Journal of Pharmaceutical Research International

32(38): 47-59, 2020; Article no.JPRI.63169
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Development, Feasibility Assessment and *in-vitro* Evaluation of Diclofenac Potassium Multilayered Tablets

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Authors' contributions

This work was carried out in collaboration among all authors. Author JA designed performed the study and wrote the first draft of the manuscript. Authors NHR, SM and FJS performed the statistical analysis. Authors MY, AA and SHL managed the analyses of the study. Authors YQ, JJ and ZA managed the literature searches. All authors contributed, read and approved the final manuscript equally.

Article Information

DOI: 10.9734/JPRI/2020/v32i3831012
Editor(s):
(1) Dr. R. Deveswaran, M.S.Ramaiah University of Applied Sciences, India.
Reviewers:
(1) Sohan Lal Solanki, Tata Memorial Hospital, India.
(2) Anubhav Chauhan, Shri Lal Bahadur Shastri Government Medical College, India.
(3) Debarshi Kar Mahapatra, Dadasaheb Balpande College of Pharmacy, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/63169

Original Research Article

Received 25 September 2020
Accepted 29 November 2020
Published 01 January 2021

ABSTRACT

Introduction: Diclofenac potassium has widely been utilized as an analgesic and anti-inflammatory agent. To achieve rapid onset of action with prolonged therapeutic action is an immense need of time. In present project a study was conducted on preparation with physicochemical determination

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of diclofenac potassium tablets, this unique tablet have duel characteristics like rapid onset of action due to orodispersible coat and extended release of API due to sustained release core.
Methodology: As diclofenac potassium is not sensitive to water so wet granulation method was efficiently employed to prepare the granules of sustained release core, while direct compression was done to prepare orodispersible outer coat layer in order to give rapid release.
Results and Discussion: In evaluations granules characteristics and tablet properties were studied. Result of both pre compression and post compression studies were coming in pharmacopeia acceptable ranges. The orodispersible layer disintegrated with in 18sec, which gives sufficient amount of API as loading dose, in order to maintain the plasma drug concentration in therapeutic range the core will release drug in sustained manner within 10 hours in gastrointestinal tract (GIT) fluid (pH 6.8). The results of kinetic models were complying with Higuchi model.
Conclusion: In present work, a rapid release outer dispersible layer of drug was constructed on a sustained release core. Results of study gives expected outcomes to maintained initial concentration of drug which persist for long time. The combination of sodium starch glycolate, dry starch, and cross povidone exhibited promising super disintegrant efficiency while Hydroxypropylmethyl cellulose K15 showed excellent sustained release properties.

Keywords: Diclofenac potassium; compression coating; direct compression; orodispersible coat; sustained release core; sustained release.

ABBREVIATIONS

GIT : Gastrointestinal Tract
HPMC : Hydroxypropylmethyl cellulose
USP : United States Pharmacopoeia
API : Active Pharmaceutical Ingredient

1. INTRODUCTION

Synthesis or discovery of innovative active pharmaceutical ingredients are proving to be an expensive process, which divert the attention of inventors to design diverse pharmaceutical products having released profile which modified according to require therapeutic effect. Among all pharmaceutical dosage forms, oral administration of the drug is considered as the earliest route for delivering the therapeutic agent. This route is more preferable than others due to certain reasons like convenience to use, and nontechnical. There are certain limitations also associated with the oral drug delivery system, like the massive amount of drug destroy when passing through the liver by hepatic metabolism, further harsh environment of GIT (pH and enzymes) also leads to deactivate major amount of active pharmaceutical ingredient. Enzymes and unfavorable pH impart more negative effect on some pH-sensitive agents like peptides and proteins [1,2].

To overcome the problems related to oral dosage form various strategies are being applied by a researcher, development of orodispersible dosage forms are considered as a successful step to limit the relevant problems. Orodispersible is an emerging technique to enhance the release of drug from dosage device, it gives rapid and abrupt release when place the tablet on the tongue, saliva from oral cavity penetrated tablet and interact with super disintegrant which ultimately disintegrate the tablet rapidly. Lag time for these dosage forms is very less, which is due to fast disintegration and dissolution, the dissolved amount will rapidly have absorbed through GIT lining which leads to produce a rapid action. In contrast with conventional release dosage forms, the modified release dosage forms like fast and extended-release dosage forms ensure improved patient compliance because these dosage forms are easy to use and reduce the dosing frequency, this is particularly beneficial in the case of a patient with chronic disease [3].

