IPP

Innovations in Pharmaceuticals and Pharmacotherapy

www.innpharmacotherapy.com

eISSN: 2321–323X

Original Article

Formulation and evaluation of diclofenac sodium effervescent tablet

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Abstract

Ten different formulations were prepared (F1-F10) that contain citric acid, sodium bicarbonate and sodium carbonate, PVP K 30, PEG 6000, different flavors by wet granulation method with an objective to minimize the side effects of diclofenac sodium on gastric mucosa by preparing the diclofenac tablet using effervescent techniques. The prepared tablets were evaluated for various pre and post compression characteristics as per official and non- officials procedures. Among all the formulations, batch F10 showed that maximum drug release upto 94.86 % within 3 min. Selected as optimized batch kept for accelerated stability study for 90 days. The result of stability study indicates no significant difference between the parameters tested before and after stability studies. FTIR Spectroscopy of formulation F10 did not show any additional peaks for new functional groups indicating no chemical interaction between drug and excipient used in formulation.

Keywords: Effervescent tablet, diclofenac Sodium, FTIR, PVP-K 30, wet granulation.

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1.Introduction

The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolong. This can be overcome by administrating the drug in liquid from but many APIs have limited level of stability in the liquid form. For achieving a prolonged and predictable drug delivery profile in the gastrointestinal tract is to control the gastric residence time using a gastro retentive dosage forms that will provide as with new and important therapeutic options so effervescent tablets act as an alternative dosage form [1].

Effervescence is defined as the evolution of bubbles of gas from a liquid as the result of a chemical reaction. Effervescent mixture have been known and used medicinally for many years. Effervescent powder used as saline. Cathartics were available in the eighteenth century and were subsequently listed in the official compendia as compound effervescent powder [2] Effervescence is the evolution of gas bubbles from a liquid, as the result of a chemical

reaction. The most common reaction for pharmaceutical purpose is the acid base reaction between sodium bicarbonate and citric acid. Acid-base reactions between alkali metal bicarbonates and citric or tartaric acid have been used for many years to produce pharmaceutical preparations that effervesce as soon as water is added [3, 4] For example: the reaction of Citric acid and Sodium bicarbonate.

Diclofenac Sodium is NSAIDs that exhibits anti-inflammatory, analgesic, and antipyretic activities. It is used for treatment of primary dysmenorrheal, for relief of mild to moderate pain, for relief of the signs and symptoms of osteoarthritis and rheumatoid arthritis [5, 6, 7]

The main aim of the this study is to formulate and evaluate Diclofenac Sodium effervescent tablets by using different ratios of carbonates and acids by wet granulation and direct compression method that help in obviating the demerits of slow release and slow absorption and to reduce the gastrointestinal side effects and to increase the release and immediate effect.

2. Material and Method

Diclofenac Sodium was obtained as kind gift sample by Shree Krishna Chemical (Maharashtra) India. Sodium Bicarbonate & citric acid were obtained as gift sample by Sujata Chemical, Surat. All other materials and solvents used were of analytical grade.

Methods-

Characterization of Drug

The characterizations of drugs were carried out by conducting various physico-chemical tests including Physical Tests,IR Spectrometry.

Color and Appearance [8]

Determination of color of Diclofenac Sodium was made visually, against white background.

Melting point [8]

Melting point of Diclofenac Sodium was determined by Differential scanning calorimetry study.

Determination of pH of Diclofenac Sodium Solution [6]

pH of 1% w/v solution of Diclofenac Sodium was measured with the help of pH meter.

Infrared Spectroscopy [9, 10, 11]

The infrared spectrum of Diclofenac Sodium was recorded by Potassium bromide dispersion technique using FT-IR with diffuse reflectance attachment on IR Affinity-1. Drug sample was mixed along with IR grade KBr in equal proportion and IR spectrum was recorded.

Drug Excipient Compatibility Study [12, 13]

Drug excipient compatibility testing was performed by mixing drug with polymer in equal proportion then, mixture was kept under accelerated stability condition (i.e. 40ºC and 75±5% RH) for a period of 15,30 and 45 days in a glass vial. It was hermetically sealed with rubber stopper using molten carnauba wax. IR spectrum was noted for mixture after 15, 30 and 45 days.

The IR spectra of samples were recorded by potassium bromide dispersion technique 2-3 mg of sample was mixed with previously dried IR grade potassium bromide and kept in sample cell, the cell was then fitted on sample holder, spectra were recorded with FT-IR instrument and the spectral analysis was done.

