FORMULATION AND *IN VITRO* EVALUATION OF FAST DISSOLVING TABLETS CONTAINING ACECLOFENAC

Bimanjyoti Baisahya*[1], V. Rajashekhar[1], R. Manasa Deepa[1], C. Dabbara[1], K. Sridhar[2]

[1]*Department of Pharmaceutics, East West College of Pharmacy, Bangalore, Karnataka, India.
[2]Department of Pharmacology, East West College of Pharmacy, Bangalore, Karnataka, India.

ABSTRACT

Oral disintegrating tablets have proved to be an alternative to conventional dosage forms, as it has better patient compliance. The FDT's are solid dosage forms that dissolve or disintegrate rapidly in the oral cavity. This results in solution or suspension without the need of water. The main motive of our work was to formulate and evaluate fast dissolving tablets of aceclofenac coming under the category of NSAIDS. With the help of FTIR studies it was found that aceclofenac was compatible with a wide range of excipients. FDT's were prepared using different concentration of super disintegrating agent like kollidon CL, kyron T-314, doshion P544-DS by direct compression method and evaluated for hardness, thickness, friability, disintegration time, and percentage of drug release. The results were found satisfactory. Formulation KC_2 made of 4% kollidon CL showed highest release rate of 99.31% at the end of 15 min.

KEYWORDS

Aceclofenac, Oral disintegrating tablets, Superdisintegrants, Kollidon CL, Kyron T-314 and Doshion p544-DS.

Author for Correspondence:

Bimanjyoti Baisahya,

Department of Pharmaceutics,

East West College of Pharmacy, Bangalore, Karnataka, India.

Email: bimanjb7@gmail.com

INTRODUCTON

Oral route is one of the most preferred route for drug administration. But in case of oral conventional drug delivery swallowing difficulties are seen in various age group of patients (elders and children) as well as mentally retarded, un cooperative, nauseating patients. But formulation of fast dissolving tablets have helped to overcome the above mentioned difficulties[1,2].

FDTs are also known as Orodispersible tablets. Moreover this delivery system also has many other advantages like faster absorption which results in rapid onset of action, greater bioavailability.

Drawback of this system is bitter drug can be able to formulate in the form of ODT's only with the aid of taste masking agents such as sodium saccharin, aspartame and sucralose etc[3].

Many formulation techniques has been applied for the preparation of fast dissolving tablets which includes, freeze drying, molding, cotton candy process, mass extrusion, spray drying, phase transition, melt granulation, sublimation and direct compression. Here the drug aceclofenac is formulated in the form of fast dissolving tablet by direct compression technique using super disintegrants (Kollidon CL, Kyron T-314, Doshion P544-DS)[4,5]. Aceclofenac is chemically 2-[2-[-2[(2, 6-dichlorophenyl) amino] phenyl]acetyl] oxyacetic acid with a biological half-life of 4-5hrs, which is indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis[6].

MATERIAL AND METHODS
Materials
Kollidon CL (BASF Germany), Kyron T-314 (CORELPHARMA-CHEM, Ahmedabad) Aceclofenac, Doshion-P-544DS, Mannitol, Avicel R 102, Lactose, Microcrystalline cellulose, Saccharin sodium, Talc, Magnesium stearate (KAPL, Bangalore) and all other chemicals are analytical grade.

Preparation of tablets
Tablets containing Aceclofenac were prepared by direct compression technique. The drug and all other excipients, except magnesium stearate were previously sieved through a sieve#60 mesh, and are mixed for 30 mins. The resulting mixture was mixed with magnesium stearate for 15 min. Powder blend were then directly compressed using 8 mm, round shaped tooling in an 8 station tablet compression machine (Riddhi pharma instrument Ltd., Ahmedabad, India)[7]. The formulations of prepared batches were shown in Table No.1.

FTIR Study
FTIR analysis is the most important analytical tool for checking drug excipient interaction of the formulation. The samples of KC, KY, DO and physical mixtures were prepared in the form of KBR pellets and were subjected for scanning from 4000-400 cm^{-1} using FTIR spectrophotometer. The results obtained were recorded and shown in the Figure No.1[8,9].

