Formulation and Evaluation of Diclofenac Sodium Fast-Dissolving Tablet by Using Natural Super disintegrant

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ABSTRACT

The emergence of the fast-dissolving drug delivery system stemmed from the desire to offer patients a more convenient method for taking medication. Many individuals find it challenging to swallow tablets and hard gelatin capsules. The primary aim of this research was to develop a consistent formulation for fast-dissolving tablets of Diclofenac sodium, a therapeutic molecule already in use. The objective was to improve its effectiveness while avoiding side effects such as gastric irritation. Various batches of tablets were formulated using the direct compression method, incorporating different concentrations of natural super disintegrants Ocimum sanctum seed powder. The study examined the impact of altering the natural super disintegrant and its concentration on the formulation. The optimized batches were compared to determine the most effective super disintegrants for the Diclofenac sodium Fast-dissolving tablets (FDT) formulation. The tablets underwent evaluation for hardness, thickness, drug content, friability, weight variation, in-vitro disintegrating time study, and in-vitro drug release study.

Keywords: FDT, Holy Basil, Ocimum Sanctum Seed Powder, Natural Superdisintegrant, Diclofenac Sodium.

INTRODUCTION

The oral route is the most convenient and preferable route of administration and its advantages or important like high versatility, ease of administration, self-medication, accurate dosing, and most importantly patient compliance. The most important popular solid unit dosage forms are capsules and tablets. One of the disadvantages of these dosage forms for some people or patients is the difficulty to swallowing the dosage. Difficulty in swallowing is a main common problem of all age, especially in the pediatrics and elderly patient. Fast-dissolving drug delivery system is rapidly gaining acceptance as an important novel drug delivery technology which main objective is to enhance efficacy and safety of drug molecule by formulating novel drug delivery systems that have convenient dosage form for administration and achieve better patient compliance. FDT are an innovative type of tablet that dissolves or disintegrates rapidly in saliva within few seconds without the need for water. When FDTs are introduced or placed in the oral cavity, saliva penetrates quickly into the pores of a tablet and causes rapid disintegration leading to their suitability for pediatric and geriatric patients. The different polymers and natural gum are widely used in pharmaceutical industries. Seed powder is used in various contexts such as a binder, super disintegrant, gelling agent, thickening agent as well as suspending agent, etc. Natural substances are preferred over semi-synthetic and synthetic materials due to their free availability, low cost, non-irritating nature, non-toxic, and environment friendly. [1]

MATERIAL AND METHODS:

Materials: Holy Basil seed was purchased from Bhu Tatva Agro, Indore, (M.P.), Diclofenac sodium was purchased from Balaji Drugs, sodium starch glycolate, sodium saccharin and talc was purchased from Loba Chemie Pvt. Ltd., Mumbai, Vanillin was purchased from s d fine-chem Ltd., Mumbai., Magnesium stearate was purchased from Milton Chemicals, Mumbai., Avicel PH 102 was purchased from Modern Industries, Nashik

Methods:

Preparation of Diclofenac sodium FDT: The direct compression method was used to prepare FDTs containing 50 mg of diclofenac sodium. The formulae used in the study are shown in Table 1. The formulation contains different proportions (for optimization) of Ocimum sanctum seed powder as a natural super disintegrant along with Avecil PH 102 as

directly compressible diluents and sodium saccharin as a sweetening agent. To compare the disintegration efficiency of Ocimum sanctum seed powder widely used synthetic super disintegrants i.e., croscarmellose sodium, and sodium starch glycolate was used. All the ingredients were passed through sieve no # 60 individually to attain homogeneity and mixed thoroughly. Using an 8-station rotating tableting machine, the mixture was immediately compressible into tablets with a 9 mm punch. [2]

Table No. 1: Formulation quantities of tablet (mg)

Composition	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diclofenac sodium (mg)	50	50	50	50	50	50	50	50	50
Ocimum sanctum seed powder (mg)	15	30	45	--	--	--	7.5	15	22.5
SSG (mg)	--	--	--	15	30	45	7.5	15	22.5
Sodium Saccharin (mg)	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Talc (mg)	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Magnesium Stearate (mg)	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Vanilin (mg)	12.50	12.50	12.50	12.50	12.50	12.50	12.50	12.50	12.50
Avicel PH 102 (mg)	253.75	238.75	223.75	253.75	238.75	253.75	253.75	238.75	253.75
Total (mg)	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**

Note: All values are taken in mg

Evaluation parameter:

Pre-compression parameters (Evaluation of powder blend): The following parameters were determined.

