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Design, Formulation and In-Vitro Evaluation of Ibuprofen Fast Disintegrating Tablets By Using Natural Polymer Moringa Oleifera

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ABSTRACT: IbuprofenisaNon-steroidalanti-inflammatorydrug(NSAID)withanti-inflammatory and analgesic properties. It can also be used in the treatment of rheumatoid arthritis, osteoarthritis and primary dysmenorrheal.The aim of the present work is to formulate a tabletwhich disintegrate and dissolve rapidly and give its rapid onset of action so the present study wasto formulate and in-vitroevaluation of fast disintegrating tablets of Ibuprofen by using Natural polymer such as Moringa oleifera gum by direct compression method by using3 different concentrations of 2%W/W, 4%W/W & 6%W/W and the selected synthetic polymer Hydroxy Propyl Methyl Cellulose (HPMC) 6%W/W. Each formulation was evaluated forvarious pre and post compression parameters such as Flow property,Bulk density,Tappeddensity,Weight variation, Hardness, Friability,Wetting time, Disintegration time, Assay,in-vitro dissolution. Among the 04 formulations 'F3' formulation Ibuprofen with 6% W/W of Moringa oleifera gum showed less disintegration time and better dissolution ratestudies. In-Vitro dissolution studies showed (99.98%) release of drug within 20 minutes so selected natural polymer acts as a Fast disintegrant action.

Keywords: Ibuprofen,NSAID,Moringa oleifera, HPMC.

I. INTRODUCTION

Fast disintegrating tablets are those which disintegrate rapidly and get dissolved to release the medicaments.[1].A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the break up of the compacted mass when it is put into a fluid environment.In many cases disintegrants have the major role in the disintegration and dissolution process of rapidly disintegrating tablets made by direct compression these are agents added totablets and some encapsulated formulations to promote breakup of tablets and capsules slugs into smaller fragments in the aqueous environment thereby increasing the available surface area and promote more rapid release of drug substance.[2,3,4].

Natural polysaccharides and their derivatives represent a group of polymers widely used in the pharmaceutical fields for the controlled release, Immediate release of of drugs from the formulation based on the Concentration. The Natural polymers are non-toxic, less expensive, biodegradable, and freely available in Nature.[5,6]

II. METHODOLOGY

Isolation ofMoringa olifera Natural Polymer[7]

The Moringa oleifera gum was collected by making an incision on the tree stem upto 5cm – 10cm depth. A small plastic cover bag was hanged at the incision area part and it was left for 5 days the liquid exudates were collected. After collecting the exudates, they were dried, to reduce the size of the exudates by grinding process. Dried raw gum was stirred in distilled water continuously for 6-8 h at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were also added to separated supernatant. The procedure was repeated 4-6 times. Finally, the supernatant was added to some amount of water and treated withtwice the volume of acetone with continuous stirring it indicates complete precipitation of the gum and total separation from water. This process has removed organic compounds dissolved in the

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supernatant. The precipitated material was washed with distilled water and dried at 50-60^{0}C under vaccum to obtain pure Moringa oleiferagum polymer. Finally, the dried purified gum was size reduced by grinding process and passed through sieve 80# and stored in a desicator at 30^{0}C.

III. METHODOLOGY[8-19]

Organoleptic Properties of Drug

Colour

:Asmallamountofpowderwastakeninbutterpaperand Ibuprofenwasviewedinwellilluminatedplace.

Odour& taste: very less quantity of drug was used to get taste with the help of tongue as well assmelledtogettheodour.

Determination of melting point: Melting point was determined by taking small amount ofdrug in a capillary tube closed at one end. The capillary tube was placed in an electricallyoperated melting point

PreCompressionEvaluationParameters:

Angle of repose: The angle of repose of powder blend was determined by the fixed funnel method. The accurately weighed quantity of powder was taken in a funnel. The height of funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder were allowed to flow through the funnel freely onto the surface. The diameter of powder cone was measured and angle of repose was calculated using the following equation.

Tanθ = h/r

θ = tan-1(h/r)

Where θ is the angle of repose
h is the height of cone in cm
r is the radius of the cone base in cm

Bulk density (eb): Bulk density was determined by pouring the powder into a graduated cylinder. The bulk volume (Vb) and mass (m) of the powder was determined. The bulk density was calculated by using the following formula.

