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Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium by Using Two Different Superdisintegrating Agents

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ABSTRACT

The main objective of present investigation is to formulate fast dissolving tablets of Diclofenac sodium and to evaluate flow, mechanical and release properties of diclofenac sodium tablets formulated by using two different super disintegrating agents namely sodium starchglycolate and microcrystalline cellulose. Two batches of formulations were prepared. F_1 to F_4 are formulated by using SSG with varying concentrations of 10 mg, 20 mg, 30 mg & 40 mg. similarly next four formulations (F_5 to F_8) were formulated by taking MCC as superdisintegrant with varying concentrations of 10 mg, 20 mg, 30 mg & 40 mg. All the eight formulations are having good flow properties and are prepared by direct compression technique. Compatibility studies were conducted by using FTIR and all the excipients used in the formulation were compatible with the drug. All the eight formulations shows first order release. The dissolution kinetics was presented in Table 5. The dissolution rate followed first-order kinetics as the graphs drawn between log % drug unreleased vs time were found to be linear. The dissolution rate of diclofenac sodium was found to be effected by the concentration of the superdisintegrant (sodium starch glycolate) used in the preparation of tablets. Based on the dissolution rate, the order of drug release from the four formulations was F_4> F_3> F_2> F_1. The formulation prepared with 40 mg of sodium starch glycolate (F_4) was offered relatively rapid release of diclofenac sodium when compared with other concentrations employed in this investigation.

Keywords: Diclofenac sodium, SSG, MCC, Direct compression method.

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INTRODUCTION

Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID). It is used for relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and relief of mild to moderate pain and is used in chronic and acute conditions of pain and inflammation. As its serum concentrations and analgesic effect are correlated, rapid absorption of diclofenac sodium could be a prerequisite for the quick onset of its action. Rate of bioavailability of Diclofenac sodium is highly variable due to their low aqueous solubility. The major problems with drug are its very low solubility in biological fluids and its short biological half-life of 1.2- 2 h.[1]

The orally disintegrating property of tablet is attributed to a quick ingress of water into the tablet matrix, which creates porous structure and result in rapid disintegration. Some tablets are design to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate[2]. When put on tongue, these tablets disintegrates instantaneously, releasing the drug, this dissolves or disperses in saliva. Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach. [3, 4]

MATERIALS AND METHOD

Diclofenac sodium, Croscarmellose sodium, Aerosil is a gift sample from Sarvotham care Ltd, Hyderabad, Sodium starch glycolate, Microcrystalline Cellulose, Polyvinyl pyrolidone, Sodium Saccharin, Talc are procured from LOBA chem. pvt Ltd, Mumbai. Lactose, Magnesium stearate was procured from S.D. Fine chem. Ltd, Mumbai. Menthol was obtained from Moly. Chem. India pvt Ltd, Mumbai. Citric acid was procured from Thermofisher scientific India pvt. Ltd. A single punch tablet press (Cadmach machinery Co. Pvt. Ltd., Ahmedabad); disintegration test apparatus (2-USP-305), Camphbell electronics, Mumbai); dissolution test apparatus (DT 03071009, lab India- Mumbai, 2000); and UV-visible spectrophotometer (SL159, Elico Ltd., Hyderabad) were used in research work.

Preparation of Diclofenac sodium tablets:

Different batches of tablets were prepared by direct compression method. Four different batches of tablets are prepared by taking superdisintegrant Sodium starch glycolate of concentrations 10,20,30,40 mg, of each and compare with four different batches of tablets prepared by taking superdisintegrant Microcrystalline cellulose of concentrations 10,20,30,40 mg. Thus the total eight batches were prepared in different concentrations as shown in the table 1. All the ingredients were

co ground in a pestle motor. The resulting blend was lubricated with magnesium stearate and compressed into tablets using the Cadmach single punch (round shaped, 7mm thick) machine.