Angle of repose: The funnel method was employed to determine the angle of repose of granules. A carefully measured quantity of granules was placed in a funnel. The height of the funnel was adjusted to ensure that its tip made contact with the highest point of the granule heap. Subsequently, the granules were allowed to flow naturally through the funnel and onto the surface. The diameter of the resulting cone of powder was measured, and the angle of repose was calculated using the provided equation**.** [3]

$$\tan\theta = \frac{h}{r}$$

Bulk density and tapped density: Both the loose bulk density (LBD) and tapped bulk density (TBD) were determined. Each formula was subjected to a 2 g quantity of powder, which had been previously lightly shaken to disperse any clumps. The powder was placed into a 10 ml measuring cylinder, and the initial volume was recorded. The cylinder was then

dropped from a height of 2.5 cm onto a hard surface at 2 second intervals. Tapping continued until there was no further change in volume observed. The LBD and TBD were calculated using the following formula equations: [3]

$$\text{LBD} = \frac{\text{Weight of powder}}{\text{Volume of powder}}$$

$$\text{TBD} = \frac{\text{Weight of powder}}{\text{Tapped Volume of powder}}$$

Compressibility index: The compressibility index of the granules or powder was determined by Carr's compressibility index. [2]

$$\text{Carr's index (\%)} = \frac{\text{T. D.} - \text{B. D.}}{\text{T. D.}} \times 100$$

Hausner's ratio: The Hausner's ratio is a number that is associated with the ease of flow of a powder or granular material. [2]

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Post-compression parameter (Evaluation of tablets):

Thickness: Vernier calipers (Omega Instruments Ltd.) were used to measure the thickness of the prepared tablets. [4]

Hardness: The hardness of each formulation is measured by a Monsanto hardness tester (Dolphin). The hardness is measured in kg/cm^2. [5]

Friability: Friability of the tablets was measured by using Roche friabilator (Electrolab). Friabilator equipment was rotated at a 25 revolution per minute for 4 minutes. [2]

$$\text{\% Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight variation: The prepared tablets were tested for weight uniformity or weight variation. 20 tablets were weighed collectively and individually. The average weight was determined from the total weight. The weight of each tablet was then compared to the average weight to determine whether it was within the allowed range or not. [6]

$$\text{(\%) Weight Variation} = \frac{\text{A.W.} - \text{I. W.}}{\text{A. W.}} \times 100$$

Drug content: Take 20 tablets were weighed and powdered. An amount of powder equivalent to 50 mg of diclofenac sodium was dissolved in 100 ml of pH 6.8 phosphate buffer solution, filtered and diluted appropriately. The drug content was analyzed by spectroscopy at 276 nm. [7]

***In vitro* disintegration test:** In vitro disintegration time of the tablets was determined by using USP disintegration test apparatus with simulated Saliva (pH 6.8 Phosphate buffer, 900 ml at 37.0 ± 0.5°C) as the disintegration medium. To pass the test, all tablets must dissolve within 3 minutes as per official requirements. The test was carried out in triplicate. [8]

***In vitro* dissolution studies:** Dissolution rate or time were studied by using type II USP paddle dissolution apparatus, pH 6.8 Phosphate buffer, 900 ml at 37.0 ± 0.5°C at 50 - 75 rpm. At regular time intervals, aliquot of the dissolving medium were withdrawn and the same volume of freshly prepared, pre-warmed (37.0 ± 0.5°C) dissolution medium was replaced. After suitable dilution, the samples were filtered, and the drug content of diclofenac sodium was analyzed in each sample using a Shimadzu UV-spectrophotometer at 276 nm. [6,8]

Wetting time and water absorption ratio: In Petri dish a double folded tissue paper was placed. The Petri plate was filled with 6 ml of water containing the water-soluble dye (eosin). On the tissue paper, a pre-weighed tablet was carefully placed. The wetting time was calculated as the time required for water to reach the tablet's upper surface. After weighing the wet tablet, the water absorption ratio (R) was calculated using the following equation: [9]

$$R = \frac{(Wb - Wa)}{Wb} \times 100$$

Where,

W_a = Weight of tablet before (dry weight) and W_b = weight of tablet after water absorption (wet weight).

Drug and excipients compatibility studies:

Differential Scanning Calorimetry (DSC) Study: DSC study was used to find out the compatibility of ingredients. DSC of Diclofenac sodium was taken for identification. Finally physical mixture of all above ingredients was scanned for DSC.

Infrared spectroscopy: The infrared spectra of pure Diclofenac sodium were recorded by Shimadzu IR Affinity (class 1 lesser product) spectrometer. The directly place on the lesser point and examined in the transmission mode. Spectrum was measured over a frequency range of 4000-400 cm-1. The peaks obtained in the spectra were then compared with corresponding functional groups in the structures of Diclofenac sodium.