Pre-compression parameters
Angle of Repose
The angle between the surface of the pile of the powder mixture and the horizontal surface is coined as the term angle of repose. A funnel was fixed to a burette stand at a particular height. A graph paper was placed below the funnel on the table. Then the powder mixture was passed through the funnel, the height and radius of the pile was measured[10-11]. Angle of repose of the blend was calculated by using the formula given below:

Angle of repose $(\Theta) = \tan^{-1}(h/r)$

Where h = height of the pile

r = radius of pile

Bulk Density
To determine bulk density a weighed amount of powder blend was placed in a graduated cylinder and its initial volume was noted. Then the mass of the sample to the volume it occupied was calculated[10-13].

Bulk density (g/cc) = Mass of the blend/Bulk volume

Tapped Density
A weighed amount of powder blend was placed in a measuring cylinder and its initial volume was noted. Then the measuring cylinder was fitted into a tapped density apparatus and was tapped. Final volume was noted and then tapped density was calculated by the formula[10-13].

Tapped density (g/cc) = Mass of the blend / Tapped Volume

Carr's Index
It is used to determine the flow property of the powder blend. Carr's index can be measured by tapped density apparatus. It can be calculated by using the following formula[10-13].

%Carr's index = (Bulk density - tapped density/Bulk density) $\times$ 100

Hausner's Ratio
It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powder is called Hausner's ratio[13].

Hausner's ratio = Tapped density / Bulk density

Post-compression parameter

Weight Variation Test

20 tablets were taken from each batch and their individual weight and average weight of the 20 tablets were calculated. The batch of the tablet are said to pass the test if the individual weight were in the monograph limits as mentioned below[14-17].

Percentage deviation allowed for tablets

Hardness test

This test is generally carried out to check the breaking point of a tablet. 10 tablets each from the respective samples were used for checking the hardness. It was checked by using Pfizer hardness tester. Where by the tablet is placed between anvil and piston, then pressure is applied by the handle which is identical to a plier. The pressure applied is measured by a force reading gauge[14,15].

Thickness

Thickness of the tablets was determined using Vernier calipers. Six tablets from each batch were used, their average value was taken[14,15].

Friability test

20 tablets were randomly selected and weighed. The weight of each individual tablet was noted and was dropped into the friability tester and test was continued as per USP. And finally the friability of the tablets was noted[14,15].

Formula for friability:

% Friability = $(W_1-W_2)/W_1 \times 100$

Where, W_1 = Initial weight of 20 tablets

W_2 = weight of 20 tablets after testing

Disintegration test

Tablets from each formulation were placed in the tubes of the basket. Purified water was used as immersion liquid. The temperature of the liquid was maintained at $37^0C \pm 2^0C$, if 1 or 2 tablets fail to disintegrate completely repeat the test on 12 additional tablets. Test passes if at least16 out of total 18 tablets disintegrate completely. (Limit: Should be disintegrated within 3 mins)[15,17-19].

Wetting time

Wetting time of FDTs gives an idea about the disintegration properties of the tablets. The wetting time of the tablets are measured by placing five circular tissue papers of 10 cm diameter on five different petridish. 10 mL of water soluble dye solution is added to each petridish. Tablets are carefully placed on the surface of the tissue papers and the time required for dye solution to be taken up by the tablet is noted as the wetting time[15-19].

Water absorption ratio

A tablet was weighed, placed in a tissue paper (internal diameter 5.5cm) and wrapped. Then the tissue paper along with the tablet was placed in a petridish consisting of 6mL of purified water. As soon as the tablet gets wet its final weight was measured. Water absorption ratio, R was determined according to the following equation[15-19].

R=100 (Wa-Wb)/Wb

Where, Wa = Initial weight of tablet.

Wb = Final weight of tablet.

Drug content

Twenty tablets from each batch were selected and powdered. A weighed quantity of powder was transferred into a 100 ml volumetric flask consisting of 100mL of 6.8 pH phosphate buffer and sonicated for 5mins. Then the solution was analyzed for drug content at 275nm in UV VIS-Spectrophotometer (Shimadzu 1601, Japan)[15-19].

