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FORMULATION AND EVALUATION OF PRESSED COATED TABLETS OF DICLOFENAC POTASSIUM

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ABSTRACT

The main objective of the studies described was to develop a time-controlled release formulation based on a press-coating technique. The intention was that the formulation is administered in the evening at 22:00, which provides treatment for diseases in which symptoms are experienced in the early morning hours (i.e. chronopharmacotherapy). The Diclofenac potassium pressed coated tablets were prepared using direct compression method. The coats contained a hydrophilic polymer (hydroxypropylmethylcellulose) to control drug release. Cores were immediate-release formulations containing all or most of the drug dose. The time-controlled release dosage form containing HPMC allows time to peak plasma level to be adjusted to 6 to 8 hours after administration. Amount of HPMC used, HPMC viscosity grades selected were most important factors controlling drug release and absorption from the dosage form. The pressed coated tablets were evaluated for post compression studies such as hardness, friability, drug content, weight variation and dissolution studies. The kinetic data also applied to the dissolution. All the prepared tablets formulations were found to be good without capping and chipping. Post Compressionalparameters (hardness, friability, thickness and drug content) was within the acceptable limit. FTIR Spectroscopicstudies indicated that the drug is compatible with all the excipients. The *in vitro* drug release of polymer coated tablet of Diclofenac Potassium prepared by direct compression F2 method were found to be 96.60% at 8 hrs. Among the all formulations F2 formulation was found to be promising with controlled drug release. The inner Core tablets prepared with Superdisintegrant exhibited good disintegration characteristics. tablets having CP as the disintegrant showed faster dissolution rates and higher efficiency values.

KEYWORDS: Diclofenac potassium, Compression coated, Tablets, FTIR, HPMC, Crosspovidone.

INTRODUCTION

The goal in drug delivery research is to develop formulations to meet therapeutic needs relating to particular pathological conditions. Variation of physiological and pathophysiological functions in time has brought a new approach to the development of drug delivery systems. Research in chronopharmacological field has demonstrated the importance of biological rhythms in drug therapy. Optimal clinical outcome cannot be achieved if drug plasma concentrations are constant. If symptoms of a disease display circadian variation drug release should also vary over time. Utilisation of different technologies in development of time-controlled, pulsed, triggered and programmed drug delivery devices has been undergoing recent years. Another point raised by circadian variation of physiological function is that drug pharmacokinetics can also be time-dependent (i.e. chronopharmacokinetics). Both variations in a disease state and in drug plasma concentration need to be taken into consideration in developing of drug delivery systems intended for treatment of disease with adequate dose at appropriate time.[1]

The category of controlled release formulations can be divided into subgroups of rate-controlled release, delayed-release and pulsed-release formulations. Delayed-release formulations include time-controlled release and site-specific dosage forms. When constant drug plasma levels need to be avoided, as in chronopharmacotherapy, time controlled or pulsed release formulations are preferable, especially in the treatment of early morning symptoms. By timing the drug administration, plasma peak is obtained at an optimal time. Number of doses per day can be reduced. When there are no symptoms there is no need for drug.[2]

Press-coating of dosage forms has a long history. The first patent for a press coating machine was granted in at the end of the 19th century. Press coated formulations can be used to protect hygroscopic, light-sensitive, oxygen labile or acid-labile drugs, to separate incompatible drugs from each other, or to achieve sustained release. Intermittent release can also be achieved by incorporating one portion of a drug in the core and the other in the coat. Compression coating can involve direct compression of both the core and the coat, obviating

needs for separate coating process and use of coating solutions. Materials such as hydrophilic cellulose derivates can be used. Compression is easy on laboratory scale. On the other hand, for large-scale manufacture special equipment is needed.[3]

In recent years, various controlled release, especially time-controlled release;drug delivery systems based on compression coating technology have been studied. Most such formulations release drug after a lag phase, followed by a rapid dissolution of a core. Have developed a press-coated device in which the inner core contains the drug and the outer coat is made of different types of polymers. The outer barrier, controlling drug release can be either swellable or erodible. Lag times can be varied by changing the barrier formulation or the coating thickness. To achieve time-controlled delivery a press-coated formulation containing a swellable core and a less water permeable coat has been developed. The core contains drug and disintegration agent. The outer shell delays commencement of drug release.[4]

After a lag time of one to 10 hours release in vitro is rapid. Lag times depend on the composition of the blend used for coating. Pharmaceutical coatings are an essential tool to achieve the desired formulation of pharmaceutical dosage forms. Coatings are applied to achieve superior aesthetic property of a dosage form (e.g. color, texture, mouth feel and taste masking), physical and chemical protection for the drugs in cores, and modified drug release characteristics. Coating techniques mostly used in pharmaceutical industry are aqueous or organic coating, which present some disadvantages: time consuming, stability for heat labile and hydrolysis of degradable drug and polluted environment problem. Thereby, non-solvent coating is introduced as alternative coating technique to overcome these disadvantages. Non-solvent coatings have been categorized as press coating, hot melt coating, supercritical fluid spray coating, electrostatic coating, dry powder coating and photocurable coating. Among these techniques, compression coating is the absolute dry coating without solvent and heat use. Aditionally, compression coating has no limitation for the cores and hence overcomes the adhesion problem found in spraying methods.[5]

MATERIALS AND METHODS

Materials

Diclofenac potassium as a gift sample from Emcure Pharmaceuticals Ltd, Pune, Hypromellose, Ethyl Cellulose, Crospovidone andMicrocrystalline Cellulose (Avicel PH 102) were obtained from SD Fine Chem, Mumbai.