Table I Composition of ingredients for Diclofenac sodium fast dissolving tablets

S.No	Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Diclofenac Sodium	25	25	25	25	250	25	25	25
2	Sodium starchglycolate	10	20	30	40	-	-	-	-
3	Microcrystalline cellulose	-	-	-	-	10	20	30	40
4	Crospovidone	10	10	10	10	10	10	10	10
5	Mannitol	30	30	30	30	30	30	30	30
6	Croscarmellose sodium	-	9.5	5.72	7.0	-	9.5	5.72	7.0
7	Lactose	168	148.5	142.28	131.0	168	148.5	142.28	131.0
8	Citric acid	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
9	Aerosil	3.4	3.4	3.4	3.4	3.4	3.4	3.4	3.4
10	Menthol	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
11	Talc	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
12	Magnesium stearate	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4
13	Total weight	260	260	260	260	260	260	260	260

EVALUATION OF DICLOFENAC SODIUM TABLETS

a) Weight variation test [5]:

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight.

b) Drug content [6] :

Twenty tablets were powdered, and powder equivalent to 100 mg of diclofenac sodium was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 5 ml methanol was added and shaken for 10 min. Then, the volume was made up to 100 ml with 6.8 phosphate buffer. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 283 nm.

c) Disintegration Time[7]:

The disintegration time was determined in distilled water at 37 ± 0.5^0 C using disintegration test apparatus USP ED-2L (Electro lab, Mumbai).

d) Friability [8]:

Roche friabilator was used to determine the friability. Pre weighed tablets were placed in friabilator and rotated at a speed of 25 rpm for 4 minutes or up to 100 revolutions. The tablets are dropped from a distance of 6 inches in each revolution. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

$$\% \text{ friability} = \frac{\text{Weight before friabilation - Weight after friabilation}}{\text{Weight before friabilation}} \text{ X } 100$$

e) Hardness [9]:

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning threaded bolts until the tablet fractured. Then the final reading was recorded. The hardness was computed by deducting the initial pressure from the final pressure.

f) Wetting Time [10] :

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. 10 mL of water-containing amaranth a water soluble dye is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

g)Water Absorption Ratio [11]:

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.

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

Where, Wb and Wa were the weights of the tablet before and after water absorption.

j) Dissolution studies [12]:

Dissolution studies for Diclofenac sodium fast dissolving tablets were performed in pH 6.8 phosphate buffer using USP dissolution test apparatus (Electrolab, Mumbai, India) with a paddle stirrer. The paddles are allowed to rotate at speed of 100 rpm. The dissolution medium was maintained at a temperature of $37 \pm 0.5\ ^{O}C$ and samples are withdrawn at an interval of every 5 min the volume of the withdrawn samples are replaced by fresh dissolution medium in order to kept the volume of the dissolution medium as constant. The withdrawn samples are filtered and absorbance was measured at absorption maxima of 283 nm using UV-visible spectrophotometer.

k) In-vitro dissolution kinetic studies [13, 14]:

The drug release data were plotted and tested with zero order (cumulative % drug released Vs time), First order (Log % remained Vs time). The in vitro dissolution kinetic parameters, dissolution rate constants (K), correlation coefficient (r), the times (t_{50}) for 50 % drug released (half-life) and dissolution efficiency [D.E]. were calculated. From the slopes of linear plots, the dissolution rates were calculated.

RESULTS AND DISCUSSION

Micromeritic properties:

Micromeritic properties of the blends were studied and results were shown in Table 2.All the blends exhibited good flow properties and suited for direct compression.

The compatibility studies were conducted by FTIR and the results shows the compatible nature between the drug and excipients.

Table II: Micrometric properties for formulation blends:

Formulation code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (θ)
F_1	0.440	0.515	14.56	1.17	29.80
F_2	0.445	0.526	15.39	1.18	26.10
F_3	0.459	0.530	13.39	1.15	25.45
F_4	0.478	0.565	15.39	1.18	28.29
F_5	0.449	0.523	14.14	1.16	26.34
F_6	0.440	0.521	15.54	1.18	27.79
F_7	0.444	0.525	15.42	1.18	26.21
F_8	0.460	0.531	13.37	1.15	25.40

Influence of superdisintegrants on Diclofenac sodium fast dissolving tablets:

