 and coating of pellets with Opadry tm coating solution:

Uniform coating on granules was not possible as they have improper size and shape and further an increased coating level will be required when compared to that of pellets. As pellets will have uniform shape and size coating will be uniform for each and every pellet. So Extrusion Spheronization process was used for the production of pellets by using an extruder screen of 0.5mm. An attempt was made to formulate Ibuprofen pellets with microcrystalline cellulose and PVP K-30 solution as binder. Microcrystalline cellulose (Avicel PH 101) was used as a spheronization aid in the pellet production. A 0.5mm (500μ) extruder screen was used to get pellets of 0.5mm.The pellets formulated were further dried and sifted through #35(500μ), #40(425μ) and #60(250μ) sieves. The pellets retained on #40 were taken for coating in FBP. Fluidization of pellets was good when compared to that of granules and taste masking was achieved at 20% coating level.

Evaluation of Mouth Dissolving tablets of Ibuprofen:

The parameters of all formulations F01-F07 was found to be satisfactory and all were within pharmacopeias limits.

The Hardness for all formulations found to be 3.0±0.5 kp

The thickness of tablet was found to be between 4.42±0.3 to 4.49±0.3 mm.

The Friability was found to between 0.76±0.05 to 0.88±0.01 %.

The Weight variation was found to between 500±1.0 to 500±1.6 %.

Assay values of the formulations were observed in the range of 98 to 101%.The results are shown in Table j).

Water absorption ratio and Wetting time:-

The wetting time and water absorption ratio which are the important criteria for determining the capacity of disintegrates to swell in presence of little water. By using different superdisintegrants the water absorption ratio and wetting time in the formulations F01 to F07 were found to be in the range of 41.6% to 70.56% and 16.5 to 29.58 sec respectively. The results are shown in Table j & Figure c & d. The best result has been shown by batch F7 tablets, it showed the water absorption ratio and wetting time was 68.4 % and 16.5 seconds. Thus the results indicated that the preparation was more water absorption ratio and minimum wetting time, so it will take less time for disintegrating.

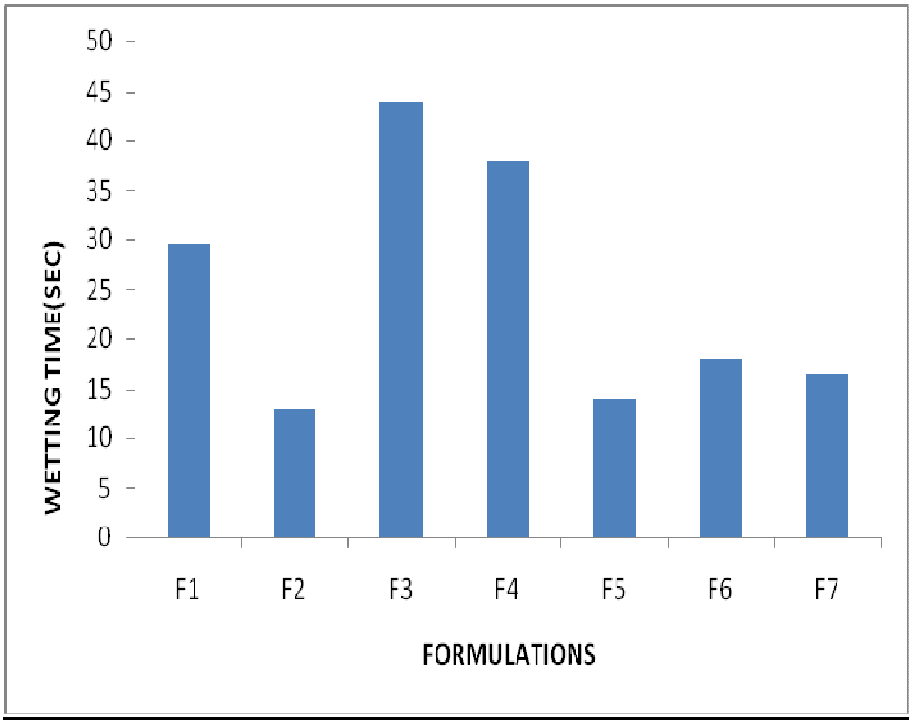

Figure-c: Wetting time of the F01-F07 Formulations.