Formulation of Core Tablet

Diclofenac potassium tablet cores (6 mm diameter tablets: 50 mg drug, 2 mg crospovidone,5 mg magnesium stearate, 43 mg microcrystalline cellulose) were prepared by direct compression.

Formulation of press-coated tablet

6 mm diameter drug cores were compression-coated into 10 mm diameter tablets with HPMC K4M:ethylcellulose (20:80, 30:70, 45:55, 55:45, 70:30 and 85:15). The compression-coated tablets (core: coat, 1:2) were prepared by first filling one-half (125 mg) of the polymer powder in the die cavity, then centrally positioning the tablet core on the powder bed followed by filling the remaining half (125 mg) of the polymer powder on top and then followed by compression.[6-7]

Table 1: Composition of Core Tablets (100mg)

Sr. No.	Formulation	Qty (mg)
1	DiclofenacPotassium	50
2	Cros povidone	2
3	Magnesium stearate	5
4	Microcrystalline cellulose	43

Table 2: Composition of press-Coated Tablet

Formulation		Coating Material (250mg)	Ratio (%)
Formulation No.	Core Table		
F1	C1	HPMCK4M:EC	20:80
F2	C1	HPMCK4M:EC	30:70
F3	C1	HPMCK4M:EC	45:55
F4	C1	HPMCK4M:EC	55:45
F5	C1	HPMCK4M:EC	70:30
F6	C1	HPMCK4M:EC	85:15

Preformulation Studies

Preformulation study is desired to ensure the development of a stable as well as the therapeutically effectiveandsafe dosage form. Preformulation testing is designed to assess the influence of physicochemical properties of drug substances and excipients on formulation properties of dosage form, method of manufacture, and pharmacokinetic-biopharmaceutical properties of the resulting product. A thorough understanding of physicochemical properties may ultimately confirm that no significant barriers are present for the formulation development.

Bulk Density

Bulk density or apparent density is defined as the ratio of mass of a powder to the bulk volume. The bulk density of a powder depends primarily on particle shape, particle size distribution and the tendency of the particles to adhere to one another.

API was accurately weighed and sifted through 18 # and transferred in a 100 ml graduated cylinder. The level was observed without compacting and noted as apparent volume (V_0). The bulk density was calculated by the formula

$$BD=M/V_0$$

Where, M=Mass of powder taken.
V_0= Apparent untapped volume.

Tapped Density

The tapped density is a limited density attained after "tapping down" usually in a device that lifts and drops a volumetric measuring cylinder containing the powder from a fixed distance. Tapped density was determined by using Electrolab USP Apparatus.

API was accurately weighed and sifted through 18 # and transferred in 100 mL graduated cylinder. The cylinder was placed on the tapped density tester and was mechanically tapped. The cylinder was tapped for 500 times initially and the tapped volume (V_1) was measured to the nearest graduated units. The tapping was repeated for additional 750 times and the tapped volume (V_2) nearest to graduated units was noted. The tapped density was calculated by the formula

$$TD=M/V_2$$

Where; M= Weight of powder,
V_2= Tapped volume (after 500+750 taps)

Hauser Ratio

Hauser's ratio gives an idea regarding the flow of the blend. It is the ratio of tapped density to the bulk density. Hausner ratio is calculated as:

HR= Tapped density / Bulk density

Compressibility Index

The compressibility index measures of the propensity of powder to be compressed. The packing ability of drug was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It is indicated as Carr's compressibility index (CI) and can be calculated as follow.

$$CI(\%) = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Bulk Density}} \times 100$$

Flow Properties

Irregular flow of powders from the hopper produces tablets with non-uniform weights. As a result content uniformity and dose precision cannot be achieved in production of Tablets & capsules. Flow properties depend on particle size, shape, porosity and density of bulk powder. The flow characteristics are measured by angle of repose. The relationship between angle of repose and powder flow is given in table. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle that can be obtained between the freestanding surface of a powder heap and the horizontal plane.

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

Where; h = height of pile.
r = radius of the base of pile.
θ = angle of repose.

A funnel was held with a clamp such that the stem of the funnel is 2 cm above the graph paper that is placed on a horizontal surface. Weighed amount of powder (5g) was taken and poured in to the funnel keeping the orifice of funnel blocked. The powder was allowed to flow by removing the blockage until the apex of the conical pile just touches the tip of the funnel. Height of pile (h) and average of six diameters formed by the pile of the powder was measured with the help of a ruler and the angle of repose was determined.[42-43]

EVALUATION OF TABLETS

Hardness test

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.[8]

Friability

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition.