To study the influence of superdisintegrants on the performance of Diclofenac sodium, a set of eight formulations (F_1 to F_8) were prepared using three different superdisintegrants *viz*, sodium starchglycolate , microcrystalline cellulose respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table 3. All the tablets complied with the pharmacopoeial standards. The dissolution data was presented in Table 4. and Figure 1 & 3. The *In-vitro* dissolution kinetics was presented in Table 5. The dissolution rate followed first-order kinetics (Figure 2 & 4) as the graphs drawn between log % drug unreleased vs time were found to be linear. The dissolution rate of Diclofenac sodium was found to be effected by nature of the superdisintegrant used in the preparation of tablets. Based on the dissolution rate, superdisintegrants can be rated as SSG < MCC. The formulation prepared with **SSG** was offered relatively rapid release of Diclofenac sodium when compared with other superdisintegrant used in this investigation.

Table III: Physical parameters of Diclofenac sodium fast dissolving tablets

S.No	Parameters	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Average weight(mg)	258±0.2	258±0.1	258±0.2	260±0.2	259±0.1	260±0.1	259±0.2	257±0.3
2	Drug content (%)	98.5	99.1	97.9	99.64	99.31	99.98	98.45	98.55
3	Disintegration time(sec)	91	84	76	46	50	49	44	39
4	Friability (%)	0.82	0.87	0.73	0.86	0.6	0.78	0.72	0.73
5	Hardness(kg/sqcm)	3.5	3	4	4	3.5	4	4	4
6	Wetting time (sec)	46	45	47	40	38	33	35	31
7	Water absorption Ratio	53	68	70	89	95	103	98	96

Table IV: *In-vitro* dissolution data of Diclofenac sodium fast dissolving tablets

Sl.No.	Sampling time (min)	Percentage of drug released ($\overline{X}$ ± S.D.)							
		F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	2	63.01±0.08	65.73±0.07	70.62±0.05	75.52±0.07	60.29±0.04	65.18±0.06	66.81±0.04	71.17±0.02
3	4	65.36±0.06	72.08±0.09	77.80±0.02	86.46±0.05	64.28±0.06	69.69±0.03	75.10±0.05	78.34±0.05
4	6	69.30±0.04	74.11±0.02	84.90±0.04	99.96±0.06	66.07±0.04	70.38±0.08	80.60±0.07	85.98±0.07
5	8	72.65±0.05	76.69±0.04	87.63±0.03	-	69.44±0.07	73.19±0.07	83.35±0.07	91.38±0.05
6	10	77.03±0.07	83.64±0.07	97.77±0.05	-	73.31±0.03	77.56±0.05	95.65±0.06	96.71±0.06

Table V: *In-vitro* dissolution kinetics of Diclofenac sodium fast dissolving tablets

S.No.	Formulation	T_{50} (min)	T_{90} (min)	DE_{10} (%)	K (min^{-1})	Correlation coefficient values	
						Zero Order	First order
1	F_1	13.32	44.28	61.77	0.052	0.775	0.861
2	F_2	10.82	35.98	64.63	0.064	0.782	0.887
3	F_3	5.09	16.93	73.97	0.136	0.825	0.943
4	F_4	1.64	5.47	70.66 (DE 8%)	0.421	0.827	0.965
5	F_5	15.06	50.06	37.38	0.046	0.767	0.836
6	F_6	13.58	45.15	39.55	0.051	0.751	0.830
7	F_7	6.18	20.50	48.65	0.112	0.835	0.942
8	F_8	5.29	17.88	49.26	0.131	0.824	0.976