In vitro dissolution studies

In vitro dissolution study of aceclofenac was carried using Electro lab TDT-08L USP dissolution apparatus. Samples from each batch were collected and dropped into the basket of the dissolution apparatus containing 900mL of 6.8pH phosphate buffer, 5 ml solution was withdrawn at predetermined time interval from each basket and equivalent amount of fresh medium was replaced to maintain a constant volume i.e sink condition. Each sample withdrawn at different time intervals were analyzed spectrophotometrically at 275 nm against suitable blank using UV-visible spectrophotometer (1800, Shimadzu, Kyoto, Japan). The *in vitro* drug release profile for Aceclofenac FDTs was mentioned in Table No.4. Graphs were plotted between % CDR and Time for all the formulations and shown in Figure No.5-7[17-20].

RESULTS
FTIR Studies

S.No	Average weight of tablet (mg)	% deviation allowed
1	130 or less	10%
2	From 130 to 324	7.5%
3	>324	5.0%

Table No.1: Formulation of FDTs of Aceclofenac

S.No	Ingredients (mg)	Formulation codes								
		KC1	KC2	KC3	KY1	KY2	KY3	DO1	DO2	DO3
1	Aceclofenac	100	100	100	100	100	100	100	100	100
2	Kollidon-cl	3	4	5	-	-	-	-	-	-
3	Kyron t-314	-	-	-	3	4	5	-	-	-
4	Doshion p544-ds	-	-	-	-	-	-	3	4	5
5	Avicel 102	60	59	58	-	-	-	-	-	-
6	Lactose	31	31	31	-	-	-	62	61	60
7	Mcc	-	-	-	60	60	60	30	30	30
8	Mannitol	-	-	-	31	30	29	-	-	-
9	Magnesium stearate	2	2	2	2	2	2	2	2	2
10	Talc	1	1	1	1	1	1	1	1	1
11	Sodiun saccharin	1	1	1	1	1	1	1	1	1
12	Vanilla	2	2	2	2	2	2	2	2	2
13	Total weight	200	200	200	200	200	200	200	200	200

Table No.2: Pre-compression parameters of the powdered blend

| S.No	Formulation Codes	Angle of repose (θ)	Bulk density (gm/cm^3)	Taped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
1	KC1	27.61±0.68	0.371±0.005	0.421±0.01	11.87	1.13
2	KC2	28.94±0.91	0.353±0.002	0.409±0.006	13.69	1.15
3	KC3	27.76±0.51	0.342±0.005	0.398±0.007	14.07	1.16
4	KY1	28.36±0.44	0.378±0.005	0.420±0.004	10	1.11
5	KY2	30.25±0.65	0.386±0.003	0.459±0.000	15.90	1.18
6	KY3	30.67±0.49	0.353±0.006	0.448±0.004	13.83	1.16
7	DO1	26.92±0.31	0.353±0.002	0.409±0.006	13.69	1.15
8	DO2	27.01±0.45	0.358±0.005	0.416±0.007	13.94	1.16
9	DO3	29.35±0.66	0.368±0.009	0.433±0.004	15.01	1.17

Table No.3: Post-compression parameter of direct compression FDTs

Formulation Code	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)	Wetting Time (sec)	Water abs. ratio (%)	Disintegration Time (sec)	Drug Content (%)
KC1	3.01±0.05	3.23±0.05	0.21	200.2±0.62	38.00±2.00	52.66±2.51	15.6±1.52	99.3±0.77
KC2	2.96±0.01	3.36±0.15	0.25	199.2±1.03	18..66±1.52	44.66±1.52	18.6±1.52	99.3±0.98
KC3	3.03±0.05	3.40±0.17	0.26	200.1±0.67	26.00±2.00	58.33±1.52	30.3±2.51	98.1±1.38
KY1	3.00±0.02	2.90±0.17	0.83	198.4±2.10	30.66±081	52.66±2.51	33.2±0.94	98.2±0.15
KY2	3.02±0.06	2.83±0.05	0.75	198.0±1.87	48.00±2.00	61.33±1.52	55.6±0.47	98.8±0.69
KY3	2.99±0.01	2.96±0.11	0.88	200.2±1.34	67.66±2.51	48.00±2.51	67.6±1.15	99.5±0.53
DO1	2.99±0.01	3.46±0.05	0.75	203.0±2.40	28.66±3.05	62.00±2.00	58.7±1.06	99.1±0.54
DO2	3.02±0.06	3.40±0.10	0.80	197.6±1.97	34.00±2.00	57.00±2.00	78.9±1.11	98.6±0.082
DO3	3.01±0.01	3.43±0.11	0.89	200.0±1.02	38.00±2.00	61.33±1.52	92.6±1.15	98.36±0.95