UV spectroscopy analysis: The absorbance maxima have been specified is determined by using UV. From the U.V analysis, it was concluded that the compound had shown λmax at 276 nm. Therefore, the observed λmax of Diclofenac sodium 276 nm has selected for further experimental work in pH 6.8 Phosphate buffer.

RESULT AND DISCUSSION:

Calibration curve of Diclofenac Sodium: The absorbance vs. concentration plot was shown in Fig. 1 and 2. The solution followed Beer-Lambert's law over the concentration range of 10 to 50 µg/ml. A minimum R^2 of 0.998 was achieved. The regression equation of diclofenac sodium was Y = 0.041x + 0.034. This was used to determine drug release of different Diclofenac sodium formulation was given in Table No. 2 and 3.

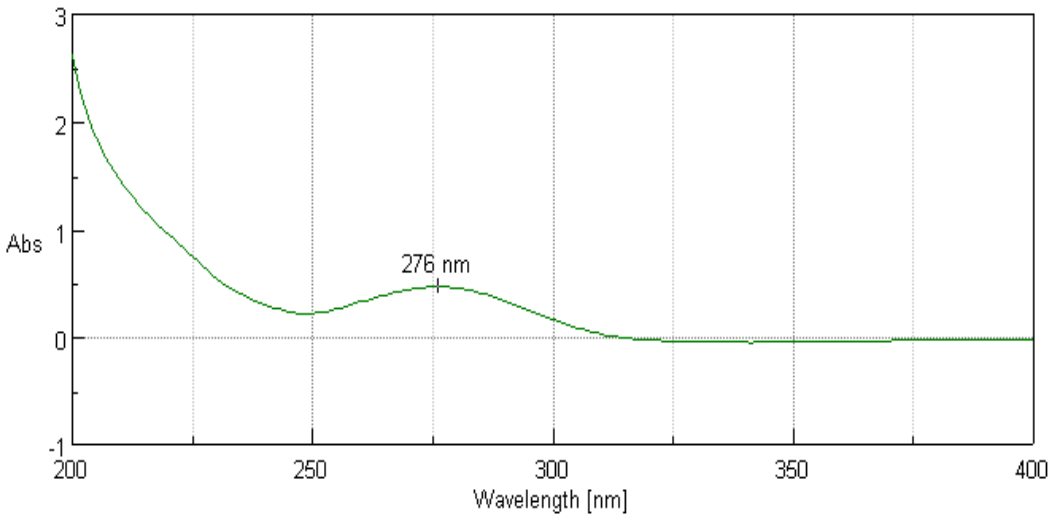

Fig. 1: UV Spectra of Diclofenac Sodium

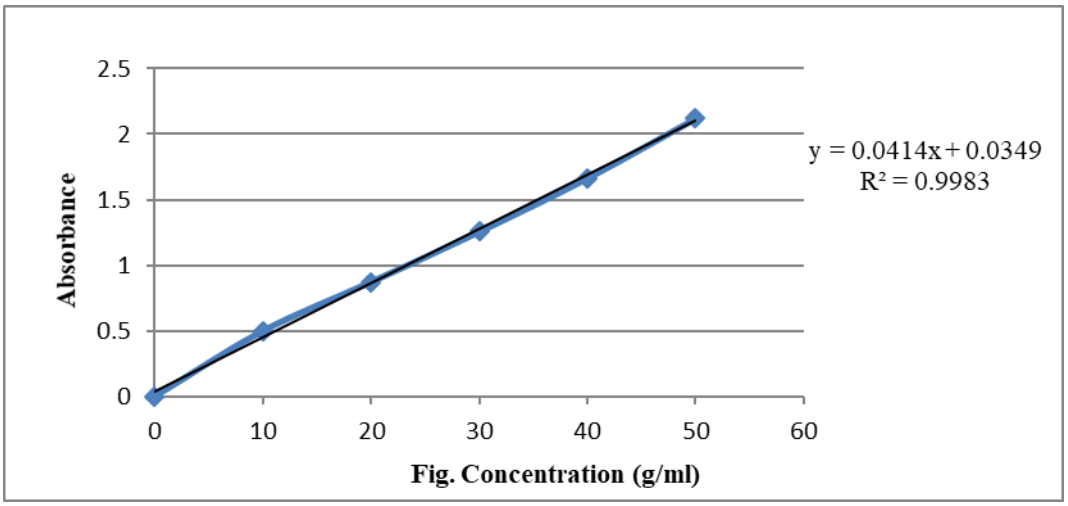

Fig. No. 2: Calibration Curve of Diclofenac sodium

Table No. 2: UV parameter for calibration curve in pH 6.8 buffer solution

Sr. No	Parameters	Value in pH 6.8 phosphate buffer solution
1	Absorbance maximum (λmax) in nm	276 nm
2	Slope	0.041
3	Intercept	0.034
4	Correlation Coefficient	0.998
5	Equation	Y= 0.041x+ 0.034