Formulation Studies

From the preliminary study, on the trial basis, the following batches were prepared.Effervescent tablet of diclofenac sodium was prepared by wet granulation technique using varying concentrations of polymers as shown in Table No.1. All the ingredients were accurately weighed. Different formulations were made in order to achieve desired friability, thickness, hardness and drug release. The tablets were formulated using drug, diluent, and release rate retarding polymer, binder, and lubricant.

The wet granulation method involves

Part I, Part II Process [14, 15]

First Part I- Process involves sifting of the Diclofenac sodium, citric acid, PVPK 90 through sieve #60 and transfer the sifted material in RMG & mix for 5 min at slow speed then add binder solution (sodium saccharin +water) and mix for 2 min at slow speed then do racking and again mix for 3 min at slow speed and followed by 2 min at

high speed. Dry the material up to 70°C by using tray dryer till LOD NMT 0.2% at 75°C. then sift the dried granule of Part I through 24#.

Second Part II-Involve mix Glycine with IPA and add this mixed solution with sodium bicarbonate and dry material in tray dryer for 60°C to 70°C till LOD NMT 0.2% at 75°C then sift the dried granule of Part II through 24# Transfer the sifted lubricant Materials such as sodium carbonate, aspartame, PEG6000 pineapple flavor & part I, part II dried granule in poly bag and mix manually for 10 min and then load for compression. The weights of the tablets were kept constant for all formulation.

Table No. 1: Formulation of Diclofenac Sodium Effervescent tablet

Ingredients (gms)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Diclofenac sodium	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Citric acid (Anhydrous)	0.215	0.233	0.228	0.23	0.231	0.231	0.231	0.226	0.202	0.178
Sod.bicarbonate	0.244	0.244	0.244	0.244	0.244	0.245	0.246	0.248	0.270	0.295
Sod saccharin	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
PVP-K 30	0.008	0.008	0.012	0.011	0.01	0.009	0.008	0.008	0.008	0.008
water	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
Sodium Bicarbonate	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Glycine	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
IPA	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
Sodium Carbonate	0.022	0.022	0.022	0.022	0.022	0.022	0.022	0.022	0.022	0.022
Aspartame	0.006	0.006	0.006	0.006	0.006	0.006	0.006	0.008	0.008	0.008
PEG 6000	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002
Trusil Orange Flavour	0.004	0.004	0.004	-	-	-	-	-	-	-
Lemeon Flavour	-	-	-	0.004	0.004	0.004	-	-	-	-
Strawberry Flavour	-	-	-	-	-	-	0.004	0.004	-	-
Pineapple Flavour	-	-	-	-	-	-	-	-	0.006	0.006
Total Wt.	0.554	0.573	0.573	0.573	0.573	0.573	0.573	0.573	0.573	0.573

All ingridients are taken in Gms. Q.S. Stand for Quantity sufficient.

Evaluation of precompression parameter of powder blend:

The flow properties of granules were characterized in terms of angle of repose, Carr index and Hausner's ratio. The bulk density and tapped density were determined and from this data Carr's index and Hausner's ratio were calculated [16, 17].

Evaluation of Diclofenac Sodium Effervescent tablet:

Tablets from all the formulations were evaluated for various properties like hardness, Friability and weight variation [18]

Disintegration Test

It was performed in disintegration apparatus at 37 C temperatures and time was noted. Place

one tablet into each tube and suspend the assembly in to the 1000 ml beaker containing water maintained at 37±2°C and operate the apparatus. Remove the assembly form the liquid. Observe the tablets, if one or two tablets fail to disintegrate completely; repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated.

Uniformity of Content

Twenty tablets were accurately weighed and finely powdered. A quantity equivalent to 10 mg of Diclofenac sodium was transferred to a 200 ml volumetric flask. To it, 50 ml of methanol was added and shaken to dissolve drug. Resulting solution is diluted to volume with methanol and filtered. 20 ml of filtrate diluted to 100ml with methanol and mixed. Absorbance of the resulting solution at maximum at about 273 nm was measured uv spectroscopically.

