International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

Formulation and Evaluation of Diclofenac Sodium Fast Disintegrating Tablets Using Natural Polymer Tangerine Peels

T Anjali*[1], M Srikanth[2], N Srinivas[3], P.SS. Prasanna kumar[4], D Rohit [1], K Nirmala[1] ,
MD Rabiya Basri[1], P Prasad[1], T Mani kumar[1], U Hemanjali[1]
[1,4] *Department of Pharmaceutics, A K R G College of Pharmacy, Nallajerla. W.G. Dist, A.P-534112*
[2] *Department of Pharmacognosy,A K R G College of Pharmacy, Nallajerla. W.G. Dist, A.P-534112*
[3] *Department of Pharmacology,A K R G College of Pharmacy, Nallajerla. W.G. Dist, A.P-534112*

Date of Submission: 15-07-2021 Date of Acceptance: 30-07-2021

ABSTRACT:
Diclofenac sodium is a Non-steroidal anti-inflammatory drug (NSAID) with Anti-Inflammatory, Anti-pyretic and Analgesic properties. The aim of the present work is to design and formulate a tablet which disintegrate, dissolve rapidly and it gives rapid onset of action by using Tangerine peel powder obtained from **Citrus Reticulata** and investigate the fast-disintegrating property. The reason for choosing a natural polymer is due to disintegrating property, nontoxicity, low cost, reliable, free availability, eco-friendly, potentially degradable and compatible. The present study was to Formulate and evaluation of fast disintegrating tablet of Diclofenac sodium using Tangerine peel powder extracted from "**Citrus Reticulata**" by direct compression technique in 04 different concentrations of 2%W/W,4%W/W,6%W/W & 8%W/W. Each formulation was Evaluated for various pre and post compression parameters such as Flow property, Bulk density, Tapped density, Weight variation, Hardness, Friability, Wetting time, Disintegration time, In- vitro dissolution. Among the 04 formulations, F4 formulation Diclofenac with 8%w/w of Tangerine peel powder showed the best dissolution rate studies. In-Vitro dissolution studies showed (99.98%) release of drug within 25 minutes. It was concluded that the fast disintegrating tablets are prepared by Tangerine peel powder extracted from C.Reticulata acts as a Fast disintegrant and the tangerine peel powder showed excellent disintegration time

Keywords: Diclofenac sodium, NSAID, Citrus Reticulata (Tangerine) extract powder, Superdisintegrant.

I. INTRODUCTION

Fast disintegrating tablets (FDT's) are those solid dosage forms when put on tongue, disintegrate or dissolve instantaneously, releasing the drug, within a few seconds without the need of water. Fast disintegrating tablets (FDT's) aim for designing dosage forms, convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, to achieve better patient compliance. Fast disintegrating tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product life extension in the many elderly persons which have difficulty in taking conventional oral dosage form (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. [1]

II. METHODOLOGY

Isolation of Citrus Reticulata tangerine peel powder Natural Polymer [2]

Mature tangerine fruits were purchased from Market. Tangerine (Citrus reticulata) fruits were cut into four parts and the peels removed (a soft white substance inside the skin of citrus fruits). The peels were cut further into smaller pieces for easy drying and then washed with large volume of water to remove foreign matter, bitter taste of the peels, and also to remove the residues of the pesticide spray. Afterwards, they were air dried for 24 hours, blended powder was obtained and kept in a polythene bag for future use.

The peel powder was measured (30 g) and transferred into a beaker (1000 mL) containing 450 mL of water, and 2.6 mL hydrochloric acid was added to give a pH of 1.27. Each of the fruit peel

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

samples were then boiled for one hour. Thereafter, the residues were removed from the extracts by filtering through a cheese cloth. The cakes were washed with 250 ml boiled water and the combined filtrate was allowed to cool to 25°C to reduce heat degradation of the pectin. Extracted pectin was precipitated by the addition of 200 ml 95% isopropanol to 100 ml of the extracted pectin with thorough stirring, and left for 30 min to allow the pectin float on the surface. The gelatinous pectin flocculants were then filtered off. The pectin extract was purified by washing in 200 ml isopropanol and pressed on nylon cloth to remove residue HCl. The obtained extracted pectin powder kept in a polythene bag in desiccator at 30^0C.