The friability of tablets was determined by using Electro lab, USP EF 2 friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 100 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} x100$$

% Friability of tablets less than 1% is considered acceptable.[9]

Weight variation test

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Uniformity of thickness

The crown thickness of individual tablet may be measured with a vernier calliper, which permits accurate measurements and provides information on the variation between tablets. Other technique employed in production control involves placing 5 or 10 tablets in a holding tray, where their total crown thickness may be measured with a sliding caliper scale. The tablet thickness was measured using screw gauge.[9]

Drug content uniformity

Four tablets weighted and crushed in a mortar then weighed powder contain equivalent to 50 mg of drug was taken and dissolved in 100 ml methanol, from this solution 1 ml of solution was diluted to 10 ml methanol again 1 ml solution from this diluted up to 10 ml with methanol and assayed for drug content at 276 nm.[10]

***In vitro* disintegration time**

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 I.P. specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 maintained at 37°±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37°±2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.[10]

***In vitro* dissolution studies**

In vitro-dissolution studies were performed on the press-coated tablets prepared by direct compression method at 37±0.5°C using 6.8 phosphate buffer in USP apparatus I with the paddle speed 100 rpm. 5 ml of filtered aliquot was withdrawn at pre- determined time intervals and replaced with 5 ml of fresh 6.8 phosphate buffer solution maintained at the same temperature. The sample wereanalyzed at276 nm using UV Spectrophotometer. The lag time and percentage release was determined for each formulation.[10]

Kinetic Study

Zero Order Kinetics: Azero-order release would be predicted by the following equation.

$A_t = A_0 - K_0 t$ …….1

Where:

A_t = Drug release at time 't'

A_0 = Initial drug concentration.

K_0 = Zero-order rate constant (hr^{-1}).

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K_0.

First Order Kinetics: Afirst-order release would be predicted by the followingequation

$$\text{Log } C = \text{Log } C_0 - \frac{K_t}{2.303} \quad \text{……..2}$$

Where:

C = Amount of drug remained at time 't'

C_0 = Initial amount of drug

K = First-order rate constant (hr^{-1}).

When the data is plotted as log cumulative percent drug remaining versus time yields a straight line, indicating that the release follows First-order kinetics. The constant 'K' can be obtained by multiplying 2.303 with slope values.

Higuchi's Model: Drug released by diffusion has been described by following Higuchi's classical diffusion equation.

$$Q = \left[\frac{D\varepsilon}{\tau}(2A-\varepsilon C_S)C_S t\right]^{½} \quad \text{……..3}$$

Where:

Q = Amount of drug released at time't'

D = Diffusion coefficient of the drug

A =Total amount of drug in unit volume

Cs = The solubility of the drug in the diffusion medium

ε = Porosity

τ = Tortuosity

t = Time (hrs) at which 'Q' amount of drug is released.

Equation-3 may be simplified if one assumes that D, Cs and A are constant. Then equation-3 becomes

$Q = Kt^{1/2}$ ……..4

When the data is plotted according to equation-4 i.e., cumulative drug released versus squareroot of time, yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to 'K'.

Korsmeyer and Peppas Mode:The release rates from controlled release polymer can be described by the equation (5) proposed by Korsmeyeret a1.

$Q = K_1 t^n$ …….5

Q is the percentage of drug released at time't',K is a kinetic constant incorporating structural and geometric characteristics of the tablets and 'n' is the diffusionalexponent indicative of the release mechanism.[11]

RESULTS AND DISCUSSION

Identification of pure Drug

The FTIR spectrum of pure Drug was found to be similar to the reference standard IR spectrum of Diclofenac Potassium given in British Pharmacopoeia. The API used for product development has been characterized by

different physicochemical tests shown in Table No.3. API complies as per the specification. Based on the above data it was concluded that the API has excellent property.

Table 3: Physical property of API.

Parameter	Observation
Bulk Density	0.477g/ml
Tapped Density	0.805g/ml
Carr's Index	40.74%
Hausner Ratio	1.107
Angle of Repose	30

FTIR Studies

FTIR spectrum of the pure drug Diclofenac K exhibits characteristic peaks at 1559, 1368, 1279 cm^{-1} due to carboxylic acid salt (COOH), tertiary amine (C-N stretching) respectively. The presence of above peaks confirms undistributed drug in the formulations. Hence there are no drug-excipient interactions. The excipients used in the formulation were crospovidone, MCC, Magnesium Stearate, and polymeric coating of hydroxy propyl methyl cellulose and ethyl cellulose. Pure form of HPMC exhibited peaks at 1058 cm^{-1} due to C-O, 3549 due to C-OH, 2924 due to C-H and at 1058 due to C-C. Pure form of crospovidone exhibited peaks at 1656 cm^{-1} due to C= O, 1287 due to C-N, 2926 due to C-H and at 932 due to C-C. The presence of above peaks confirms undisturbed structure of drug and excipients in the above formulation. Hence, there are no drug-excipient interactions.