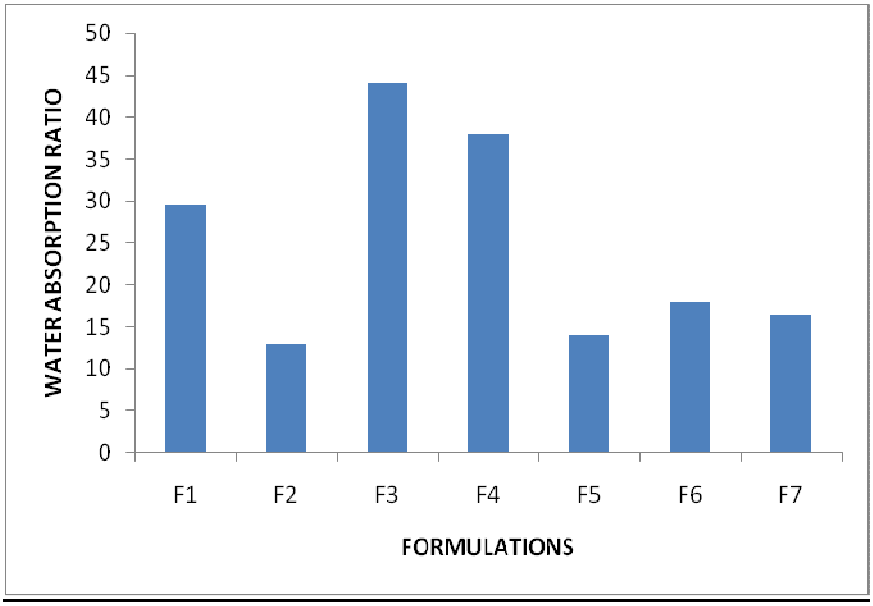

Figure-d: Water Absorption Ratio of the F01-F07 Formulations.

***In- vitro* disintegration time:**

The disintegration time of mouth dissolving tablets should be less because in a very short time it should be totally disintegrates. By using different superdisintegrant disintegration time in the formulations F01 to F07 were found to be in the range of 13.5±1.67 to 27.5±1.45 sec. The results are shown in Table j. The best result has been shown by batch F7 tablets, it showed the disintegration time was 13.5seconds.In conclusion, with increase in concentration of superdisintegrant disintegration time decreases.

***In-vitro* dissolution study:**

Dissolution rate studies showed that about 94-99% drug release within 60 minutes for all formulations with using the superdisintegrant. The tablets prepared with superdisintegrant i.e. Ac-Di- Sol (5%), Polyplasdone (5%), Sodium Starch Glycolate (5%), L-Hydroxy Propyle Cellulose (5%), Polyplasdone (3%) Polyplasdone (7%) and Polyplasdone (5%) in the formulations F1 to F7 showed the complete release of drug i.e.94.85%, 96.30%, 95.33%, 94.52%,95.63%, 96.42% and 98.85% respectively within the 60 minutes. The comparison of dissolution profiles of all formulations i.e. F1 to F7 are shown in Figure e.

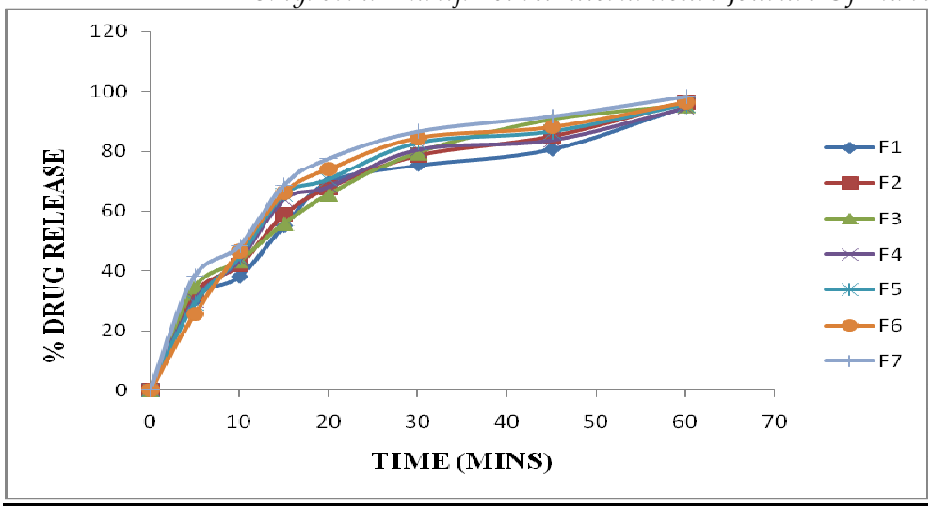

Figure-e: % Cumulative drug release of F01-F07 formulations.