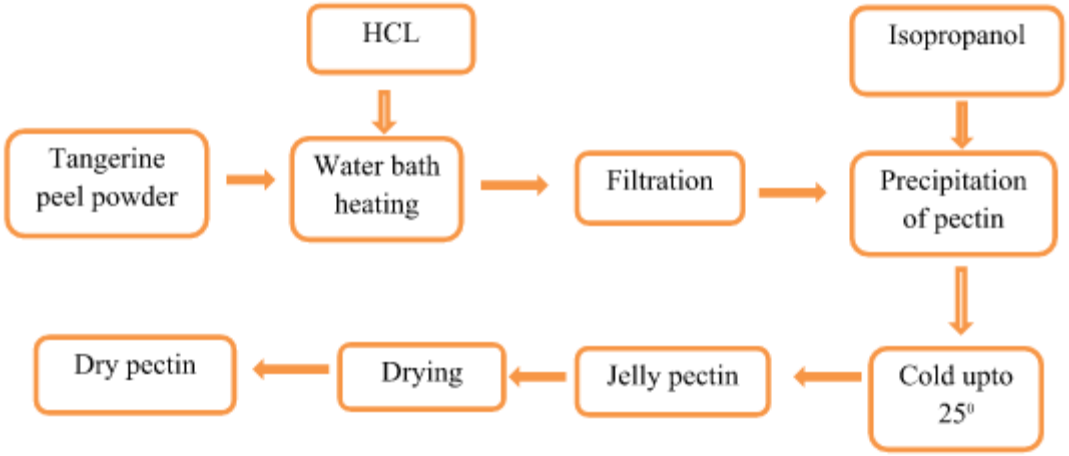

Fig No:1 Extraction procedure for pectin from tangerine peels

III. METHODOLOGY

Organoleptic Properties of Drug

Colour: A small amount of powder was taken in butter paper and Ibuprofen was viewed in well illuminated place.

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

Determination of melting point: Melting point was determined by taking small amount of drug in a capillary tube closed at one end. The capillary tube was placed in an electrically operated melting point and the temperature at which the drug melts was recorded. This was performed thrice and average values were noted.

Solubility Analysis: To Prepare supersaturated solutions of Ibuprofen drug with water, 0.1N HCl, Phosphate buffer-pH 6.4, Phosphate buffer- pH -6.8, Phosphate buffer- pH -7.2 separately. All the solution kept a side for 24 hrs and filter the solution. Collect the filtrate and measure the absorbance at 221 nm.

The solubility of the drug can be calculated by using the following formula.

Solubility = $(A_T/A_s)\times C_s\times (D_t/W_d\times 1000)\times 100$

Where A_t is the Sample(test) absorbance.

A_s is the Standard absorbance

C_s is the standard concentration of drug.

D_t is the dilution factor.

W_d is the Weight of the drug.

Pre-Compression Evaluation Parameters:

Angle of repose: The angle of repose for blended powder was determined by the fixed funnel method. The accurately weighed quantity of powder was taken in a funnel and height of funnel was adjusted that the tip of the funnel just touch the apex of the heap of the powder. The powder was 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.

$\mathbf{Tan\theta = h/r}$

$\mathbf{\theta = tan\text{-}1(h/r)}$

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

Bulk density (ρ_b) = Mass of the powder (M) / Bulk volume of powder (V_b)

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

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 (ρ_t) = Mass of powder (M) / Tapped volume of powder (V_b)

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 = $\rho_t - \rho_b / \rho_t \times 100$

Where ρt is the tapped density of powder
ρb 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 = ρ_t / ρ_b

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 Ibuprofen with polymer. Disappearance of Ibuprofen peaks or shifting of peaks in any of the spectra was studied

Standard Calibration Curve of Diclofenac sodium:

The λmax was obtained at 273 nm in Phosphate buffer at pH 6.8. The standard calibration curve for Diclofenac sodium with regression value of 0.9967 was shown in Figures 7.5 respectively. The relation between drug concentration and absorbance is linear and the curve obeys Beer – Lamberts law within the concentration range of 1 to 10 µg/mL of Diclofenac sodium. The calculation of In-vitro drug release and Assay was based on this calibration curve.