This novel approach advent sustained release dosage forms a good option for drugs with a narrow therapeutic window. Direct compression, wet granulation, and solid dispersion are commonly used methods for the fabrication of sustained-release tablets. To optimize the release of API from the dosage device an appropriate proportion of hydrophobic and hydrophilic polymers are necessary. The concentration of each polymer is adjusted according to the desire release rate and release patron of drug from tablets, commonly using polymer in preparation of tablets is Hydroxypropylmethyl cellulose (HPMC). Many others also available such as polyvinyl alcohol, polyvinyl pyrrolidone and carbomer etc. Preparation of a hydrophobic/hydrophilic polymeric matrix followed by uniform distribution

of the drug is considered as a simple and efficient method for extending the drug release profile. Release of drug from polymeric tablet can be achieved by two mechanisms including solvent activated drug release and gel-forming method. In the case of solvent activated drug delivery, the release carried out by absorption of body fluid by polymer leads to cause plasticization, swelling or degradation, and erosion of the polymer. While gel-forming release mechanism involves swelling of hydrophilic polymer which become plasticized and results in volume expansion in contact with GIT fluid, that causes release of drug by diffusion from the gel layer. In preparation of sustained-release tablets to achieve a rapid onset of action is a great problem, to resolve it a system has been developed to prepare domperidone tablets having sustained action coupled with a fast release which is beneficial to achieve convenient administration, and rapid response with the advantage of prolonged duration of action, simultaneously [4]. Among non-steroidal anti-inflammatory (NSAID) drug, Diclofenac is commonly used as an analgesic and antipyretic. Short duration of action in diclofenac is attributed to rapid clearance of the drug from the system which makes it a strong candidate to prepare into an extended-release dosage form to prolong the duration of action and reducing the dosing frequency which ultimately leads to enhance the patient convenience [5]. When diclofenac administers orally it absorbs completely, but due to the first-pass effect in the liver up to 50% of API will lose which causes poor bioavailability in systemic circulation, use of appropriate polymers in optimized concentration can prove beneficial in resolving the problem. To obtain a longer duration of action the prepared tablet should remain unbroken, reside for extended duration in GIT with release of drug at predetermine controlled rate [6,7]. The release of the drug from the matrix occurs as a result of interaction between the dosage form and GIT fluid by wetting, swelling, absorption, diffusion, and dissolution. Numerous hydrophilic polymers are using in preparation of water-soluble matrix among HPMC is a cellulose derivative and considered as a better option for many years in preparation of hydrophilic matrix tablets as sustained release polymer. For the preparation of rapid release formulations, the disintegrant is an integral part of the system that enhances disintegration and dissolution, sodium starch glycolate has been successfully using as a disintegrant in oral dosage form since a long time. Primogel is commonly employed in tablet development either through wet-granulation or direct-compression in various concentrations [8]. The present research work is related to the formulation and evaluation of multilayered diclofenac potassium tablet with orodispersible coating, and sustained release portion as a core.

The purpose of the present research work is to enhance the efficacy of the drug in the systemic circulation, which will provide rapid relief from pain with minimizing side and adverse effects. Various ratios of polymers (HPMC) are used to control the release of drugs from sustained-release core while sodium starch glycolate is used as disintegrate orodispersible coat for rapid release to gives quick onset of action.

2. MATERIALS AND METHODS

2.1 Materials

Diclofenac potassium (gifted from Saffron Pharmaceuticals (Pvt.) Ltd.), Lactose (DMV-Fonterra Germany), Starch (Rafhan Maze products Pakistan), HPMC K-15 (Zhongbao chemicals (Ltd.) China), Magnesium stearate (Peter Greven Asia Malysia), Cross Povidone (Basf, Germany), Primogel (Mingtai chemical, Taiwan), Avicel PH-200 (Mingtai chemical, Taiwan), Aerosil 200 (Henan Xunyu Chem Co, China), Talcum (Liaoning Jinghua new material Inc. China). All analytical grade chemicals was received as gift sample from Saffron pharmaceuticals Faisalabad, Pakistan.

2.2 Preparation of SR Layer

Active pharmaceutical ingredient diclofenac potassium, diluents lactose, and prescribed amount of polymer HPMC (Methocil) were screened through a sieve of mesh size 85. All materials blended by using a ribbon mixer, purified water were added gradually to prepare the wet mass. The wet mass was passed through a sieve no zero-mesh size, screened wet mass then transferred to SS trays and placed inside a dryer, the material was dried at 65°C a temperature. Upon completion of the drying process, the material was dry milled and sieved to achieve the desired size granules of 20 mesh. Mix magnesium stearate with excessive of HPMC K-15 and pass this mixture through 85 mesh [9]. Finally, add magnesium stearate HPMC mixture to dried granules and mix for 10 minutes in cone mixer. After accessing pre-compression parameters the mixed material was compressed by using a tableting machine. Ingredient of tablets along with quantities are enumerates in Table 1.