Table No.4: *In vitro* dissolution studies

S.No	Time (min)	% Cumulative drug release								
		KC1	KC2	KC3	KY1	KY2	KY3	DO1	DO2	DO3
1	0	0	0	0	0	0	0	0	0	0
2	5	78.29	84.25	86.12	64.06	64.58	85.64	50.23	59.40	60.59
3	10	95.94	94.28	91.37	73.93	76.46	86.94	63.21	81.48	70.63
4	15	98.59	99.31	95.42	79.28	88.51	94.95	75.53	87.74	83.52
5	20	----	---	---	83.18	89.44	97.94	91.70	85.76	92.37
6	25	----	---	---	85.14	93.13	98.18	91.23	92.04	97.11

A.
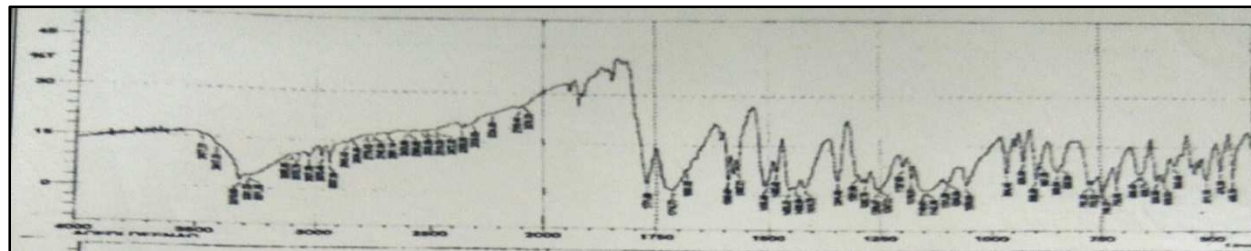
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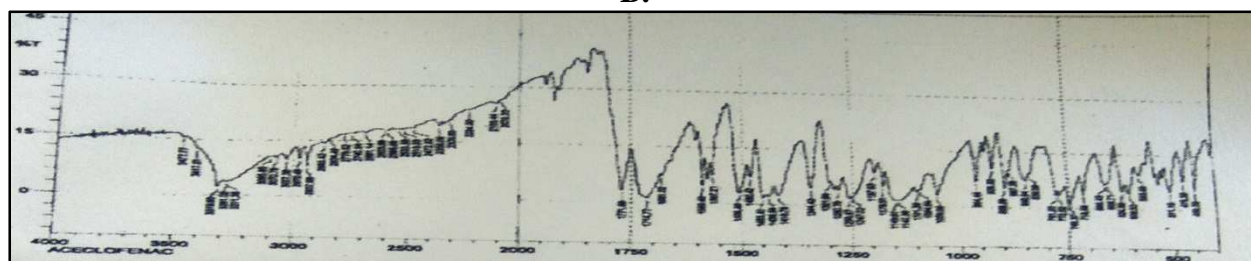
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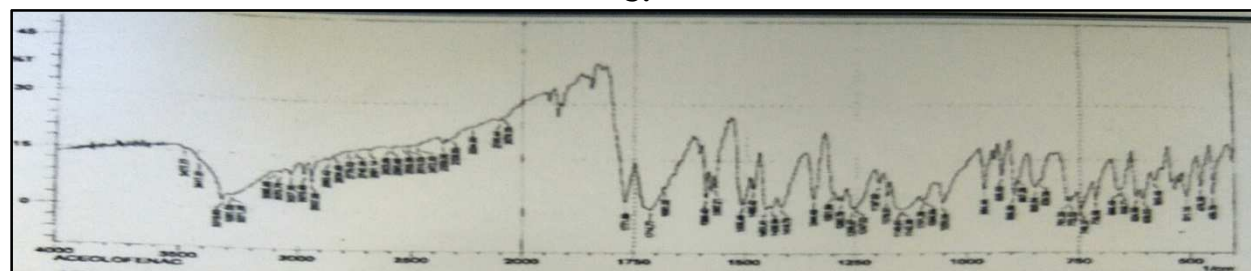
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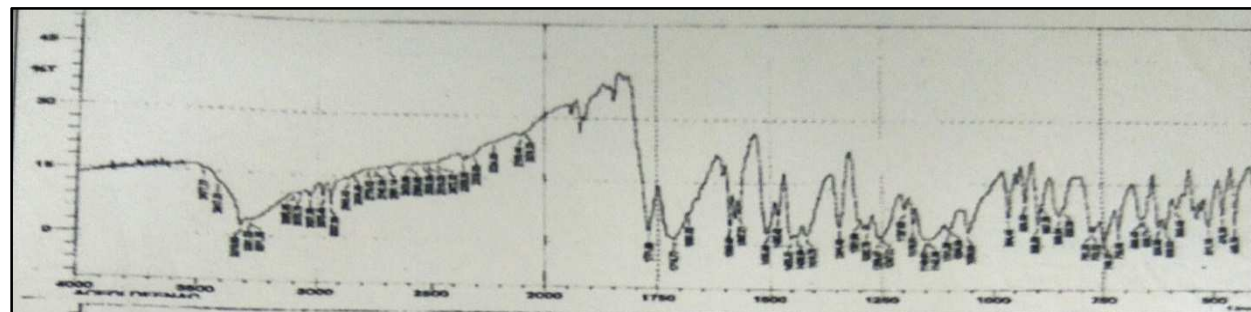
Figure No.1: FTIR spectra of: A. Aceclofenac pure drug, B. Aceclofenac-Kollidon CL and physical mixture, C. Aceclofenac-Doshion p544-DS and physical mixture , D. Aceclofenac-Kyron T-314 and physical mixture