Table No.3: Absorbance of Diclofenac Sodium

Sr. No.	Conc. (µg/ml)	Absorbance (nm)
1	10	0.4997
2	20	0.8734
3	30	1.2568
4	40	1.6654
5	50	2.1201

Differential Scanning Calorimetry (DSC) Studies: The thermal behavior of the pure drug (Diclofenac sodium) and optimized formulation was characterized by using DSC and graph was shown in Fig. 3 and 4. The DSC thermogram of Diclofenac sodium showed an exothermic peak at 289.21ºC.

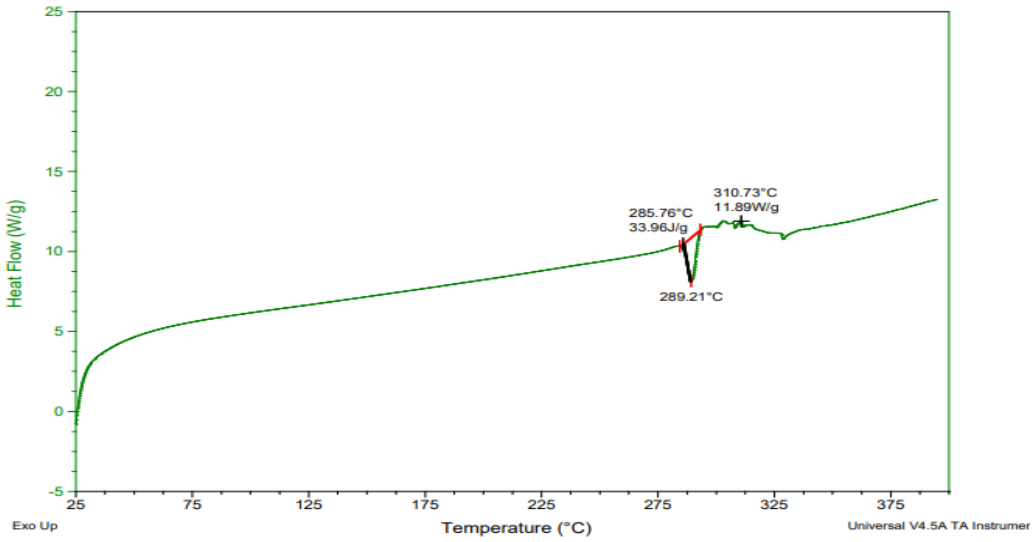

Fig. No. 3: DSC of Diclofenac Sodium

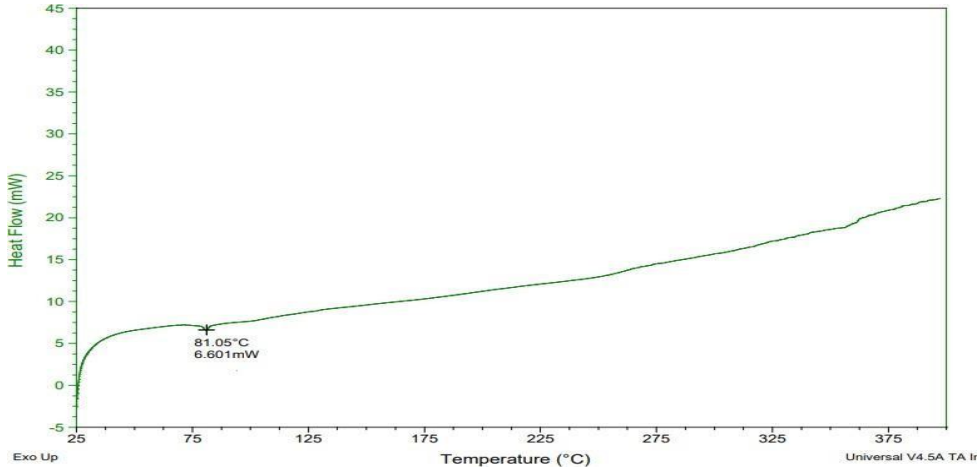

Fig. No. 4: DSC of Diclofenac Sodium and optimized formulation

Infrared spectroscopy study: The Infra-Red absorption spectrum of the finely ground sample in KBr dispersion compressed into a disc should exhibit maxima only at the same wavelengths as that of a similar preparation of working standard.