Table 1. Composition of sustained release core (final weight 105 mg)

Preparation	Diclofenac Potassium (mg)	Starch	Hydroxypropylmethyl cellulose (mg)	Talcum (mg)	Lactose (mg)	Mag. Stearate (mg)
FD-01	50	13.5	10	1.0	29.0	1.5
FD-02	50	11.5	12	1.0	29.0	1.5
FD-03	50	9.5	14	1.0	29.0	1.5
FD-04	50	7.5	16	1.0	29.0	1.5
FD-05	50	5.5	18	1.0	29.0	1.5

Table 2. Composition of orodispersible coat (Total weight 385 mg)

Preparation	Diclofenac Potassium (mg)	Primogel (mg)	Avicel PH200 (mg)	Cross Povidone (mg)	Aerosil 200 (mg)	Magnesium Stearate (mg)
FD-01	50	5.5	312.9	5.0	3.3	8.3
FD-02	50	10.5	307.9	5.0	3.3	8.3
FD-03	50	15.5	302.9	5.0	3.3	8.3
FD-04	50	20.5	297.9	5.0	3.3	8.3
FD-05	50	25.5	292.9	5.0	3.3	8.3

2.3 Preparation of Orodispersible Layer

To get a uniform mixture the measured mass of diclofenac potassium, then Cross povidone, Avicel 200, and Primogel were passed from sieve 85 mesh followed by 15 minutes mixing of all ingredients. The lubricant and glidant *i-e.* magnesium stearate and Aerosil 200 were added and further mixed for five minutes and tablets were compressed by the method previously used by Abbas et al., 2017 and Gohel et al., 2010 [10,11]. Precompression studies were conducted before final compression. Table 2 represents materials with quantities of Orodispersible coat.The correct way of writing is i.e.

2.4 Characterization

2.4.1 Pre-compression studies

The quality of finally prepared tablets depends mainly upon good flow properties and compactness of granules, so it is important to ensure the quality of uncompressed tablet material before compression. To assure these qualities tablet uncompressed granules were accessed for bulk density, angle of repose, tapped density, Carr's index, and Hausner ratio [12].

2.5 Tablet Evaluation

2.5.1 Physical Properties of tablets

Weight variation, diameter, and thickness of tablets are performed to ensure the uniform size of compressed tablets, as variation in size can lead to a change in the amount of API in each unit dosage form. Weight variation test was conducted on 20 tablets, which were weighted on an analytical balance, obtained results were subjected to calculate for mean and standard deviation [7]. Thickness and diameter of tablet were evaluated by using vernire caliper, test was conducted on 10 tablets, and obtained data was further computed for mean and standard deviation. The hardness of tablets is an important physical parameter as it has a great impact on disintegration, dissolution, and finally on therapeutic bioavailability. The test is performed to measure the tensile strength, in the present study test was conducted by using a digital hardness tester on 10 tablets. Obtained results were treated statistically to achieve mean and standard deviation. Friability is a test used to check the percent abrasion or shedding of material from a tablet, the test is performed to ensure the durability of the tablet during handling, blistering, storage, and transportation. Test was performed on 20 tablets in friability apparatus, mean, and standard deviation of the obtained result were calculated [13,14].

2.5.2 Disintegration time of Orodispersible layer

It is the time required to breakdown the tablets into fragments and these fragments must pass through the mesh which is present at the bottom of the tube in the disintegration apparatus. This test is performed to estimate the time taken by a tablet to break into their respective granules. Disintegration is directly proportional to dissolution and ultimately bioavailability of orally administered dosage forms. The test was performed in disintegration apparatus, by using water as disintegration media at a temperature of 37 ± 2°C. For this test, six tablets were individually placed in each tube of the basket of disintegration apparatus. The time at which the entire tablet disintegrated was noted [15].

2.5.3 Assay content

2.5.3.1 Sustained release core

This is an analytical procedure used to confirm the available concentration of the drug in the preparation. This test was performed by taking twenty individual tablets. The weight of selected tablets was noted and crushed together in the motor. An equivalent amount of crushed powder containing 50 mg of API was weighed by using an analytical balance and dispersed in a flask containing 100 ml of purified water. The mixture was heated for 30 minutes at 70°C with continuous stirring. This hot solution was cooled filtered and diluted accurately; a sufficient amount of filtrate was analyzed by using a spectrophotometer at wavelengths of 276 nm [10,16].