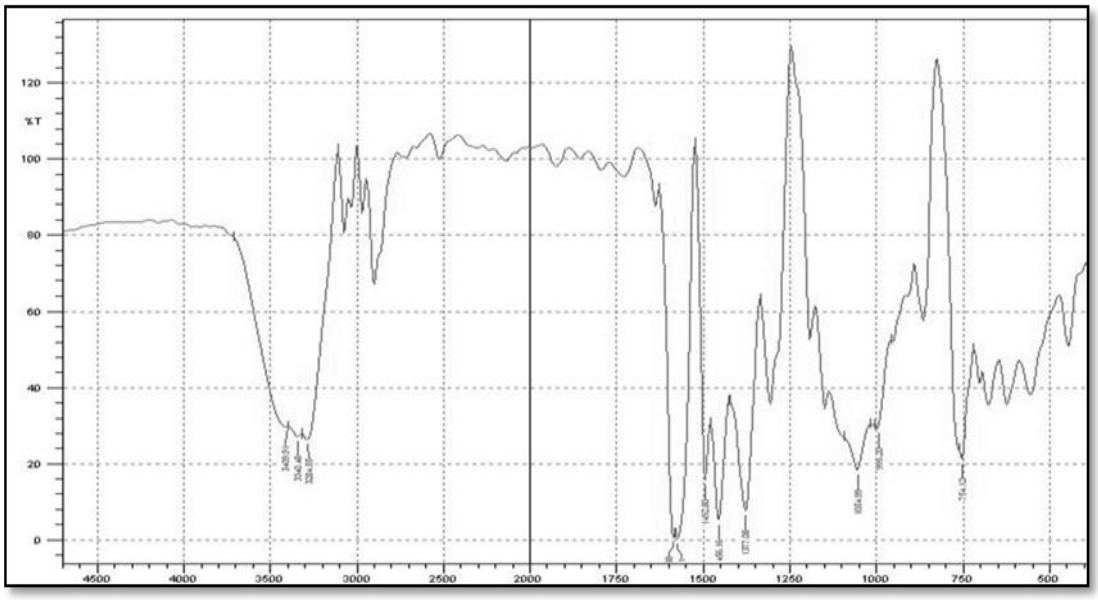

Fig. 1: FTIR spectra of Diclofenac Potassium.

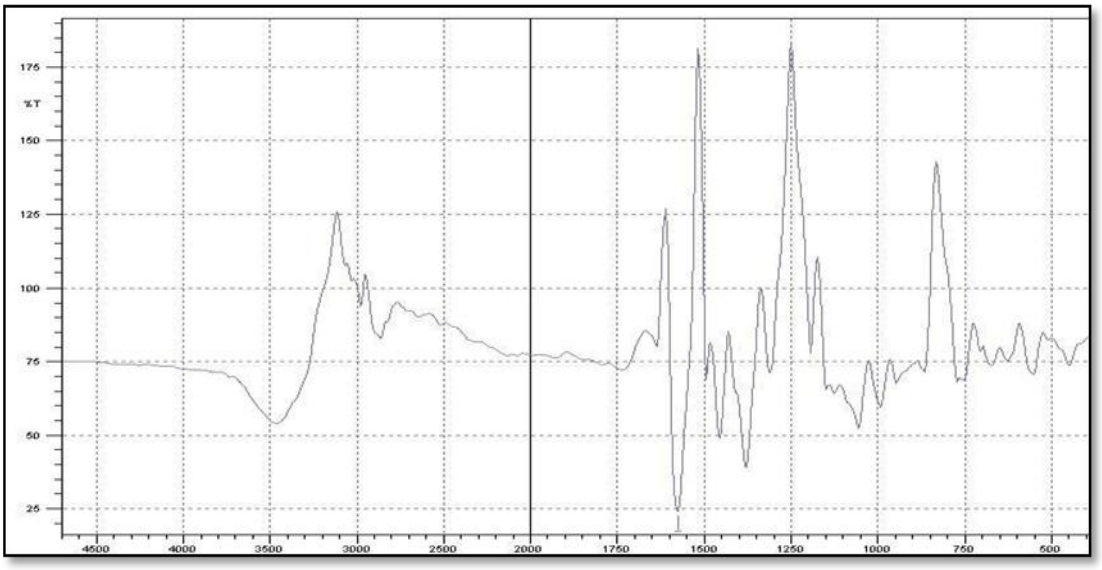

Fig. 2: FTIR spectra of Drug and Polymer.

Table 4: Post-compression Parameters of Core tablet.

Sr. No.	Parameter	Observation
1	Thickness	0.15±0.007 cm
2	Hardness	2.30±0.014 kg/cm^2
3	Average Weight	99.21±0.070 mg
4	Friability(%)	0.760±0.003 (%)
5	Drug Content	96.60 %
6	Disintegration time (min)	1.42

The prepared core tablets of Diclofenac Potassium were evaluated for various parameters like weight variation, hardness, friability, disintegration time and drug content.

All the tablet formulations were evaluated for hardness. The hardness range for core formulation was in the range of 2.05 kg/cm^2 to 2.55 kg/cm^2

Table 5: Post-compressional parameters for Press- Coated Tablet.