IR spectrum: The Infra-Red absorption spectrum was determined following procedure is described by (Prajapati *et al*, 2011). FTIR spectrum of Diclofenac sodium displays a characteristic C-N (amide) absorption peak at 1153 cm^{-1}, which is a normal range of absorption of primary amines. It exhibits a strong band for C=O stretching of carboxylic acid at 1305 cm^{-1}. The corresponding C-H stretching appears at 3080 cm^{-1}. And the graph of FTIR spectrum Diclofenac sodium and optimized formulation was shown in Fig. 5 and 6. The FTIR

spectrum of diclofenac sodium can be used to confirm the presence of various functional groups such as carboxylic acid, amide, and aromatic ring shown in Table No. 4.

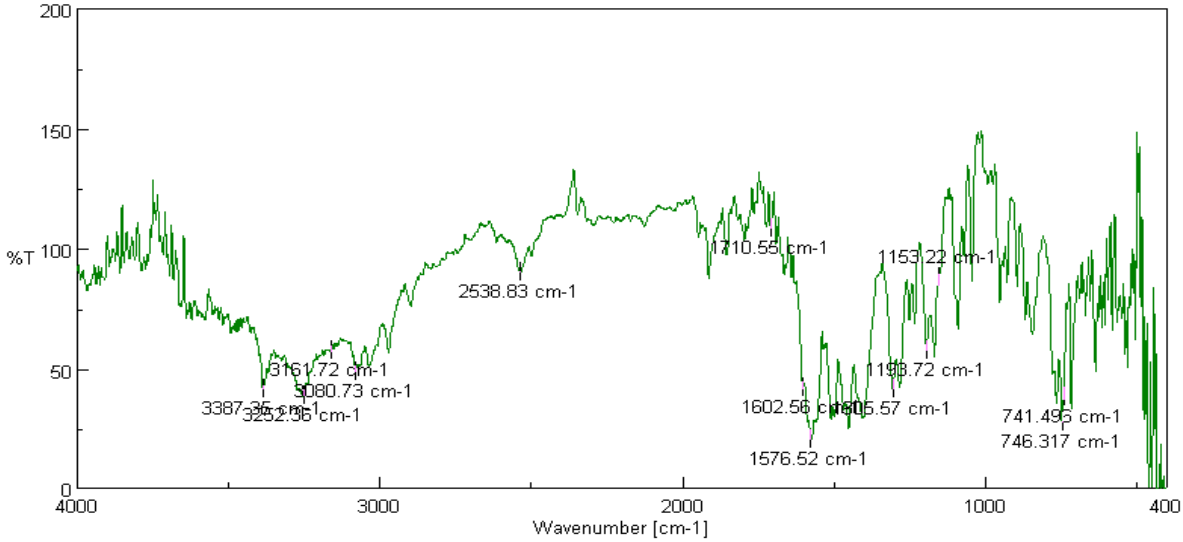

Fig. No. 5: IR Spectra of Diclofenac Sodium

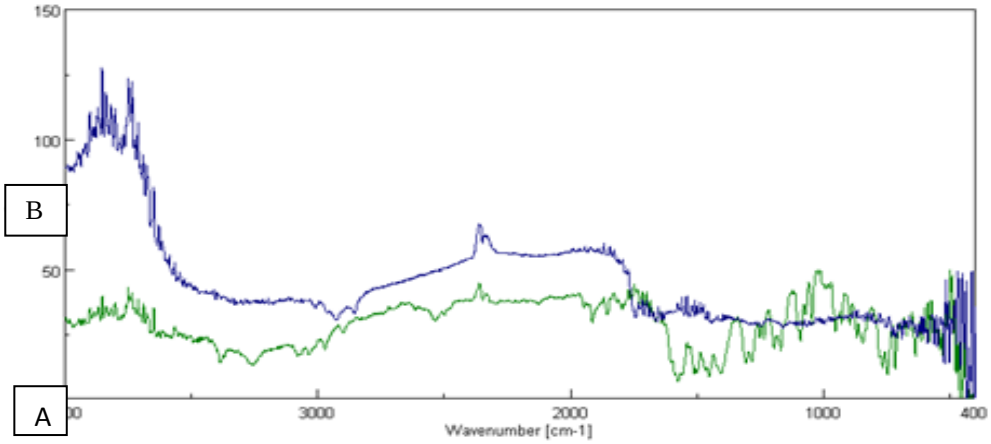

Fig. 6: IR spectrum overlay of drug and excipients
['A' represent IR spectra of diclofenac sodium and 'B' represent IR spectra of optimized formulation]