Bulk density (eb) = Mass of the powder (M) / Bulk volume of powder (Vb)

Tapped density (et) :The measuring cylinder containing known mass of powder blend was tapped 1000 times for a fixed time. The minimum volume occupied in the cylinder (Vt) and mass of the powder (m) was measured. The tapped density was measured by using the following formula.

Tapped density (et) = Mass of powder (M) / Tapped volume of powder (Vb)

Compressibility index (Carr's index): The compressibility index determines the flow property characterstics of powder developed by Carr's. The percentage compressibility of powder is a direct measure of the potential powder arc and stability. The Carr's index can be calculated by the following formula.

%Carr's index = et – eb / et ×100

Where et is the tapped density of powder
eb is bulk density of powder .

Hausner's ratio: It is the measurement of frictional resistance of the drug. It was determined by the ratio of tapped density and bulk density.

Hausner's ratio = et / eb

Drug Excipient Compatibility Studies

Fourier Transform Infrared Spectroscopy (FTIR) : Potassium bromide was mixed with drug and/or polymer in 9:1 ratio and the spectra were taken. FT-IR spectrum of Ibuprofen was compared with FT-IR spectrum of Ibuprofenwith polymer. Disappearance of Ibuprofenpeaks or shifting of peaks in any of the spectra was studied

Calibration curve of Ibuprofen:

The I stock solution was prepared by dissolving 50mg of Ibuprofen sodium in 50ml of phosphate buffer - p^H 7.2 solution (1mg /1ml or 1000 µg /1ml). From stock I solution, pipetted out 5ml of solution into a 50ml volumetric flask and make up the volume with Phosphate buffer - p^H 7.2 solution and it is consider as stock II solution (100µg/1ml).From the secondary stock solution II various concentrations such as 0,2,4,6,8,10 µg/ml were prepared by using Phosphate buffer- p^H 7.2 solution for calibrationcurve. Standard Calibration curve was plotted by taking absorbance of secondary stocksolutionsinUVdoublebeamspectrophotometerat221 nm.

SolubilityAnalysis: ToPreparesupersaturatedsolutionsofIbuprofendrugwithwater,0.1NHCl,Phosphate buffer-pH 6.4, Phosphate buffer- pH -6.8, Phosphate buffer- pH -7.2 separately. Allthe solution kept a side for 24 hrs and filter the solution. Collect the filtrate and measure theabsorbance at221 nm.

Thesolubilityofthedrugcanbecalculatedbyusingthefollowingformula.

SOLUBILITY=(AT/AS)×CS×(DT/WD×1000)×100

WhereAtistheSample(test)absorbance.

As istheStandardabsorbance

Csisthestandardconcentrationofdrug.Dtis the dilutionfactor.

WdistheWeightofthedrug.

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FormulationandDevelopmentofIbuprofenfastdisintegratingtabletsbyusingDirectCompressionmethod

Table 1:List of Formulations

S.No	Name of the Ingredient	F1	F2	F3	F4
1	Ibuprofen	200	200	200	200
2	Moringa oleifera Polymer	6	12	18	-
3	HPMC	-	-	-	18
4	Magnesium stearate	4.5	4.5	4.5	4.5
5	Talc	4.5	4.5	4.5	4.5
6	Lactose	85	79	73	73
7	**Total weight (mg)**	300	300	300	300

In-vitroEvaluationtestsforFastDisintegratingTablets:

General Appearance: The formulated tablets were assessed for its general appearance and observationsweremadeforshape,colour,texture andodour.

Thickness: The Thickness mainly depends up on die filling, physical properties of material to becompressed under compression force. The thickness of the tablets was measured by usingDigitalVernierCalipers.

Desiredthickness:2.0 -4.0mm

Hardness :Hardnessof thetabletisdefinedastheforcerequiredinbreakingatablet inadiametric compression test. In this test, a tablet was placed between two anvils, force wasappliedtothe anvilsandthecrushingstrength thatjustcausesthe tablettobreakisrecorded.Hence hardnessissometimesreferredtoasCrushingStrength. Tablets require certain amount of strength or hardness to withstand mechanical shocks ofhandling in manufacture, packaging and shipping. The hardness of a tablet, like its thickness, is afunction of the die fill and compression force. At a constant die fill, the hardness value increasesandthicknessdecreasesasadditionalcompressionalforceisapplied

Desiredhardness:4-12Kg/cm^2

Friability : Friability is defined as the loss in weight of tablet in the container due to removal of fineparticle from their surface. It is expressed in percentage (%). A preweighed tablet sample (20tablets) was placed in the friabilator chamber and rotated for 10 revolutions. In each revolutionthe tablets are carried up and are allowed to freely fall from a height of 6 inches. After 100revolutions the tablets are removed from the chamber, dusted and reweighed. When capping isobservedduringfriabilitytest,tabletsshouldnotbeconsideredacceptable,regardlessofpercentage weightloss.