| 5 sec. | 10 sec. | 15 sec. | 20 sec. | 25 sec. |
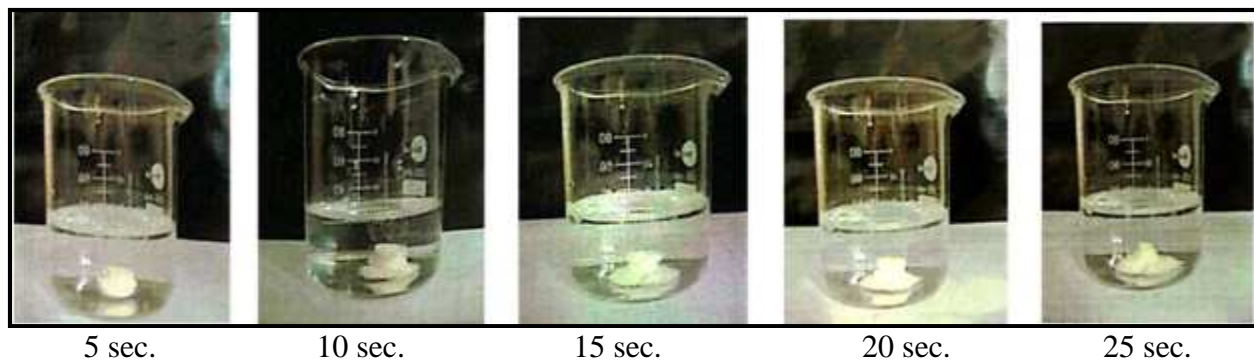
Figure No.2: *In vitro* **disintegration time profile of Kyron T-314 formulation**