Formulation Code	Hardness (Kg/cm^2)	Friability (%)	Thickness (cm)	Average Weight(mg)	Drug Content(%)
F1	5.8±0.30	0.5±0.028	0.26±0.138	346.81±0.212	99.05±0.113
F2	5.5±0.21	0.54±0.020	0.26±0.118	347.11±0.827	99.21±0.305
F3	5.4±0.20	0.52±0.022	0.27±0.104	345.55±0.874	99.64±0.413
F4	5.2±0.20	0.55±0.024	0.28±0.095	345.38±0.855	98.64±0.451
F5	5.8±0.18	0.56±0.021	0.27±0.087	347.10±0.767	98.52±0.458
F6	5.5±0.22	0.53±0.026	0.27±0.082	346.25±0.701	98.45±0.464

The prepared press-coated tablets of Diclofenac Potassium were evaluated for various parameters like weight variation, hardness, friability, disintegration time and drug content.

Weight variation: The weight of all the tablets was found to be within the Pharmacopoeial limits of ± 5 %. The weight of all the tablets was found to be uniform with low values of standard deviation. The thickness and weight variation were uniform and indicated by the low values of standard deviation. Friability values were less than 1% indicates good mechanical strength. All the tablet formulations were evaluated for hardness. The hardness range of press- coated tablets was in the range of 4.55 to 7.30 cm^2. Friability of all the tablet formulations was according to the pharmacopoeial limits of below 1 %. Drug content uniformity was performed and low values of standard deviation indicates drug content uniformity within the tablets. The percent drug content uniformity of the formulations (F1-F6) Was In The Range Of 98.45 % To 99.64 %.

Dissolution Study

In vitro release studies were performed in USP XXIII tablet dissolution apparatus I employing basket at 100 rpm at a temperature of 37 ± 0.5^{0}C. The dissolution medium used for the study was 900 ml of Phosphate buffer solution of pH 6.8. *In vitro* release studies were performed in USP XXIII tablet dissolution apparatus I employing basket at 100 rpm at a temperature of 37 ± 0.5^{0}C. The dissolution medium used for the study was 900 ml of 0.1 N HClsolution and Phosphate buffer solution of pH 6.8.The time-controlled release Press-Coated tablets containing HPMC allows time to peak plasma level to be adjusted to 6 to 8 hours after administration. HPMC viscosity grades selected were most important factors controlling drug release and absorption from the dosage form. In vitro studies show that time to peak concentration values are approximately predictable from a dissolution parameter.

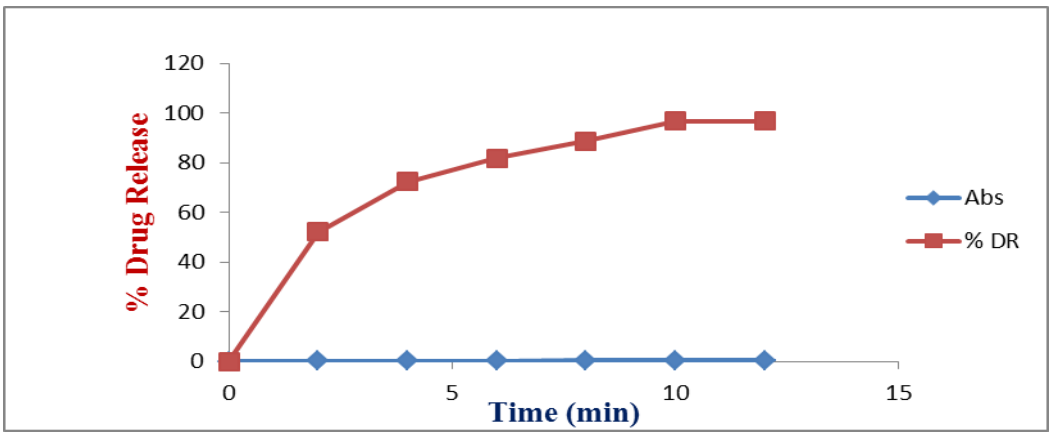

Fig. 3: Dissolution Profile of Core Tablet.

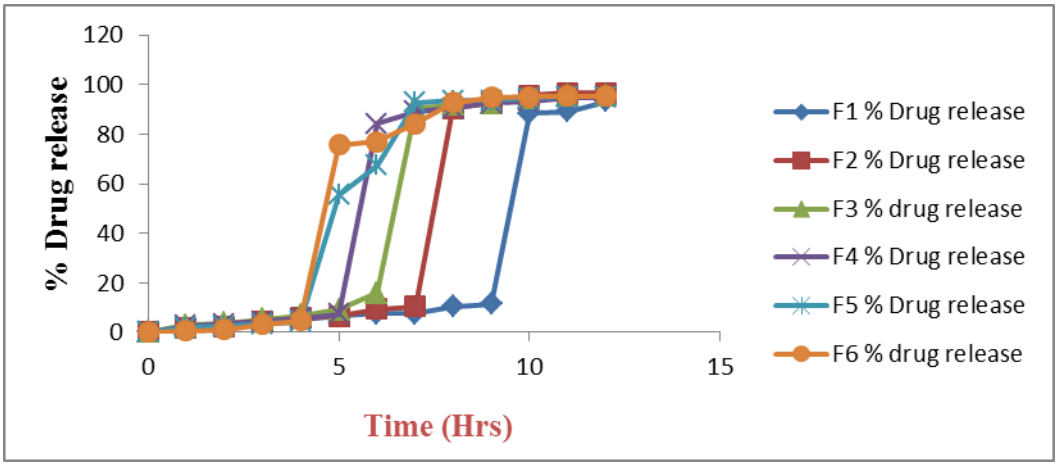

Fig. 4: *In Vitro* drug release study of Press- Coated tablet of F1-F6 Formulation.