Table No. 4: IR Interpretation

IR Absorption band (cm^{-1})	Functional group	Standard Frequency (cm^{-1})
741.49	C-Cl stretching vibration	800-600
1153.22	C-N stretching vibration	1230-1020
1602.56	C=C bending vibration	1680-1600
3252.36	O-H stretching vibration	3300-2500
3387.35	N-H stretching vibration	3500-3300
1305.57	C=O stretching vibration	1350-1300

Evaluation parameters of powder: The prepared fast dissolving tablet by direct compression method are initially evaluated for pre-compression variables like tapped density, bulk density, % compressibility Hausner's ratio, the angle of repose and the values are shown in Tables No. 5.

Table No. 5: pre compression parameter

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	% Compressibility	Hausner's ratio	Angle of repose(Degree)
F1	0.487 ± 0.33	0.625 ± 0.40	22.08 ± 0.58	1.28 ± 0.84	27.02 ± 1.25
F2	0.465 ± 0.20	0.606 ± 0.25	23.26 ± 0.45	1.30 ± 0.71	25.17 ± 1.50
F3	0.476 ± 0.12	0.587 ± 0.26	18.90 ± 0.36	1.23 ± 0.96	25.64 ± 1.13
F4	0.454 ± 0.29	0.606 ± 0.41	25.08 ± 0.79	1.33 ± 0.56	26.56 ± 1.84
F5	0.444 ± 0.45	0.587 ± 0.35	24.36 ± 0.14	1.32 ± 0.48	27.47 ± 1.74
F6	0.475 ± 0.12	0.625 ± 0.24	24.00 ± 0.67	1.31 ± 0.35	27.02 ± 1.64
F7	0.454 ± 0.13	0.605 ± 0.41	24.95 ± 0.59	1.33 ± 0.43	27.47 ± 1.57
F8	0.487 ± 0.41	0.644 ± 0.47	24.37 ± 0.05	1.32 ± 0.63	25.64 ± 1.79
F9	0.464 ± 0.65	0.624 ± 0.24	25.64 ± 0.49	1.34 ± 0.91	28.36 ± 1.98

All value are expressed in mean ±SD, Where n=3

Evaluation parameter of tablet:

Organoleptic characteristics and evaluation of tablets are included in Table No. 6 and Table No. 7 respectively.

Table No. 6: Organoleptic property

Formulation	Color	Odour	Shape
F1	White	Sweet	Round
F2	White	Sweet	Round
F3	White	Sweet	Round
F4	White	Sweet	Round
F5	White	Sweet	Round
F6	White	Sweet	Round
F7	White	Sweet	Round

Table No. 7: Evaluation parameter

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration Time (sec.)	% drug content (%)
F1	341.5 ± 0.22	3.1 ± 0.69	3.60 ± 0.77	0.19	29	98.80 ± 1.98
F2	344.0 ± 0.78	3.2 ± 0.75	3.70 ± 0.85	0.13	36	93.41 ± 2.87
F3	338.0 ± 0.43	3.1 ± 0.45	3.50 ± 0.78	0.16	50	89.47 ± 2.17
F4	334.1 ± 0.87	3.1 ± 0.32	3.50 ± 0.28	0.17	47	86.02 ± 2.11
F5	336.0 ± 0.59	3.2 ± 0.17	3.60 ± 0.43	0.19	38	91.49 ± 3.32
F6	338.3 ± 0.43	3.1 ± 0.97	3.50 ± 0.92	0.19	42	91.74 ± 1.29
F7	327.0 ± 0.57	3.2 ± 0.36	3.80 ± 0.71	0.22	37	95.05 ± 2.57
F8	344.1 ± 0.36	3.2 ± 0.11	3.70 ± 0.29	0.14	58	88.51 ± 2.97
F9	342.4 ± 0.42	3.2 ± 0.58	3.40 ± 0.39	0.23	55	90.46 ± 1.45

All values are expressed in mean ±SD, Where n=3

Dissolution studies (% drug release)

Drug dissolution profile with release pattern: The drug release of formulations prepared with super disintegrants by the direct compression method was performed by dissolution apparatus, the results were shown in Table No. 8 and graph was shown in Fig. 7. From the results, it was found that as the 15 mg Ocimum sanctum seed powder formulation F1 showed maximum release. The formulation F1 shows 95.96 % drug release in 20 min. The F1 is the optimized formulation of all these series of formulations.