| 5 sec | 10 sec | 15 sec | 20 sec |
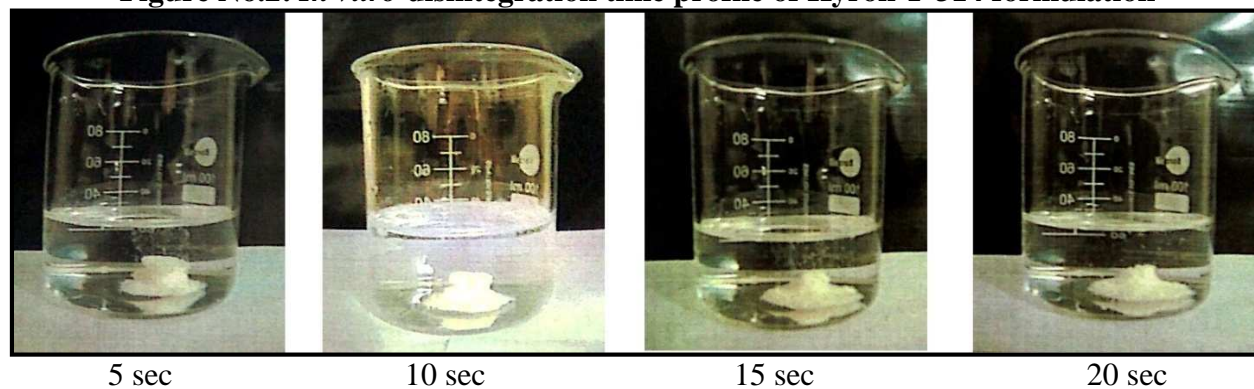
Figure No.3: *In vitro* **disintegration time profile of Kollidon CL formulation**
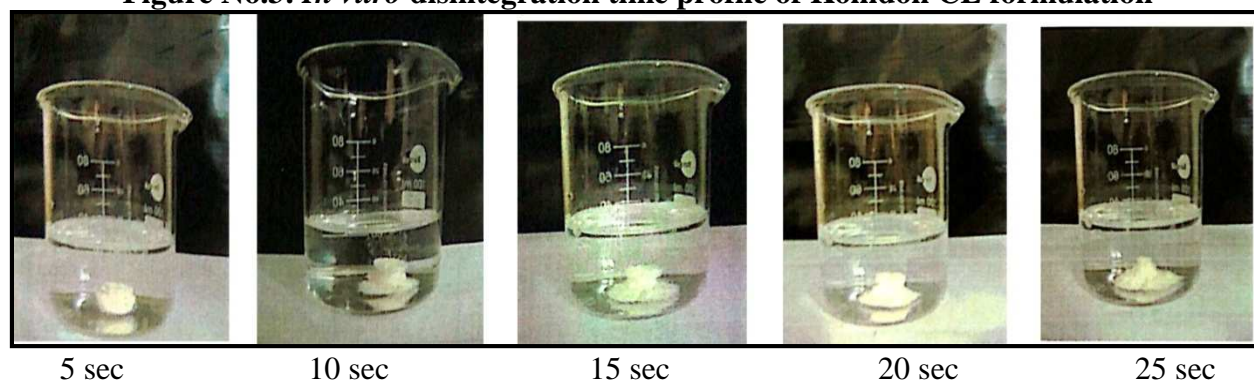

| 5 sec | 10 sec | 15 sec | 20 sec | 25 sec |

Figure No.4: *In vitro* **disintegration time profile of Doshion P544-DS formulation**
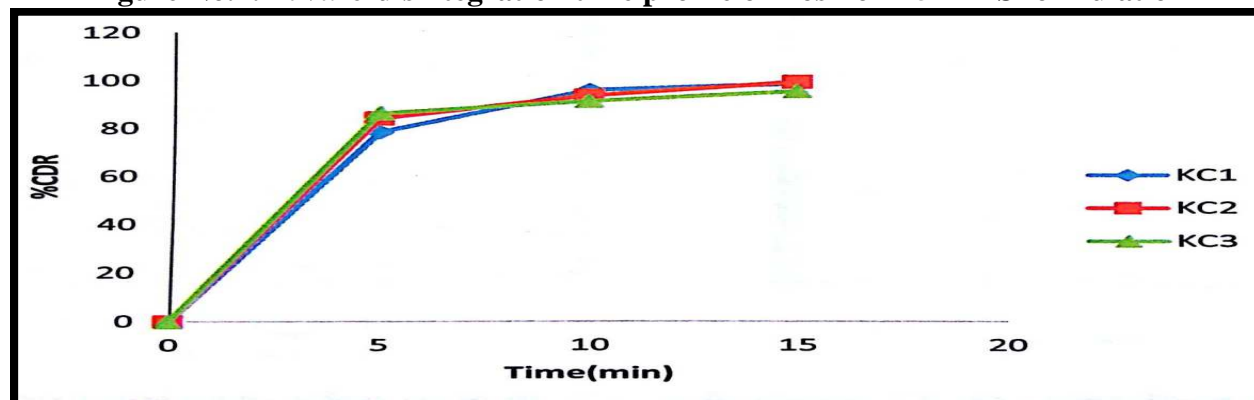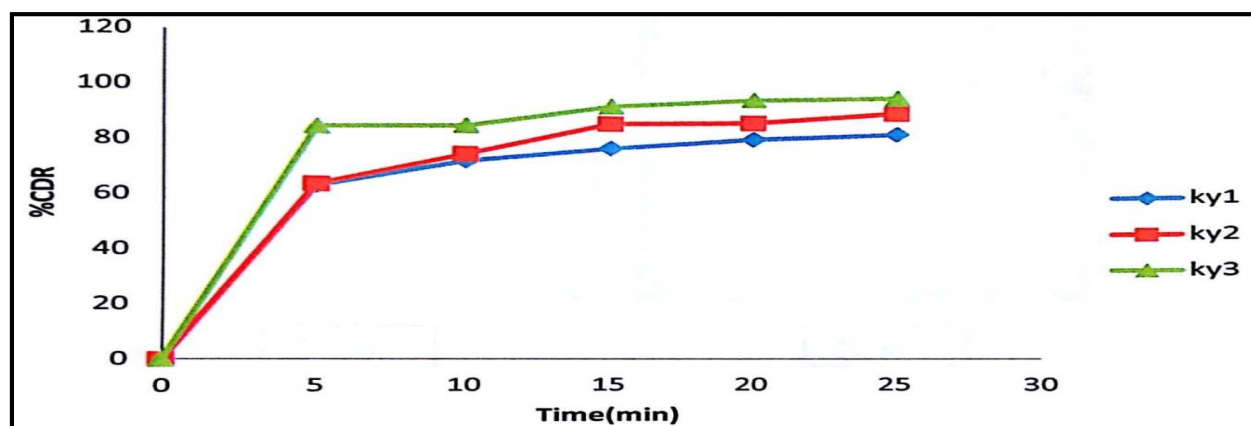