%Friabilitywasthencalculatedusingthefollowingformula:

Friability = [(Initial wt – Final wt)/ Initial wt] X 100

Limit: DesiredFriability: be less than 1%

Weight Variation: This testis not applicable to coated tablets other than film coated tablets and to tabletsthat are required to comply with the test for uniformity of content for all active ingredients. USPandNFprovidelimitsforthepermissiblevariation sintheweightsofindividualtabletsexpressedas a percentageofthe averageweightofthesample.

Individually weighed 20 tablets and calculated the average weight not more than two ofthe individual weights deviate from the average weight by more than the percentage deviationshowninTableandmore deviatedbymore thantwice thatpercentage.

Table 2: Limits for weight variation

Average Weight Of Tablets (mg)		Maximumn percentage deviation(%)
IP	**USP**	

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130 or Less	80 or Less	10
130 -324	80 -250	7.5
324 or More	250 or More	5.0

Disintegration Test: The process of breakdown of a tablet into smaller particles is called as disintegration. The in vitro disintegration time of a tablet was determined using disintegration test apparatus as per IP specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using 0.1 N Hcl or Phosphate buffer pH 7.2 as the immersion liquid and maintained a temperature at $37^{o}\pm 2^{o}C$. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

Content uniformity(Assay): Weighandpowder20tablets.Weighaccuratelyaquantityofthepowderequivalentto 50mg ofIbuprofen, shake with 60ml of methanol in a 200ml clean, dry volumetric flaskand dilute tovolume with methanol and sonicate for 30 minutes with intermittentshaking atroom temperature. Dilute 5ml of this solution to 100ml with methanol. Centrifuge the solution at10,000RPMfor 10minutes.Filterthrough 0.45µnylonmembranefilter.Tomeasuretheabsorbance at221nm.

$$\text{ASSAY}=(\text{AT}/\text{AS})\times\text{CS}\times(\text{DT}/\text{WD})\times 100$$

WhereAtistheSample(test)absorbance.
As istheStandardabsorbance.
Csisthestandardconcentrationofdrug.Dtis the dilutionfactor.
WdistheWeightofthedrug.

Wetting Time: This test was carried out by to measure the time required for the complete wetting of tablet formulations. A piece of tissue paper folded twice was placed in small petridish containing 10ml of water in which amaranth, a water-soluble dye was added. A tablet was placed on this paper. The time required for water to reach the upper surface of the tablet was noted as wetting time.

Dissolution rate studies

The drug release rate of Ibuprofen fast disintegrating tablets was determined using United States Pharmacopeia (USP) dissolution testing apparatus type-II (paddle method).The dissolution test was performed by using 900 ml of Phosphate buffer-pH 7.2, at $37^{0}\pm 0.5^{0}$ C and 50 rpm. In specified time intervals an aliquot of 5ml samples of the solution were withdrawn from the dissolution apparatus and with replacement of fresh fluid to dissolution medium. The samples were filtered through filter paper of 0.45 µ m. Absorbance of these solutions were measure data λmax 221 nm using by using UV/Visible Spectrophotometer. The drug release was plotted against time to determine the release profile of various formulations.

The % drug release of the formulation can be calculated by

% drug release = (At/As)×Cs× (Dt ×Vm/Wd×1000) ×100

Where At is the Sample(test) absorbance.
As is the Standard absorbance.
Cs is the standard concentration of drug.
Dt is the dilution factor.
Wd is the Weight of the drug.
Vm is the volume of the dissolution medium

IV. RESULTS:

Table 3: APICharacteristics

S.No	Characteristics	Results
1	Description	White
2	MeltingPoint	$76\pm 0.26^{0}c$
3	BulkDensity	0.328±0.03gm/ml
4	TappedDensity	0.378±0.09gm/ml