Kinetic Study of Diclofinac Potassium Press Coated tablet

The kinetic study was concluded that the *in vitro* drug release data is subjected to different drug release kinetic treatment zero order, first order, Higuchi's and Peppa's equations to ascertain mechanism of drug release. The results of linear regression analysis including regression co-efficient are summarized in table. The coefficient of correlation (R^2 Value) is considered as the main parameter for interoperating the release kinetic model. The formulation Batch F2 Shows Higuchi model for Best fit model of drug release.The above data it is evident that formulation displayed zero-order kinetics.

Table 6: Kinetic Study of Diclofinac Potassium Press Coated tablet.

Time (hrs)	Sq. Rt.Time	Log Time	Conc. (µg/ml)	Conc. (mg/ml)	% Release	Cum.% Release*	Log % Release
0	0.000	0.000	0.000	0.000	0.00	0.00	0.00
1	1.000	0.000	0.316	0.948	1.58	1.10	0.20
2	1.414	0.301	0.496	1.488	2.48	2.48	0.39
3	1.732	0.477	0.904	2.712	4.52	4.52	0.66
4	2.000	0.602	1.176	3.528	5.88	5.89	0.77
5	2.236	0.699	1.312	3.936	6.56	6.57	0.82
6	2.449	0.778	1.900	5.700	9.50	9.51	0.98
7	2.646	0.845	2.036	6.108	10.18	10.20	1.01
8	2.828	0.903	18.098	54.294	90.49	90.51	1.96
9	3.000	0.954	9.253	55.518	92.53	92.68	1.97
10	3.162	1.000	9.547	57.282	95.47	95.55	1.98
11	3.317	1.041	9.660	57.960	96.60	96.68	1.98
12	3.464	1.079	9.660	57.960	96.60	96.68	1.98

Table 7: *In-vitro* drug release data of formulations.

Time(hrs)	%cumulative drug released	%cum drug remaining(x)	log %cum drug remaining	(x)⅓
0	0	100	2	4.641588834
1	1.1	98.9	1.995196292	4.624506887
2	2.48	97.52	1.989093693	4.602896726
3	4.52	95.48	1.97991241	4.570574617
4	5.89	94.11	1.973635773	4.548608841
6	9.51	90.49	1.956600588	4.489522951
8	90.51	9.49	0.977266212	2.117168404
10	95.55	4.45	0.648360011	1.644826157
12	96.66	3.34	0.523746467	1.494796787

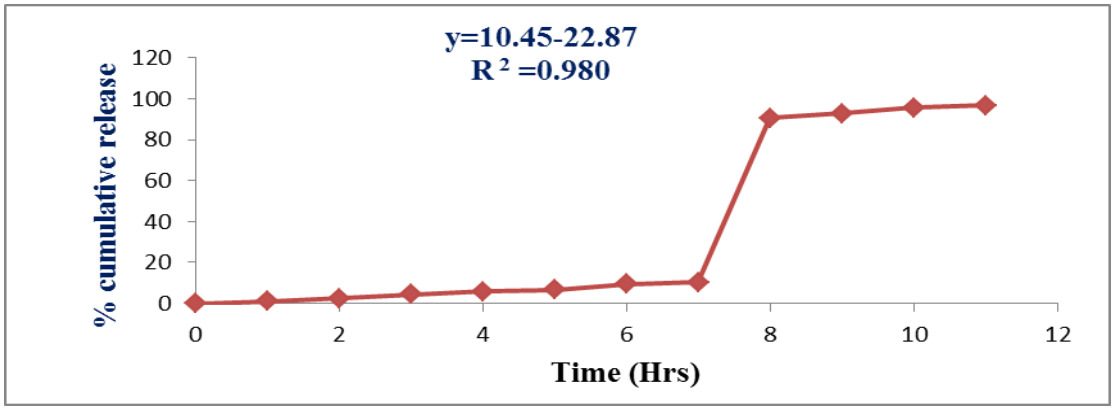

Figure 5: Cumulative percent drug released vs time (zero order) of formulation F_2.