Figure No.5*: In vitro* **drug release profile of KC1, KC2, KC3**

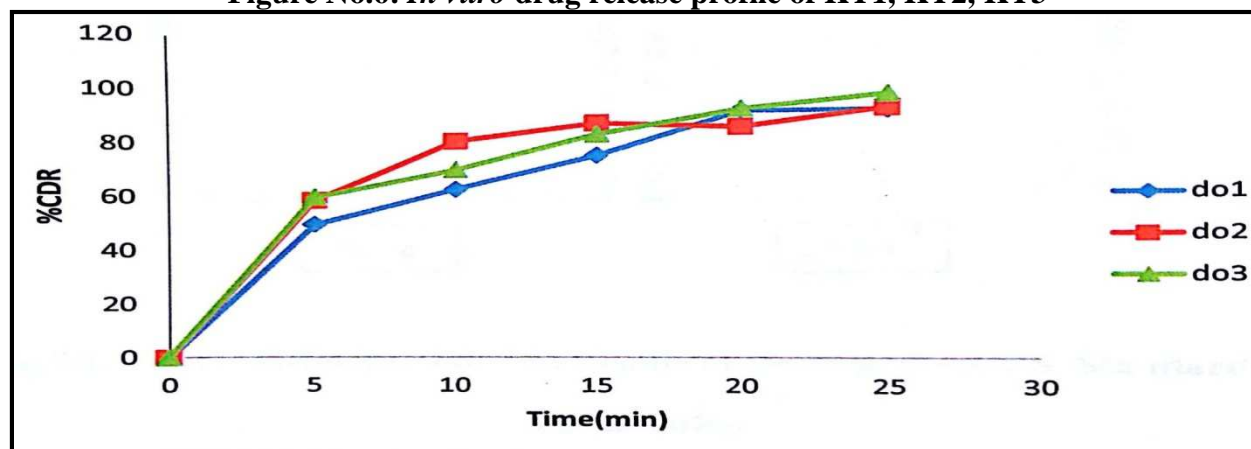**Figure No.6:** *In vitro* **drug release profile of KY1, KY2, KY3**

Figure No.7: *In vitro* **drug release profile of DO1, DO2, DO3**

CONCLUSION

Among all the formulations, tablets prepared with KC_2 Kollidon CL (KC_2) showed good release profile. This was because of the presence of higher concentration of super disintegrants. Even all the formulation showed the post compression parameters within the pharmacopoeial limits. The formulated tablets dissolve or disintegrate rapidly in the oral cavity within a matter of seconds without the need of water. Thus from this study we can conclude that FDTs of Aceclofenac can be more promising over the normal conventional tablets in terms of ease of administration as well as onset of action.

ACKNOWLEDGEMENT

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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