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5	Carr'sIndex	13.22±0.01%
6	Hausner'sRatio	1.15±0.10
7	AngleofRepose	22.58^0±0.11

Table 4: Solubility Analysis of Ibuprofenwith different solvents

S.NO	TypeofSolvent	Solubility(mg/ml)
1.	Water	0.021±0.019
2.	0.1NHCl	0.218±0.49
3.	Phosphatebuffer^H-6.4	0.980±0.028
4.	Phosphatebuffer^H-6.8	0.986±1.33
5.	Phosphatebuffer^H-7.2	0.998±0.59

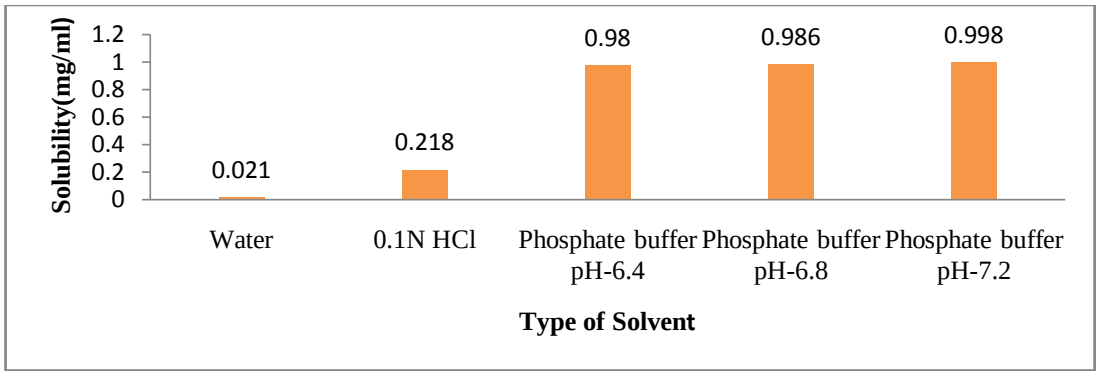

Figure 1:Solubility Analysis of Ibuprofenwith different solvents.

Table 5 : Natural Polymers Characteristics

S.No	Characteristics	Moringa Gum
1	Description	Initially white in colour but canges to Reddish brown or Brownish black on exposure
2	BulkDensity	0.76±0.06gm/ml
3	TappedDensity	0.83±0.11gm/ml
4	Carr'sIndex	8.43±0.11%
5	Hausner'sRatio	1.09±0.052
6	AngleofRepose	17.74^0±0.031

Drug-Excipient Compatability study

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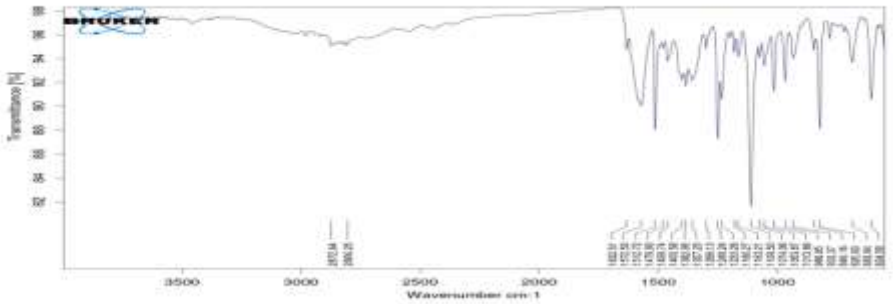

Figure 2:FTIRSpectraofIbuprofen

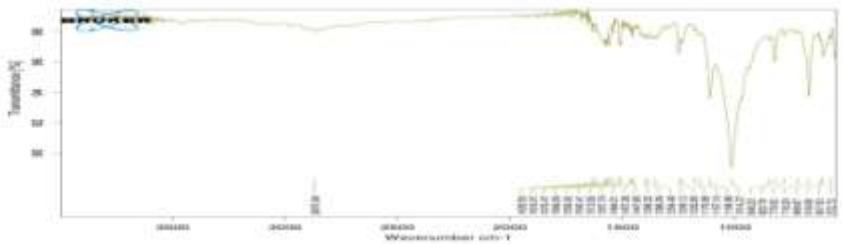

Figure3:FTIRSpectraofoptimizedFormulation

Table 6: Standard Calibration Curve Data

S.NO	Concentration (µg/ml)	Absorbance at 221nm
1.	0	0
2.	2	0.075±0.018
3.	4	0.161±0.003
4.	6	0.263±0.016
5.	8	0.350±0.025
6.	10	0.442±0.021