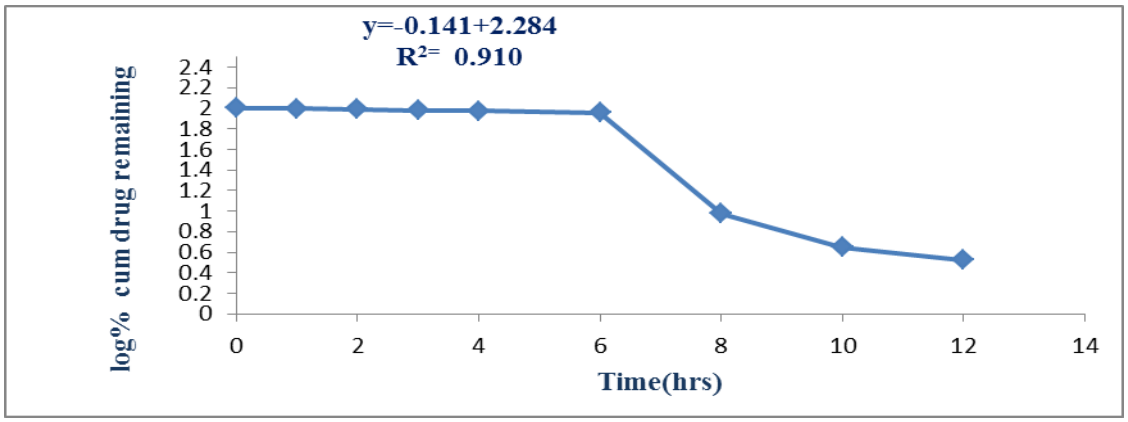

Fig. 6: Cumulative percent drug released vs time (First order) of formulation F_2.

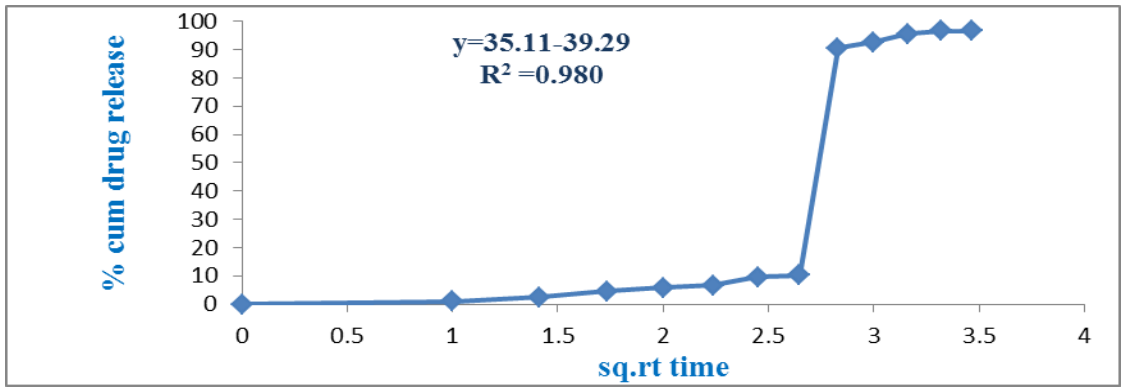

Fig. 7: Cumulative % drug released vssqure root time (Higuchis plots) of formulation F_2.

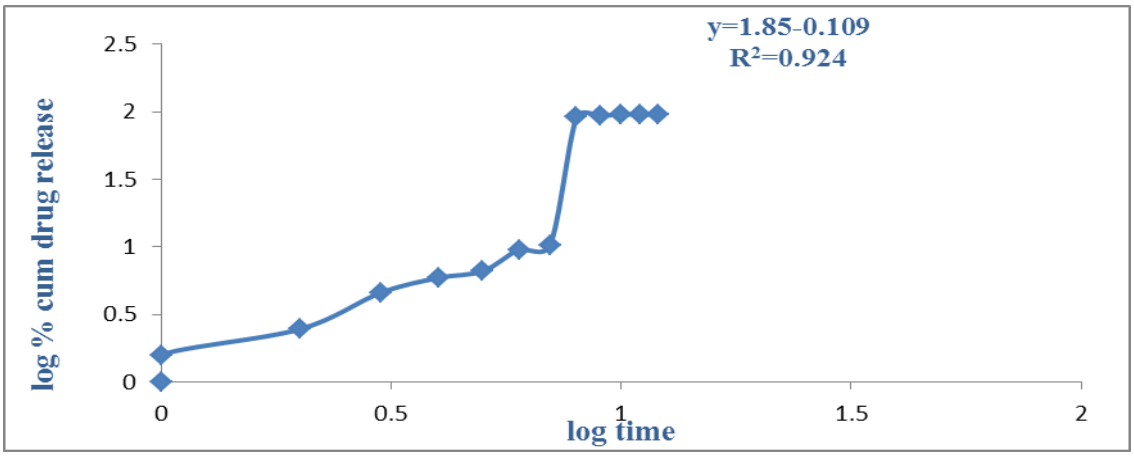

Fig. 8: Cumulative percent drug released vs log time (Korsmyer-Peppas plots) of formulation F_2.