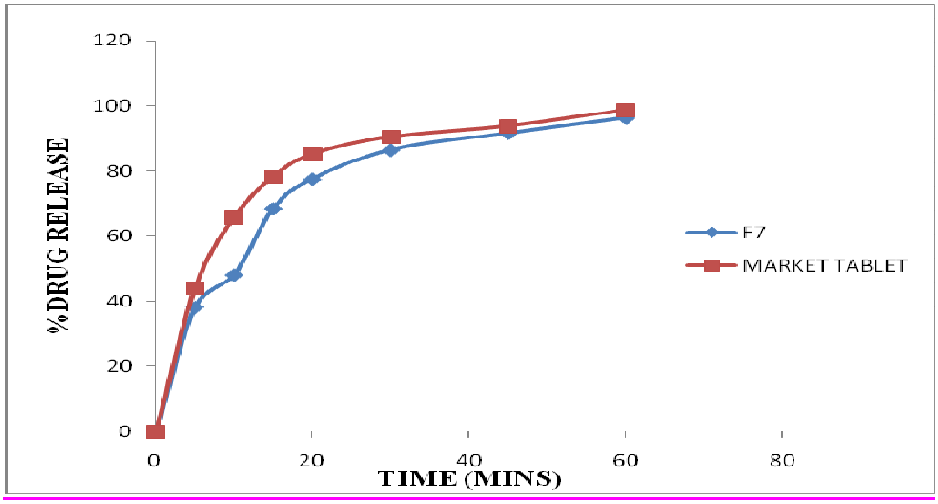

Figure-f: % Cumulative drug release of Opadry tm coated tablet and Marketed tablet.

The dissolution rate profile of marketed tablet was conducted. The comparison graphs between the marketed preparation and best formulation, F7 is shown in Figure f. The result showed that the formulation, F7 showed good result in comparison to other formulations and also marketed formulation. The evaluation parameter of marketed and optimized formulation are shown in Table k.

Table-k: Physical evaluation of Marketed and Optimized tablets.

	Marketed product	**F07**
Color	Off white	Off white
Surface	Smooth	Smooth
Thickness (mm)	4.45 ± 0.3	4.49 ± 0.3

Hardness (kP)	3.0 ± 0.5	3.0 ± 0.5
Weight (mg)	500 ± 1.0	500 ± 1.0
Assay (% w/w)	100.16 ± 1.1	98.79 ± 2.1
D.T. (sec)	8.5 ± 1.5	13.5 ± 1.67
Friaibility (%)	0.89 ± 0.03	0.88± 0.01
Wetting time	15.7 ± 0.8	16.5 ± 0.8
Water absorption ratio	55.36	68.4

F07 – Opadry tm coated Ibuprofen tablet.

Stability Studies: The stability study was conducted for the optimized formulation, F07 according to ICH guidelines, for 3 months. The percentage of drug content and *in vitro* drug release was evaluated. From the results, it was observed that there is insignificant changes in evaluation parameters. Hence it was concluded that the optimized formulation was stable.

Conclusion:

This study is aimed at formulating orally disintegrating tablets of a bitter drug i.e., Ibuprofen. It was carried out by fluid bed coating of extruded and spheronized pellets comprising of Ibuprofen, microcrystalline cellulose opadry tm was evaluated for taste masking systems. This prototype formulation (F07) had opadry tm coated taste masked pellets and selected excipients. Its disintegration time was found to be about 13.5sec. Tablets were evaluated for their disintegration time, hardness, friability, water uptake and drug release profile. It was concluded from this study that a water insoluble, system can effectively bitter drugs without unduly affecting their drug release profile.

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