Formulation and Development of Diclofenac sodium fast disintegrating tablets by using Direct Compression method

Table 1: List of Formulations

S.NO	Name of the Ingredient	F1	F2	F3	F4
1	Diclofenac sodium	200	200	200	200
2	**Citrus Reticulata** (tangerine peel powder)	**8**	**16**	**24**	**32**
3	Talc	4	4	4	4
4	Magnesium stearate	4	4	4	4
5	Lactose	184	176	168	160
	Total weight(mg)	400	400	400	400

In-vitro Evaluation tests for Fast Disintegrating Tablets:

General Appearance: The formulated tablets were assessed for its general appearance and observations were made for shape, colour, texture and odour.

Thickness: The Thickness mainly depends up on die filling, physical properties of material to be compressed under compression force. The thickness of the tablets was measured by using Digital Vernier Calipers.

Desired thickness: 2.0 - 4.0 mm

Hardness : Hardness of the tablet is defined as the force required in breaking a tablet in a diametric compression test. In this test, a tablet was placed between two anvils, force was applied to the anvils and the crushing strength that just causes the tablet to break is recorded.

Desired hardness: 4-12 Kg/cm^2

Friability : Friability is defined as the loss in weight of tablet in the container due to removal of fine particle from their surface. It is expressed in percentage (%). A preweighed tablet sample (20 tablets) was placed in the friabilator chamber and rotated for 10 revolutions. In each revolution the tablets are carried up and are allowed to freely fall from a height of 6 inches. After 100 revolutions the tablets are removed from the chamber, dusted and reweighed. When capping is observed during friability test, tablets should not be considered acceptable, regardless of percentage weight loss.

% Friability was then calculated using the following formula:

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

Limit: Less than 1%

Weight Variation: This test is not applicable to coated tablets other than film coated tablets and to tablets that are required to comply with the test for

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

uniformity of content for all active ingredients. USP and NF provide limits for the permissible variations in the weights of individual tablets expressed as a percentage of the average weight of the sample.

Individually weighed 20 tablets and calculated the average weight not more than two of the individual weights deviate from the average weight by more than the percentage deviation shown in Table and more deviated by more than twice that percentage.

Table 2: Limits for weight variation

Average Weight of Tablets (mg)		Maximum percentage deviation (%)
IP	**USP**	
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 $37^o \pm 2^oC$. 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): Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 50mg of Diclofenac sodium, shake with 60ml of methanol in a 200ml clean, dry volumetric flask and dilute to volume with methanol and sonicate for 30 minutes with intermittent shaking at room temperature. Dilute 5ml of this solution to 100ml with methanol. Centrifuge the solution at 10,000 RPM for 10 minutes. Filter through 0.45µ nylon membrane filter. To measure the absorbance at 273 nm.

$Assay=(A_t/A_s)\times C_s\times (D_t/W_d) \times 100$
Where A_t is the Sample(test) absorbance.
A_s is the Standard absorbance.
Cs is the standard concentration of drug.
Dt is the dilution factor.
Wd is the Weight of the drug.

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 Diclofenac sodium 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 λ_{max} 273 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 $= (A_t/A_s)\times C_s\times (D_t \times V_m/W_d\times 1000) \times 100$
Where A_t is the Sample(test) absorbance.
A_s is the Standard absorbance.
C_s is the standard concentration of drug.
D_t is the dilution factor.
W_d is the Weight of the drug.
V_m is the volume of the dissolution medium

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

IV. RESULTS:

Table 3: API Characteristics

S.NO	Characteristics	Results
1	Description	White
2	Melting point	284°C±0.35
3	Bulk Density	0.394±0.46 g/ml
4	Tapped Density	0.443±0.06 g/ml
5	Carr's Index	11.06±0.12%
6	Hausner's Ratio	1.124±0.06
7	Angle of repose	32.35^0±0.12