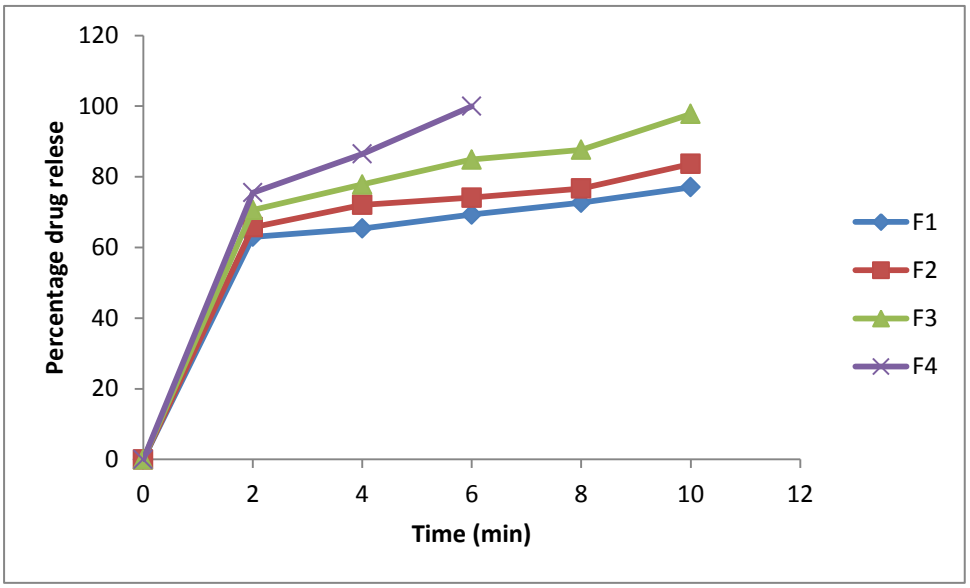

Figure I: *In-vitro* dissolution profile of Diclofenac Sodium fast dissolving tablets formulated with different concentrations of sodium starch glycolate

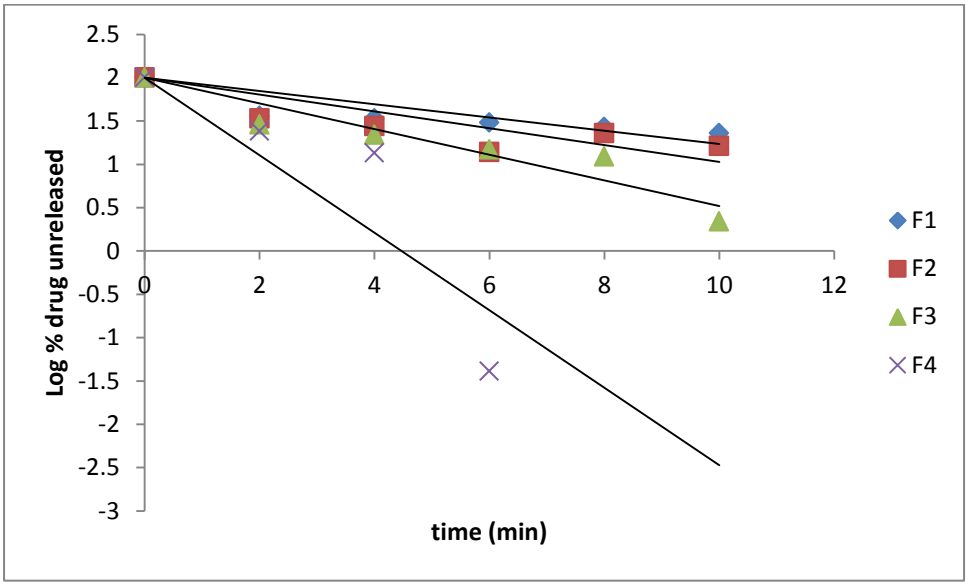

Figure II: First order plots of Diclofenac Sodium tablets formulated with different concentrations of sodium starch glycolate