***In-vitro* Dissolution Studies** [19]

In-vitro release study was carried out (USP dissolution test apparatus Type I Basket type) using 900 mL 0.1N Hydrochloride acid buffer pH 1.2 solution, for 30 min.. The Basket are rotated at 100 rpm. The medium was set at 37 ± 0.5^0 C. Aliquot (10 mL) of the solution was collected from the dissolution apparatus after 1 min and was replaced with fresh dissolution medium. The withdrawn samples were analyzed by an UV spectrophotometer (Lab India) at 273 nm using hydrochloride acid buffer pH 1.2 as a blank. Aliquots were withdrawn at one min interval from a zone midway between the surface of dissolution medium and the top of rotating basket not less than 1 cm apart from the vessel wall. Drug content in dissolution sample was determined by software (PCP disso v2.08) version.

Accelerated Stability Study [20-23]

Since the period of stability testing can be as long as two years, it is time consuming and expensive. Therefore it is essential to devise a method that will help rapid prediction of long-term stability of dosage form. The accelerated stability testing is defined as the validated method by which the product stability may be predicted by storage of the product under conditions that accelerate the change in defined and predictable manner. Stability testing of formulations was carried out to determine the stability of drug and carrier and also to determine the physical stability of formulation under accelerated storage condition at various temperatures. The prepared tablets were placed in borosilicate screw capped glass containers. The samples were kept at condition of 45°C$\pm$ 2 ^oC and 70% RH and were analyzed at 15, 30 and 45 days for their physical changes and in drug content.

3. Result and discussion

Characterization of Drug

Physical Tests:

Organoleptic Evaluation of Diclofenac Sodium

Organoleptic characters of drug was observed and recorded by using descriptive terminology. Following physical properties of API were studied.

Table No. 2: Organoleptic Evaluation of Diclofenac Sodium

Test	Observation
Color	White
Taste	Bitter
Odor	Odorless

Diclofenac Sodium was found to be white, crystalline powder.

Melting point

Melting point was noted in triplicate and was found to be 283-285°C. It was similar to the pharmacopoeial standards.

PH of Diclofenac Sodium solution (1%w/v)

PH of 1%w/v solution of Diclofenac Sodium was found to be 6.8, which complies with standard pH value mentioned in pharmacopoeia.

Infrared Spectroscopy

The IR spectrum did not show presence of any additional peaks for new functional groups indicating no chemical interaction between Diclofenac Sodium & citric acid, sodium bicarbonate, Sodium Carbonate, PVPK 30 used in

formulations. IR spectrum of, Citric acid, Sodium bicarbonate ,Sodium carbonate IR spectrum of physical mixtures of Diclofenac Sodium along with Citric acid, Sodium bicarbonate ,Sodium carbonate, PVP K30. From the IR spectrum data it showed that there was no interaction in between the drug and excipients