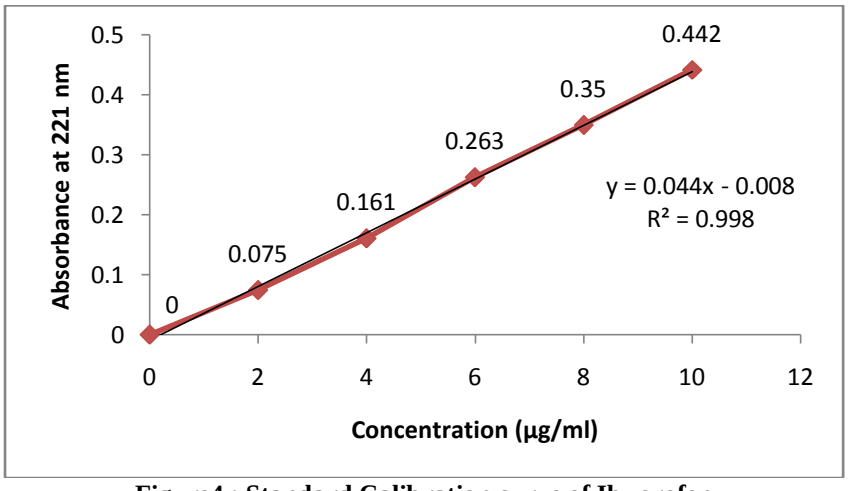

Figure4 : Standard Calibration curve of Ibuprofen

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Table 7:Evaluation of Flow properties of Formulation Blends

FormulationCode	Angle ofrepose(Θ)	Bulk Density(gm/cm^3)	TappedDensity (gm/cm^3)	Compressibility(%)	Hausnersratio
F1	28.37±0.16	0.651±0.12	0.722±0.68	9.83±0.24	1.105±0.07
F2	28.22±0.42	0.637±0.25	0.705±0.42	9.64±0.42	1.10±0.21
F3	27.54±0.25	0.671±0.32	0.730±0.35	8.08±0.24	1.08±0.16
F4	28.88±0.15	0.590±0.10	0.659±0.63	10.47±0.48	1.11±0.14

Table 8: Evaluation of Ibuprofen FD Tablets

Formulations	Weightvariation(mg)	Thickness(mm)	Hardness(kg/cm^2)	Friability(%)	Assay(%)	Disintegrationtime (Sec)	Wettingtime(Sec)
F1	Pass	2.96±0.22	4.45±0.25	0.75±0.54	99.85±0.43	108±0.52	62±0.43
F2	Pass	2.84±0.36	4.62±0.15	0.62±0.44	98.92±0.09	82±0.43	48±0.16
F3	Pass	2.94±0.28	4.56±0.10	0.82±0.26	99.92±0.17	52±0.12	29±0.09
F4	Pass	2.86±0.87	4.92±0.07	0.68±0.07	99.31±0.01	204±0.68	85±0.47