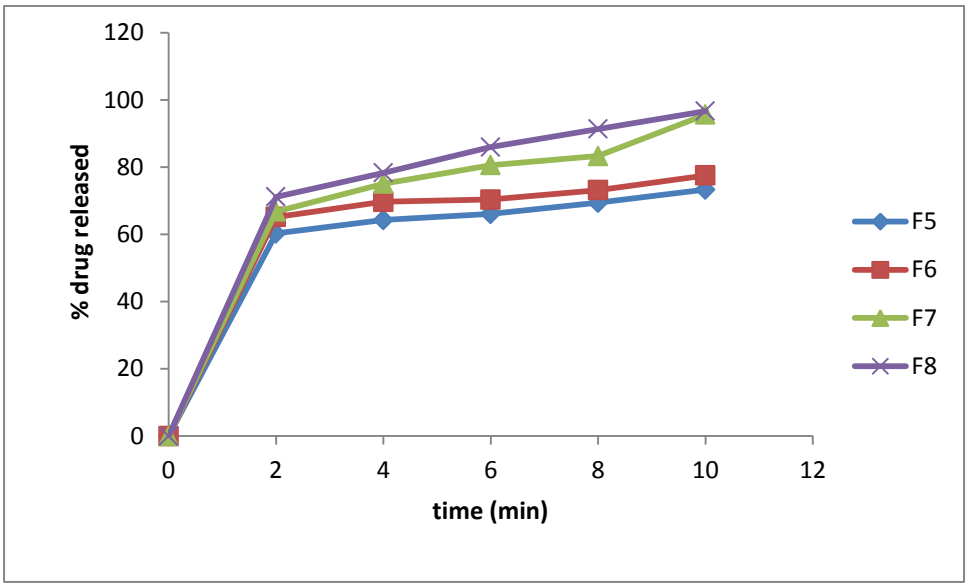

Figure III: *In-vitro* dissolution profile of Diclofenac sodium fast dissolving tablets formulated with MCC