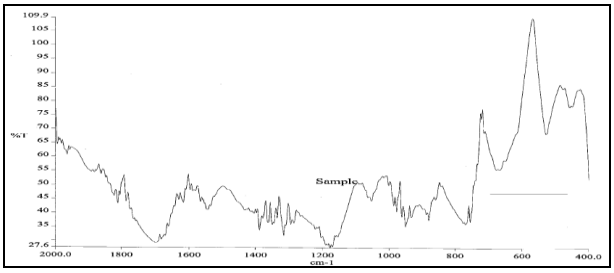

Fig No 1: FT- IR spectrum of citric acid

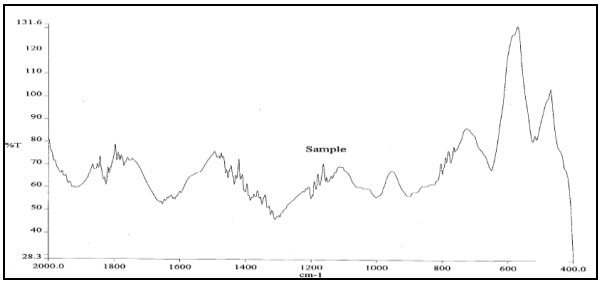

Fig No 2: FT- IR spectrum of sodium bicarbonate

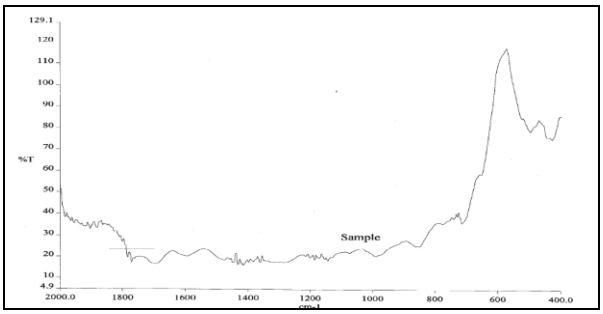

Fig No 3: FT- IR spectrum of Sodium Carbonate

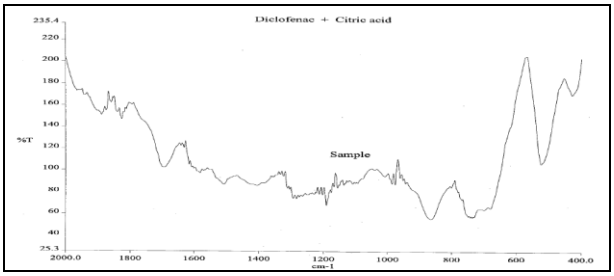

Fig No 4: FT- IR spectrum of Diclofenac Sodium + citric acid

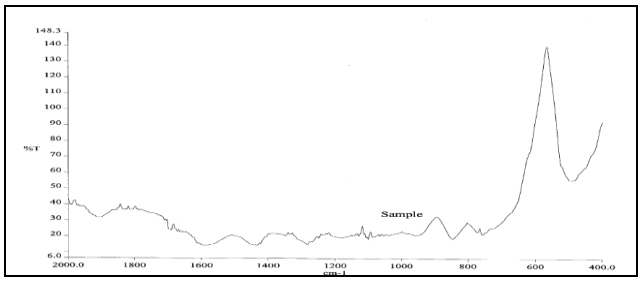

Fig No 5: FT- IR spectrum of Diclofenac Sodium + Sodium Bicarbonate

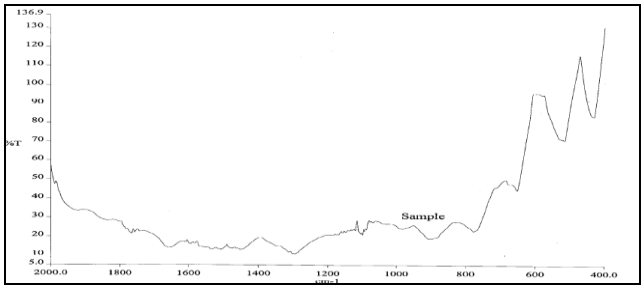

Fig No 6: FT- IR spectrum of Diclofenac Sodium + Sodium Carbonate

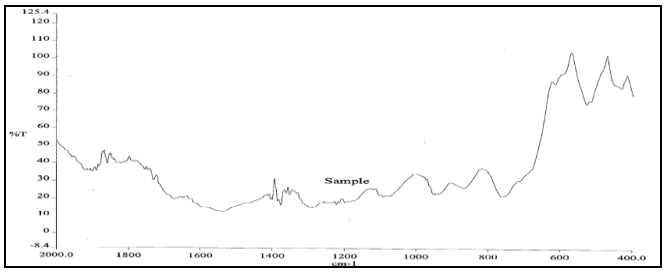

Fig No 7: FT- IR spectrum of Diclofenac Sodium + PVP K30.

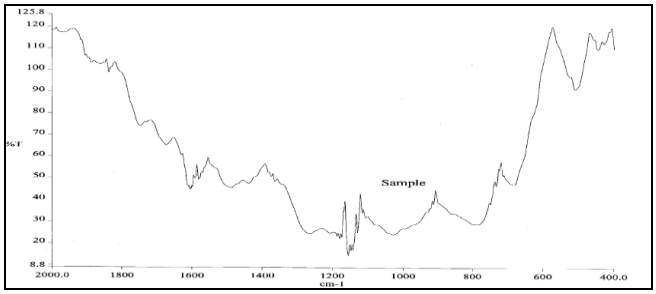

Fig No 8: FT- IR spectrum of Optimized Formulation (F10)

Evaluation of pre-compression parameters of drug and excipients.

The prepared powder mixtures were evaluated for the blend property like Bulk density, Tapped density, Carr's index, Angle of repose, Hausner ratio and LOD results obtained are as shown in Table 3.