Table No. 8: Dissolution study (%)

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	14.17	10.86	15.55	11.16	12.48	11.16	9.69	13.60	10.09
4	28.58	21.65	25.21	23.98	24.45	23.75	23.28	26.16	25.56
6	43.74	33.76	37.85	31.81	34.57	35.00	31.19	31.50	36.54
8	52.98	40.71	49.40	44.65	48.75	41.47	39.78	44.73	40.02
10	61.97	50.21	53.30	49.18	59.28	48.52	46.16	57.29	48.36
12	72.03	57.84	58.74	59.09	65.41	64.79	55.82	68.86	59.35
14	81.95	65.38	64.65	65.36	70.90	68.18	64.91	75.05	65.41
16	88.89	70.54	67.61	71.63	79.89	72.26	70.32	83.90	70.10
18	92.89	79.62	73.02	76.24	85.92	75.51	72.21	88.18	72.05
20	95.96	80.22	84.83	78.65	90.21	78.53	77.63	91.93	76.66

Note: All values are taken in %

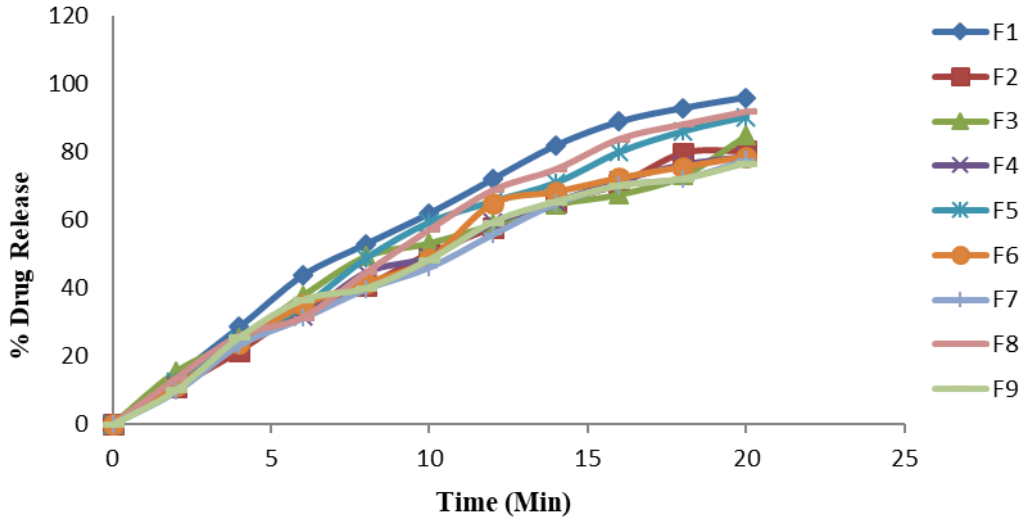

Fig. No. 7: Drug release profile of Diclofenac sodium FDT

Discussion:

Diclofenac sodium is poorly water soluble. The natural materials like Ocimum sanctum seed powder have been widely used in the field of drug delivery due to their easy accessibility, cost-effectiveness, environmentally friendly nature, soothing and non-irritating properties, non-toxicity, ability for various chemical modifications, potential for degradation, and compatibility due to natural origin. The evaluation studies showed that synthetic and natural super disintegrants differed in their ability to disintegrate the Diclofenac sodium. When oro-dispersible tablets used in different concentrations. Hence, such a difference can potentially impact the rate of drug dissolution, which is particularly beneficial for patients who have difficulty accessing water (such as travelers and mentally ill individuals) or experience swallowing problems. These tablets hold great potential for the treatment of acute pain conditions.

In summary, the study suggests that natural superdisintegrants, specifically Ocimum sanctum seed powder, can be used as pharmaceutical excipients for oral drug delivery of fast-dissolving tablets of Diclofenac sodium. The formulation F1, containing 15 mg of Ocimum sanctum seed powder, demonstrated the highest percentage of drug release at 95.96%. Therefore, it can be concluded that natural superdisintegrants like Ocimum sanctum exhibit superior or better disintegrating properties.

CONCLUSION:

Diclofenac sodium is poorly water soluble. The natural materials like Ocimum sanctum seed powder have been widely used in the field of drug delivery due to their easy accessibility, cost-effectiveness, environmentally friendly nature, soothing and non-irritating properties, non-toxicity, ability for various chemical modifications, potential for degradation, and compatibility due to natural origin. The evaluation studies showed that synthetic and natural super disintegrants differed in their ability to disintegrate the Diclofenac sodium. When oro-dispersible tablets used in different concentrations. Hence, such a difference can potentially impact the rate of drug dissolution, which is particularly beneficial for patients who have difficulty accessing water (such as travelers and mentally ill individuals) or experience swallowing problems. These tablets hold great potential for the treatment of acute pain conditions.