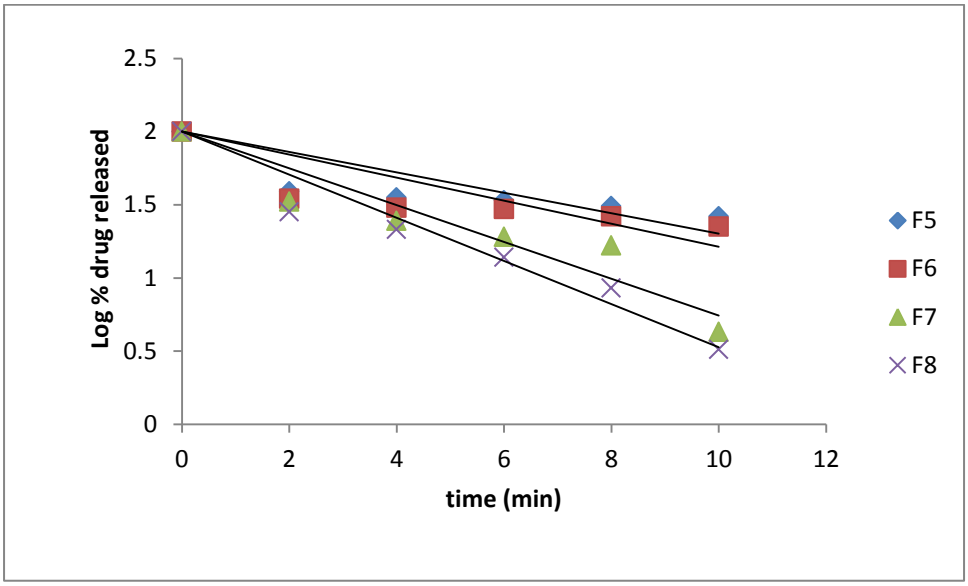

Figure IV: First order plots of Diclofenac sodium tablets formulated with MCC

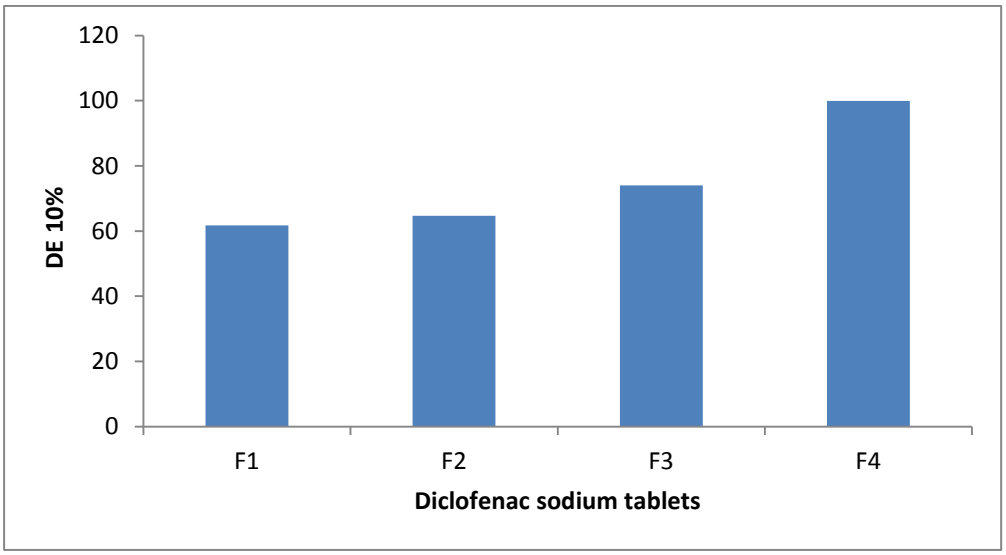

Figure V: Comparison of dissolution efficiency of Diclofenac sodium tablets formulated with different concentrations of sodium starch glycolate

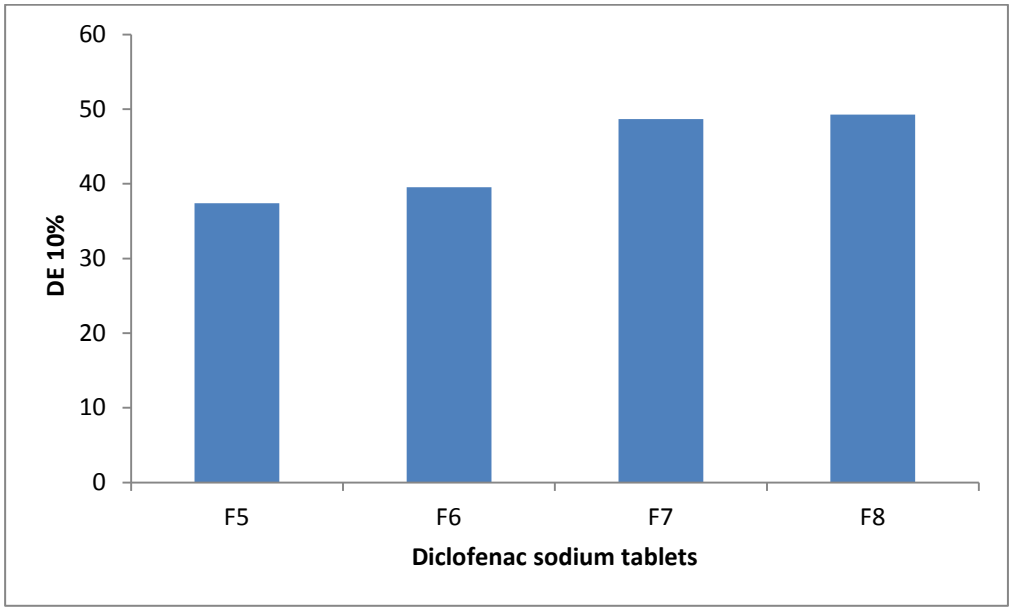

Figure VI: Comparison of dissolution efficiency of Diclofenac Sodium tablets formulated with different superdisintegrants

CONCLUSION

Nature and concentration of the superdisintegrant showed influence on the rate of dissolution. The rate of drug release was found to be increased by increasing the concentration of the superdisintegrant and found to be highest for tablets formulated with 40 mg of SSG.bAll the blends exhibited good flow properties and suited for direct compression. The compatibility studies were conducted by FTIR and the results. The results show the compatible nature between the drug and excipients. The formulation prepared with 40 mg of microcrystalline cellulose was offered

relatively rapid release of Diclofenac sodium when compared with other concentrations employed in this investigation. The formulation prepared with 40 mg of SSG was offered relatively rapid release of Diclofenac sodium when compared with other superdisintegrants used in this investigation. Based on the dissolution rate, superdisintegrants can be rated as SSG < MCC. The formulation prepared with SSG was offered relatively rapid release of Diclofenac sodium when compared with other superdisintegrant used in this investigation.

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