Table No 3: Blend Properties of Formulation of Diclofenac Sodium Effervescent Tablets

Batches	Angle of Repose (± SD)*	Bulk density (g/ml) (± SD)*	Tapped density (g/ml) (± SD)*	Compressibility(%) (± SD)*	Hausner Ratio (± SD)*	LOD of Blend (%) (± SD)*
F1	31°40'±0.67	0.751±0.52	0.864±.62	13.07±0.78	1.15±0.01	0.15±0.74
F2	30°41'±0.48	0.739±0.43	0.862±0.78	14.26±0.33	1.16±0.01	0.17±0.75
F3	31°60'±0.50	0.740±0.91	0.858±0.24	13.75±0.64	1.15±0.02	0.19±0.65
F4	26°52'±0.45	0.758±0.35	0.853±0.62	11.13±0.80	1.12±0.03	0.14±0.48
F5	32°52'±0.57	0.760±0.71	0.862±0.34	11.83±0.77	1.13±0.01	0.15±0.56
F6	31°64'±0.90	0.750±0.12	0.859±0.93	12.68±0.42	1.14±0.03	0.16±0.50
F7	29°50'±0.66	0.744±0.20	0.850±0.32	12.47±0.71	1.14±0.02	0.18±0.65
F8	31°49'±0.32	0.749±0.43	0.861±0.74	13.00±0.49	1.14±0.02	0.19±0.64
F9	29°27'±0.66	0.750±o.20	0.863±0.19	13.09±0.50	1.15±0.01	0.15±0.47
F10	27°67'±0.32	0.753±0.18	0.865±0.32	12.94±0.71	1.14±0.03	0.16±0.85

* (n=3)

Powder blend was evaluated for values of angle of repose which were found to be in the range of 26°52'±0.45 – 32°52'±0.57 indicating powder flow for all the 10 formulations were good as shown in table No. 13.Bulk density for all 10 formulations was found to be in the range of 0.739±0.43 – 0.760±0.71 g/ml while tapped density was in the range of 0.850±0.32 – 0.865±0.32 g/ml .The percent compressibility index of all batches was found to be 11.13±0.80 - 14.26±0.33% The Hausner ratio of all batches was found to be in the range of 1.12±0.03 - 1.16±0.01 .The LOD of all batches was found to be 0.15±0.47 - 0.19±0.64 These results indicated that the powder had good flow property as shown in table No. 3.

Evaluation of post-compression parameters of Diclofenac Sodium effervescent tablets.

The prepared formulations were evaluated for the physical characteristics like thickness, hardness, friability, weight uniformity and uniformity of content; the results obtained are shown in following Table. All the physical parameters of the Effervescent tablet were within pharmacopoeial limits. Compressed tablet was evaluated for values of Average Weight which were found to be in the range of 2460 mg±0.29 – 2690mg ±0.29.Thickness for all 10 formulations was found to be in the range of 4.1 mm ±0.14 – 4.5 mm ±0.67 while Hardness was in

the range of 60N ±0.28 – 130N±0.40 The friability of all batches was found to be 0.10%±0.43 - 0.19%±0.19 Disintegration time of all batches was found to be in the range of 3 min.- 8 min 30sec.The drug content of all batches tablet was found to be 97.08%±0.03 – 98.57%±0.024 which is in limits of pharmacopeial specifications as shown in table No. 4.

Table No 4: Physical Evaluation of Diclofenac Sodium Effervescent tablet

* (n=3)

Batches	Average Weight (mg)±SD*	Thickness (mm) SD*	Hardness (N) ±SD*	Friability (%)±SD*	Disintegration time	Uniformity of content ± SD*
F1	2460±0.29	**4.1±0.14**	**60±0.28**	0.19±0.29	03 min 10 sec	97.23±0.024
F2	2670±0.30	4.2±0.83	80±0.62	0.13±0.12	03 min 30 sec	97.54±0,038
F3	2690±0.25	4.5±0.67	130±0.40	0.14±0.10	08 min 30 sec	97.32±0.03
F4	2675±0.28	4.4±0.38	120±0.97	0.18±0.87	07 min 20sec	98.14±0.027
F5	2690±0.29	4.4±0.14	105±0.14	0.14±0.19	06 min 40 sec	97.54±0.035
F6	2675±0.30	4.4±0.14	100±0.95	0.12±0.26	05 min 30 sec	97.14±0.024
F7	2680±0.42	4.3±0.21	90±0.14	0.11±0.66	04 min 20 sec	98.02±0.027
F8	2670±0.54	4.2±0.23	92±0.95	0.10±0.43	04 min 20 sec	97.08±0.024
F9	2666±0.64	4.3±0.20	90±0.36	0.19±0.19	03 min 40 sec	98.00 ±0.03
F10	2665±0.38	4.2±0.22	85±0.32	0.11±0.66	03 min	98.57±0.024

The results of the dissolution studies for formulations F1 to F10 are shown in the Figure 9. The cumulative percentage drug release for F1-F9 (73.53, 80.27, 73.35, 76.75, 79.87, 89.83, 77.01, 80.41, 77.01) at the end of 5Min. respectively. Among all the Formulation batch F10 showed that maximum drug release upto 94.86 % within 3 min.