Table 4: Solubility Analysis of Diclofenac sodium with different solvents

S. NO	Type of solvent	Solubility(mg/ml)
1	Water	0.073±0.019
2	0.1N HCl	0.652±0.006
3	Phosphate buffer pH -6.4	0.922±0.028
4	Phosphate buffer pH -6.8	0.988±0.554
5	Phosphate buffer pH -7.2	0.931±0.035

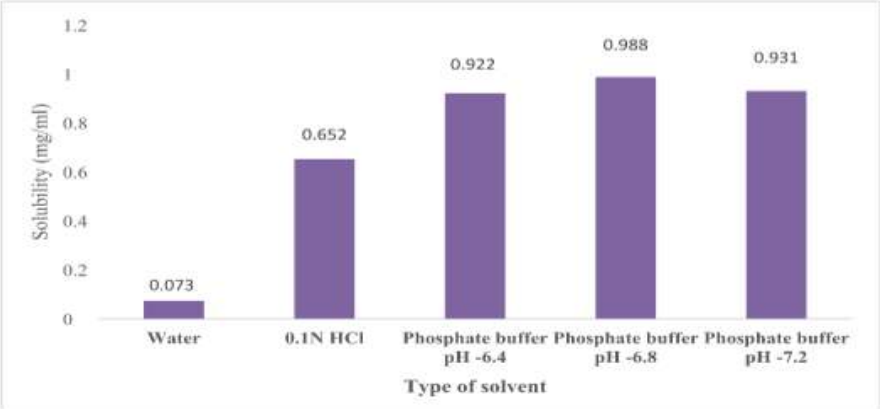

Figure 2: Solubility Analysis of Diclofenac sodium with different solvents.

Table 5: Natural Polymer Characteristics

S.NO	Characteristics	Pectin
1	Description	yellowish
2	Bulk Density	0.669±0.32 g/ml
3	Tapped Density	0.764±0.21 g/ml
4	Carr's Index	12.43±0.12%
5	Hausner's Ratio	1.14±0.14
6	Angle of Repose	29.16°±0.14