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REFERENCES:

1. Alanezi, A. A. (2014). *Development of an orally disintegrating mini-tablet (ODMTs) containing metoclopramide HCl to enhance patient compliance*. The University of Toledo.
2. Bi, Y., Sunada, H., Yonezawa, Y., Danjo, K., Otsuka, A., & Iida, K. (1996). Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. *Chemical and pharmaceutical bulletin*, *44*(11), 2121-2127.
3. Misal, N. V., & Satyam, Z. C. (2010). Formulation and evaluation of lornoxicam mouth dissolving tablets by using super disintegrants. *IJPSR*, *10*(4), 1848-1855.
4. Basu, B., Bagadiya, A., Makwana, S., Vipul, V., Batt, D., & Dharamsi, A. (2011). Formulation and evaluation of fast dissolving tablets of cinnarizine using superdisintegrant blends and subliming material. *Journal of advanced pharmaceutical technology & research*, *2*(4), 266.
5. Dixit, S., Kaur, R., Mishra, V., & Bhargava, S. (2012). Fast Dissolving Tablet-A Promising Approach For Drug Delivery: A Review. *Journal of Pharmacy Research*, *5*(3), 1508-1513.
6. Kumar, M. U., & Babu, M. K. (2014). Design and evaluation of fast dissolving tablets containing diclofenac sodium using fenugreek gum as a natural superdisintegrant. *Asian Pacific journal of tropical biomedicine*, *4*, S329-S334.
7. Lachman, L., Lieberman, H. A., & Kanig, J. L. (1976). *The theory and practice of industrial pharmacy* (pp. 412-428). Philadelphia: Lea & Febiger.

8. Malik, K., Arora, G., & Singh, I. (2012). Ocimum sanctum seeds, a natural superdisintegrant: Formulation and evaluation of fast melt tablets of nimesulide. *Polim Med*, *42*(1), 49-59.
9. Gohel, M., Patel, M., Amin, A., Agrawal, R., Dave, R., & Bariya, N. (2004). Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *AAPs PharmSciTech*, *5*, 10-15.
10. Mor, J., Chauhan, P., & Jalwal, P. (2016). Development and evaluation of oral fast dissolving tablets of Lornoxicam using superdisintegrants-A comparative study. *The Pharma Innovation*, *5*(7, Part A), 1.
11. Heer, D., Aggarwal, G., & Kumar, S. H. (2013). Recent trends of fast dissolving drug delivery system–an overview of formulation technology. *Pharmacophore*, *4*(1), 1-9.
12. Nareda, M., Sharma, A. K., Nareda, S., Ghadge, M., Garg, D. S., & Sharma, D. P. (2018). Design and Formulation of Fast Dissolving Tablet of Lornoxicam using Banana Powder as Natural superdisintegrant by direct compression method. *Wjpps*, *7*(2), 631-642.
13. Allen, L. V., Ansel, H. C., & Popovich, N. G. (2011). Pharmaceutical dosage forms and drug delivery systems. *Evaluation*, *56*, 44.
14. Aulton, M. E., & Summers, M. (2013). Tablets and compaction. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*, *5*, 520-530.
15. Chang, R. K., Guo, X., Burnside, B. A., & Couch, R. A. (2000). Fast-dissolving tablets. *Pharmaceutical technology*, *24*(6), 52-52.
16. Battu, S. K., Repka, M. A., Majumdar, S., & Rao Y, M. (2007). Formulation and evaluation of rapidly disintegrating fenoverine tablets: effect of superdisintegrants. *Drug development and industrial pharmacy*, *33*(11), 1225-1232.
17. Prajapati, B. G., Patel, R. P., & Patel, S. N. (2011). Formulation, evaluation & optimization of orally disintegrating tablet of cinnarizine using sublimation method. *Bio phys*, *38*, 4089-92.
18. Shukla, D., Chakraborty, S., Singh, S., & Mishra, B. (2009). Mouth dissolving tablets I: An overview of formulation technology. *Scientia Pharmaceutica*, *77*(2), 309-326.
19. Chakraborty, S., Khandai, M., Singh, S. P., & Patra, N. C. (2008). Comparative study on effect of natural and synthetic superdisintegrants in the formulation of fast dissolving tablets. *International Journal of Green Pharmacy (IJGP)*, *2*(1).
20. Varma, K. (2016). Excipients used in the formulation of tablets. *Research and Reviews: Journal of Chemistry*, *5*(2), 143-154.