Stability Study-

Accelerated stability studies (AST) was carried for optimized batch F10 by exposing it to 40°C/75%RH for 15, 30 and 45 days. The sample was analyzed for physical parameters color, hardness, uniformity of content, and percentage drug release. The sample was analyzed for physical parameters color, hardness, drug content, and percentage drug release and no any changes occurs in a physical parameter as shown in table No.5. Thus, formulation batch F10 was found to be stable.

Fig No 9: % Drug Release of Formulation F1 to F10.

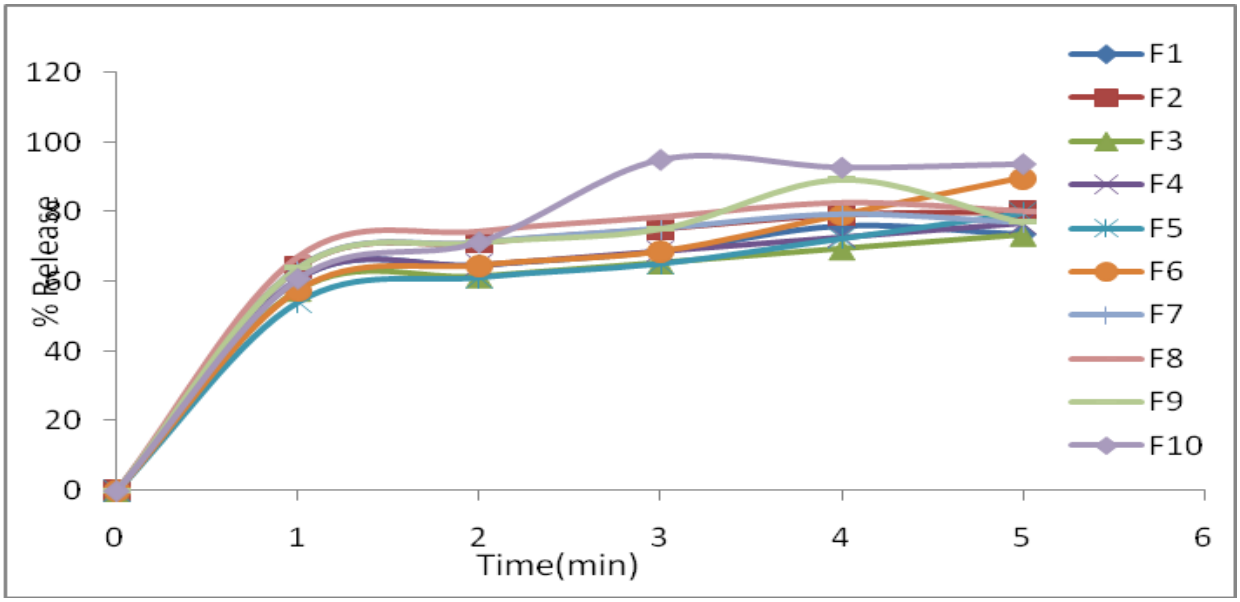

Table No. 5: Accelerated stability studies Optimized of F10

Parameters	Days			
	Initial	15	30	45
Color	No change	No change	No change	No change
Hardness ±SD	85±0.85	85±0.45	84±0.29	82±0.70
Drug Content (%) ±SD	98.57±0.54	97.52±0.31	97.07±0.46	96.12±0.95
% Release (in 3 Min)±SD	94.86±0.34	93.80±0.46	93.01±0.67	92.40±0.83

Conclusion

From the above summary it was concluded that, the effervescent tablets of Diclofenac can be formulated for quick analgesic and anti-inflammatory action by effervescence reaction using citric acid (30.57%), Sodium Bicarbonate (57.78 %) and Sodium carbonate (4.1%) gives better effervescence. The PVPK 30(1.5%) used as the binding agent.PEG 6000 (0.38%) as lubricating agent.

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