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

Drug-Excipient Compatability study

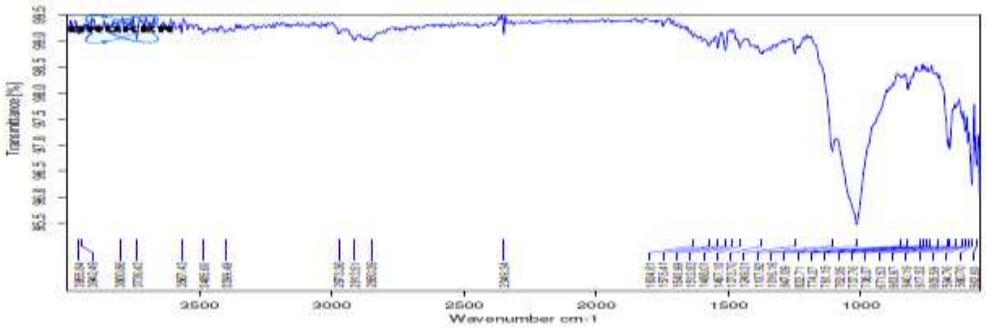

Figure 3: FTIR Spectra of Diclofenac sodium

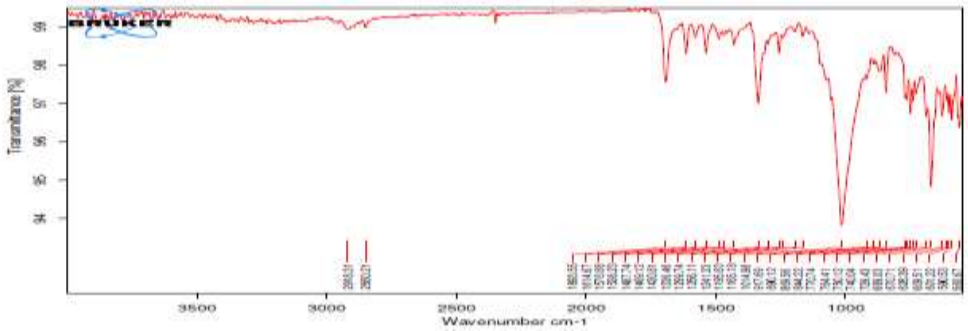

Figure 4: FTIR Spectra of optimized Formulation

Table 6: Standard Calibration Curve Data

S.NO	Concentration(µg/ml)	Absorbance at 273 nm
1	0	0
2	2	0.070±0.008
3	4	0.120±0.012
4	6	0.175±0.023
5	8	0.233±0.016
6	10	0.294±0.014

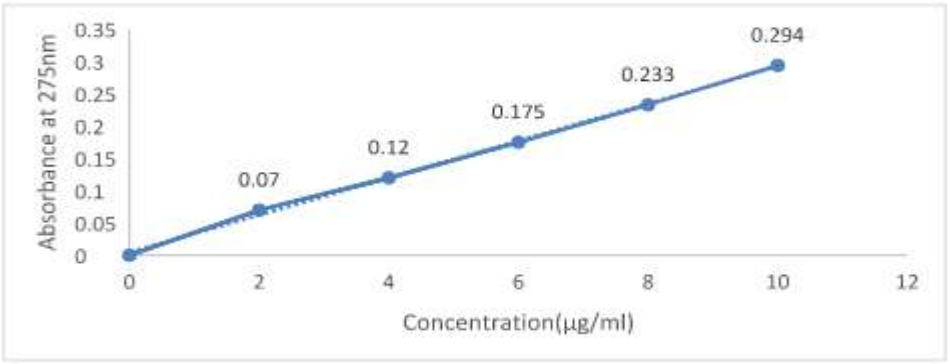

Figure 5: Standard Calibration curve of Diclofenac sodium

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

Table 7: Evaluation of Flow properties of Formulation Blends

FormulationCode	Angle of repose (Θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Compressibility(%)	Hausnersratio
F1	31.62±0.45	0.594±0.12	0.690±0.33	13.91±0.30	1.161±0.02
F2	33.54±0.59	0.585±0.20	0.670±0.24	12.68±0.13	1.145±0.03
F3	32.38±0.52	0.538±0.35	0.612±0.57	12.09±0.24	1.137±0.04
F4	34.46±0.37	0.615±0.06	0.720±0.21	14.58±0.27	1.170±0.01

Table 8: Evaluation of Diclofenac sodium FD Tablets

Formulations	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration time (sec)	Wetting time (sec)
F1	Pass	2.75±0.35	4.59±0.29	0.59±0.52	154±0.52	85±0.05
F2	Pass	2.91±0.14	4.62±0.35	0.76±0.43	82±0.43	62±0.09
F3	Pass	2.82±0.24	4.67±0.46	0.66±0.21	48±0.12	36±0.11
F4	Pass	2.69±0.36	4.38±0.66	0.72±0.03	29±0.68	20±0.18