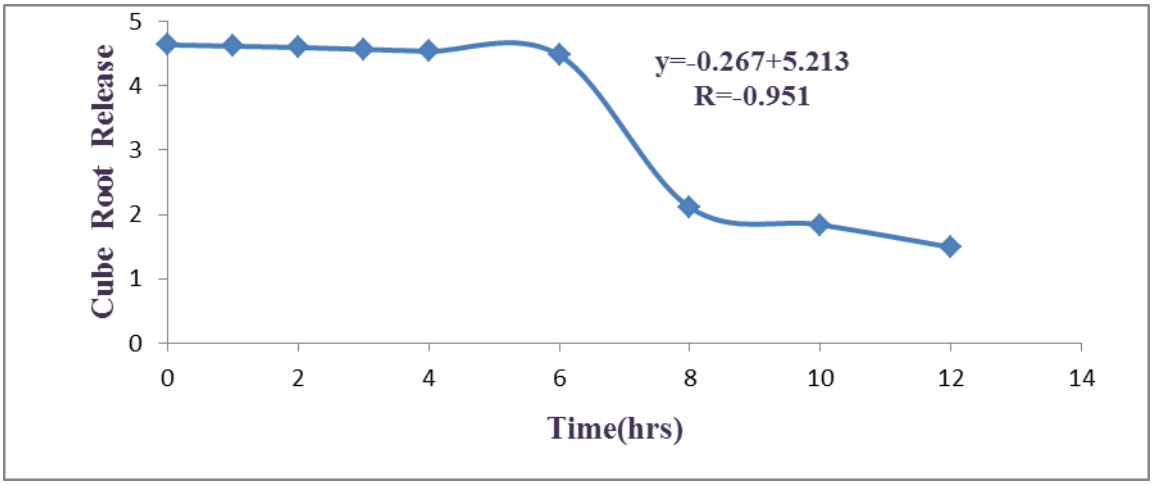

Fig. 9: Cube root release Vstime (Hixson plot) of formulation F_2.

CONCLUSION

In the present work time-controlled release Press- Coated tablets of Diclofenac Potassium were prepared by direct compression method containing inner core tablet contains superdisintegrants such as crospovidone and polymeric coating contains Hydroxy propyl methyl cellulose and ethyl cellulose. All the tablets of Diclofenac Potassium were subjected to weight variation, hardness, friability, drug content uniformity, and *in vitro* drug release.

Press- Coated tablet prepared by direct compression method byusing HPMCk4M and Ethyl cellulose polymers. All the prepared tablets formulations were found to be good without capping and chipping. Post Compressionalparameters (hardness, friability, thickness and drug content) was within the acceptable limit. FTIR Spectroscopicstudies indicated that the drug is compatible with all the excipients. The *in vitro* drug release of polymer coated tablet of Diclofenac Potassium prepared by direct compression F2 method were found to be 96.60% at 8 hrs. Among the all formulations F2 formulation was found to be promising with controlled drug release. The inner Core tablets prepared with Superdisintegrant exhibited good disintegration characteristics. tablets having CP as the disintegrant showed faster dissolution rates and higher efficiency values.

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REFERENCES

1. Conte U., Maggi L., Torre P, Giunchedi P. Press-coated tablets for time programmed release of drugs. Biomaterials, 14: 1017-1023.
2. Giunchedi P. and La Manna Ab. New oral system for timing-release of drugs. Boll. Chim. Farmaceutico, 131: 199-204.
3. Hata T., Shimazaki Y., Kagayama A., Tamura S. and Ueda S Development of a novel drug delivery system, time-controlled explosion system (TES): V. Animal pharmacodynamics study and human bioavailability study. Int. J. Pharm, 110: 1-7.
4. Ritschel W.A. and Sabouni. Permeability of [3H] water across a porous polymer material used as rate-limiting shell in compression-coated tablets J. Controlled Release, 12: 97-102.33.
5. Sangalli M.E., Maroni A., Busetti C., Zema L., Giordano F. and Gazzaniga A. In vitro and in vivo evaluation of oral systems for time and site spesific delivery of drugs technology). Boll. Chim. Farmaceutico, 138: 68-73.
6. Suhas M. Kakade et al, Formulation and evaluation of sustain release tablets of losartan potassium by direct compression techniques. Int. J. Res. Pharm. Sci., 2010; 1(3): 290-295.
7. Lachman L, Libermann HA, Joseph L. Kanig, The Theory & Practice of Industrial Pharmacy. 3rd ed. Varghese Publishing House, Bombay.
8. Kumar S, Sachdeva M, Bajpai M, Formulation and Evaluation of Extended release Tablets Sildenafil Citrate. J. Pharma. Sci. & Tech, 2010; 2(4): 202-206.
9. Rashmi Dahima, Ashish Pachori, Sanjay Netam, Formulation and Evaluation of time- Controlled release Tablets Containing Amlodipine Besilate. Int. J. ChemTech. Res., 2010; 2(1): 706-715.
10. Yunxia Bi et al, Preparation & Evaluation of a Compressed Tablets Rapidly Disintegrating in Oral Cavity. Chem. Pharm. Bull, 1996; 44(11): 2121-2127.
11. Vineet Bhardwaj, Vikesh Shukla, Narendra Goyal, MD Salim, PK Sharma, Formulation And Evaluation of Sustain release Tablets Using Different Superdisintegrants. Int. J. Pharm. & Pharma. Sci., 2010; 2(3): 89-92.
12. Lin SY, Lin KH, Li HL. "Hydrophilic excipients modulate the time lag of time controlled disintegrating press coated tablets." American Association of Pharmaceutical science Journal, 2004; 5(4): 54.