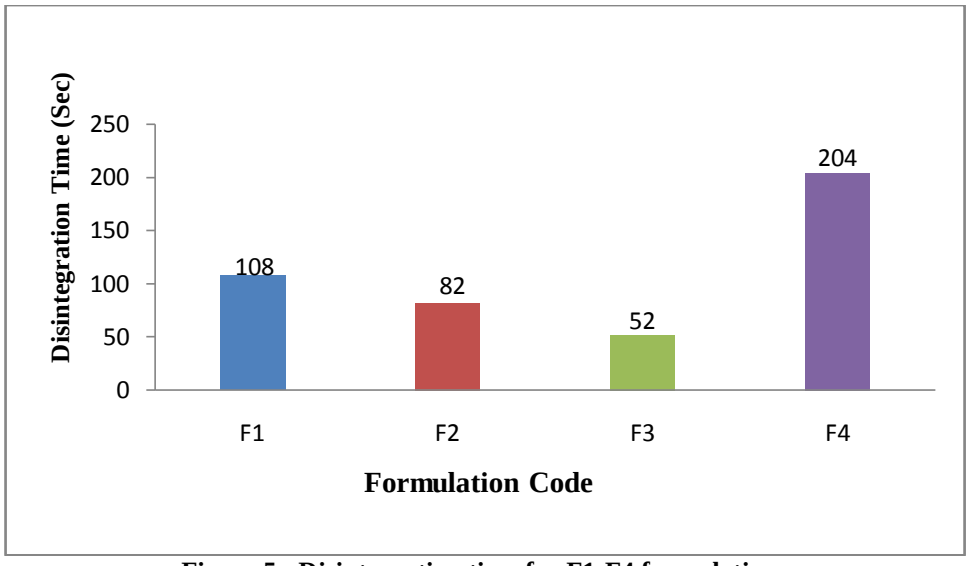

Figure 5 : Disintegration time for F1-F4 formulations

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Table 9: Dissolution profiles of formulations(F1 to F4)

Time(Min)	F1	F2	F3	F4
0	0	0	0	0
5	11.23±0.41	12.34±0.16	23.05±0.21	14.11±0.20
10	19.21±0.23	23.12±0.11	55.11±0.09	22.31±0.11
15	26.11±0.09	44.03±0.09	81.03±0.11	36.13±0.05
20	38.23±0.05	56.00±0.13	99.98±0.04	49.03±0.80
25	57.21±0.11	65.13±0.21		74.23±0.09
30	69.03±0.04	78.11±0.09		86.13±0.09
40	84.23±0.09	99.86±0.11		99.80±0.32
50	99.89±0.11			

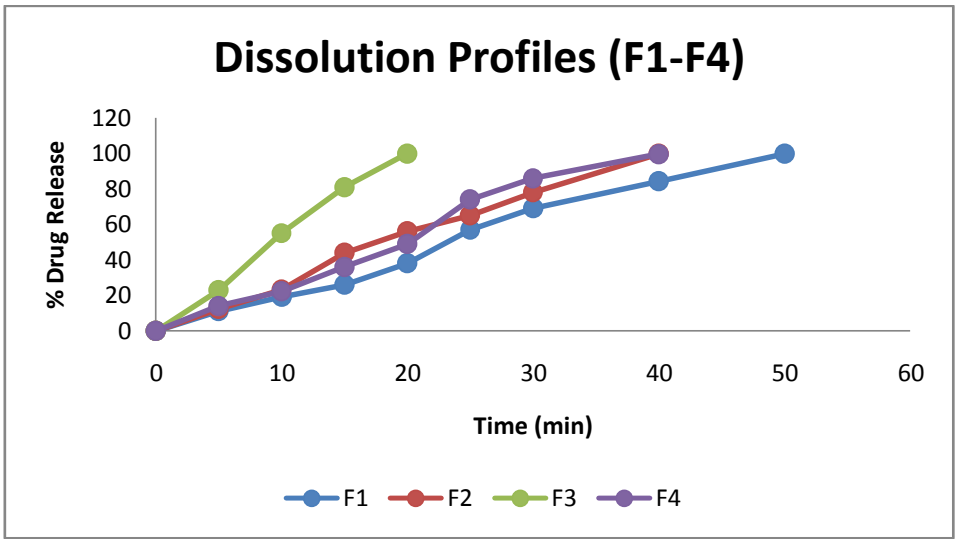

Figure 6: Dissolution graphs of 4 Formulations

V. SUMMARY AND CONCLUSION

The present study was to formulate and in-vitro evaluation of Ibuprofen usingNatural polymer such as Moringaoleifera gum in the percentage of 2%W/W, 4%W/W,6%W/W.

The powder blend were evaluated by various physical characteristic tests such as bulkdensity, Tapped density, Compressibility index, Hauser's ratio, Angle of repose. So the valueswere foundtobewithinthelimits.

Among the all formulations the Assay results, Hardness, Friability, Weight variation,Thickness,Disintegration time andWetting timeSo the values werefound tobe within thelimits. As the ratio of polymer increased then the Disintegration time was decreased. Among allthe 04 formulations the 'F3' formulation [(Ibuprofen): Moringa oelifera] showed excellent disintegration time and betterdrug release when compared to other formulations.In-Vitro dissolution studies showed 99.98%ofdrugrelease within20minutes. So it was concluded that the fast disintegrating tablets were prepared by Natural polymerMoringa oleiferagum and Synthetic polymer Hydroxy Propyl Methyl Cellulose acts as a Fast disintegrant action based on the concentration used so the Moringaoleiferagum showed excellent disintegration time and enhance the dissolution rate.

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