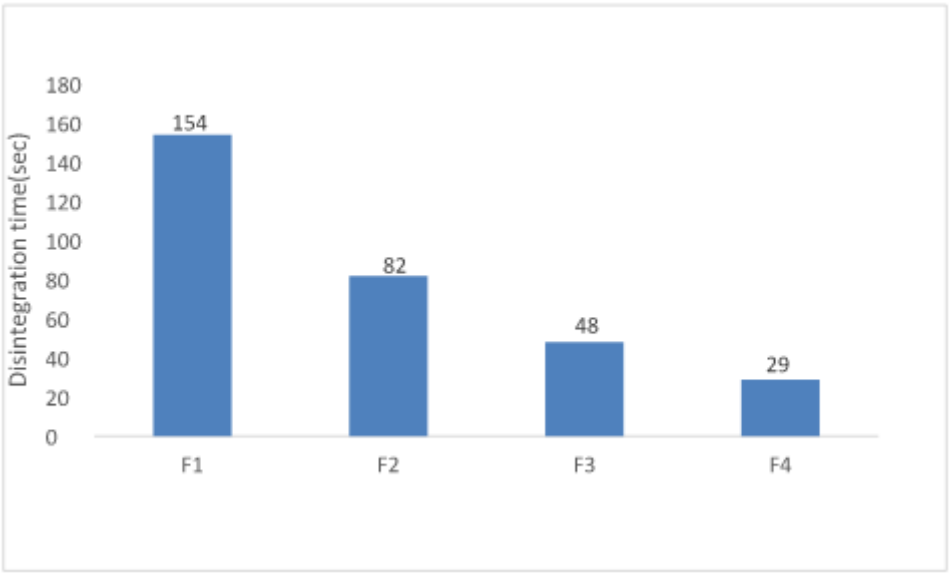

Figure 6: Disintegration time for F1-F4 formulations

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

Time (Min)	F1	F2	F3	F4
0	0	0	0	0
5	14.71±0.04	20.66±0.12	23.67±0.32	30.56±0.27
10	28.31±0.14	39.03±0.08	42.85±0.15	49.74±0.56
15	44.05±0.04	51.27±0.21	55.10±0.59	72.70±0.34
20	53.15±0.21	65.05±0.32	66.58±0.36	86.47±0.66
25	66.03±0.18	75.76±0.54	87.24±0.48	99.87±0.13
30	75.58±0.07	81.12±0.68	94.13±0.62	
40	80.02±0.19	93.36±0.25	99.70±0.20	
50	84.68±0.09	99.62±0.18		
60	99.15±0.6			

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 635-643 www.ijprajournal.com ISSN: 2249-7781

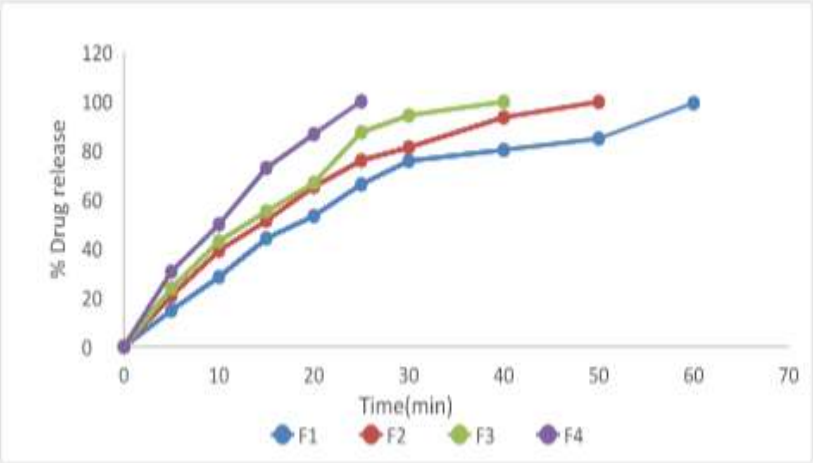

Figure 7: Dissolution graphs of 4 Formulations

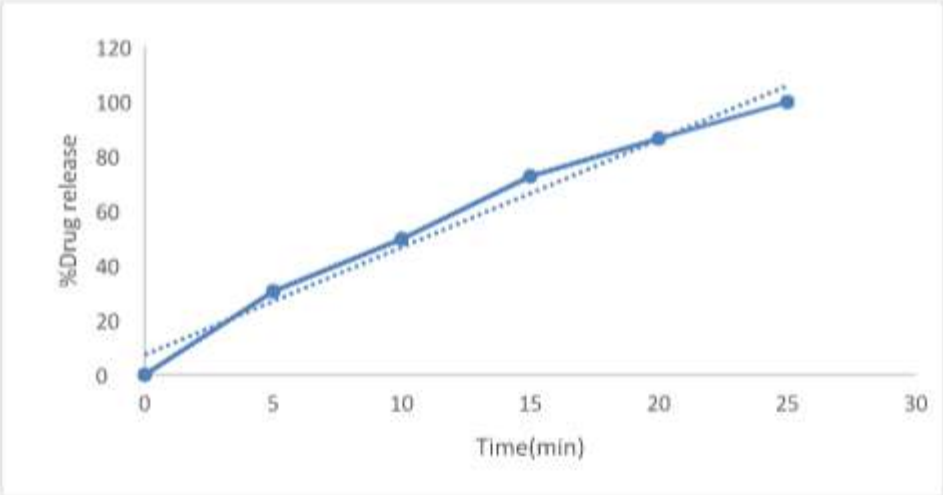

Figure: 8- Dissolution graphs of F4 formulation

V. SUMMARY AND CONCLUSION

The present study was to formulate and In-vitro evaluation of Diclofenac sodium Fast disintegrating tablets by using **Citrus reticulata** as a natural Polymer in the percentage of 2% W/W, 4% W/W, 6% W/W and 8% W/W.

The powder blend was evaluated by various physical characteristic tests such as Bulk density, Tapped density, Compressibility index, Hausner's ratio, Angle of repose. So, the values were found to be within the limits.

Among all the formulations Assay, Hardness, Friability, Weight variation, Thickness, Disintegration time and Wetting time values were found to be within the limits. As the concentration of Natural polymer increased then the Disintegration time was decreased so selected Natural polymers acts as Fast disintegrating agents.

Among all the 04 formulations the optimised formulation "F4" (8%W/W) showed better drug release when compared to other formulations. In-Vitro dissolution studies showed 99.98% of drug release within 25 minutes

REFERENCES:

[1]. Sharma Deepak, Fast disintegrating tablets: A new era in novel drug delivery system and new market oppurtunities, Journal of Drug Delivery & Therapeutics; 2012,2(3):74-86.

[2]. Hannington Twinomuhwezi et al., Extraction and characterization of pectin from orange (citrus sinesis), Lemon(Citrus limon) and Tangerine(Citrus tangerina), American journal of physical science, ISSN 2519-5549(online) Vol.1, Issue1, No.2, 2020.

[3]. Kokkula Satyanarayana, Chinmaya Keshari Sahoo, Gude Bhargavi, and Nalini Kanta Sahoo Formulation and optimization of Olanzapine sustained release matrix tablets for the treatment of schizophrenia -Der Pharmacia Lettre, 2015, 7 (4):266-273.
[4]. G.N.K. Ganesh *, R. Suresh Kumar, N. Jawahar, V. Senthil, D. Nagasamy Venkatesh and M. Shanmukha Srinivas Preparation and Evaluation of Sustained Release Matrix Tablet of Diclofenac Sodium using Natural Polymer -J. Pharm. Sci. & Res. Vol.2 (6), 2010, 360-368.
[5]. L. Lachman, HA Lieberman, Joseph L Kanig. The theory and practice of Industrial pharmacy, Verghesh publishing house, 3rd edition, 1990, 346.
[6]. Remington, the Science and practice of pharmacy, Lippincott Williams & Wilkins, 20th edition, 2002, 903-914.
[7]. Alford N Martin, Patrick J. Sinko. Martin's Physical pharmacy and pharmaceutical sciences, 2006.
[8]. Madhu EN, Karunakar R, Pavan KK, Raghunadha GC. Development and evaluation of extended-release matrix tablets of Alfuzosin HCl and its comparison with marketed product. Journal of Pharmacy Research. 2011; 4(5): 1436-1437.
[9]. A.Martin and J.Swarbrick, Physical pharmacy, 3rd edition, Mumbai: Varghese publishing house, 1993, Pg. No. 444-7.
[10]. Jagadeesh I, Padmaja B, International Journal of Pharmacy and Pharmaceutical Sciences, 2012, 4, 1, 241-248.
[11]. Jain S, Yadav SK, Patil UK, Preparation and evaluation of sustained release matrix tablet of furosemide using natural gum. Research J Pharm. and tech., 2008, 1(4), 374-376.