2.5.3.2 Orodispersible coat

To produce rapid onset of action measured drug amount has been added in orodispersible coat, amount of API in coat should also analyze to assure prescribed amount. Quantification of active pharmaceutical ingredients can be conducted by randomly selecting 10 tablets and their outer layer was detached completely from inner core and weight should be noted.

Separated coat was comminuted in motor, sufficient quantity equivalent to 50mg of API was taken, and transferred to 100 ml volumetric flask. The content was mixed in purified water by magnetic stirrer approximately for 10 minutes. From this solution one ml filtrate was withdrawn and shifted to second volumetric flask and volume was adjusted to 25ml by using purified water. The quantification was done by measuring the absorbance of solution value at 276 nm was determined using UV–Visible Spectrophotometrically [10,17].

2.5.4 *In-vitro* drug release

Amount of active pharmaceutical ingredients comes out from pharmaceutical dosage form into dissolution media, while performing test in a control environment of laboratory. In-vitro drug release test is an important evaluation as it has direct impact on *in-vivo* bioavailability. In present study USP type-II apparatus was used. Newly developed tablet having two parts inner core and outer coat, outer coat disintegrates within seconds, so it does not need to conduct release studies. Inner core without coat is subjected to perform *in-vitro* release study. The study was performed by using phosphate buffer pH 6.8 for 10 hours, the quantity of dissolution medium was 900ml in each vessel. The temperature of dissolution medium was maintained according to human body temperature *i.e.* 37 ± 0.5^{o}C throughout the process. Single tablet was put into each vessel, and paddles were rotated at 50 rpm. 5ml of dissolution medium was withdrawn after specified time interval followed by analysis by using UV-visible spectrophotometer at a wavelength of 276nm for diclofenac. The quantity of dissolution medium after withdrawal was adjusted with freshly prepared dissolution medium [18].

2.6 Release Kinetics of Drug

Various Kinetic drug release models are used to determine the release mechanism of drug from dosage device. Release amount of drug were further computed to evaluate perfect kinetic release pattern of drug, different kinetic release models with their respective equations shown bellow.

The zero-order kinetic describes the systems in which the drug release rate is independent of its concentration, Zero order rate equation $Q_t = Q_0 + K_0$ t, The first order kinetic describes the systems in which the drug release rate is concentration dependent, first order rate equation log Q_t = logQ_0 -(K/2.303) t, The Higuchi well explained the behavior of the drug release from the insoluble matrix as the square root of a time-dependent process, Higuchi model equation $Q_t = K_H$ t^(1/2), The Hixson-Crowell cube root law describes the drug release from systems in which there is a change in the surface area and the diameter of a particle present in formulation, Hixon – Crowell model Q_0 ^(1/3)-Q_t ^(1/3)=Kt. In the case of Korsmeyer-Peppas model, the drug release from such devices having constant geometry will be observed till the polymer chains rearrange to an equilibrium state, Korsmeyer Peppas Equation $Q_t / Q_\infty = K_t$ ^n [19].

3. RESULTS AND DISCUSSION

3.1 Evaluations of Granules

Flowability of material before compression is an important property, as it has a great impact mostly on the physical parameters of final compressed tablets. In this work angle of repose was measured and obtained results for orodispersible granules and sustained release granules were up to 31°C and 30°C respectively. The results represent that concerning flowability material fall in a good range. Results of the study are mentioned in Tables 3 and 4. The Carr's index values were founded up to 20 and 20.62 for both granules respectively. Carr's index result co-related with Hausner's ratio, the obtained results showed less than 1.25 and 1.22, respectively [20].

3.2 Compressed Tablet Characterization

3.2.1 Physical characterization of obtained tablets

In physical parameters, tablets were checked for their weight variation, thickness, and hardness. Results of the study shown that the weight of prepared tablet was 490 ± 1- 1.22% while 105 ± 1% for sustained release core, thickness was 5.10mm-5.15mm while 3.10mm–3.21mm for sustained release core,. Hardness of tablet was tested to estimate the possible effect on the drug release from a tablet, as hardness in inversely proportional to disintegration of tablets [21,22].

Table 3. Pre-Compressional properties of diclofenac potassium sustained release core granules

Preparation	Bulk Density (g/cc)	Tapped Density (g/cc)	Carr's Index (%)	Angle of Repose (°)	Hausner Ratio
FD-01	0.87	1.08	19.44	30	1.24
FD-02	0.85	1.05	19.04	31	1.25
FD-03	0.86	1.05	18.10	29	1.22
FD-04	0.88	1.07	17.76	30	1.22
FD-05	0.86	1.06	20.00	29	1.23

All obtained data was calculated as mean average± standard deviation (n= 3)

Table 4. Pre-Compressional properties of orodispersible coat granules

Preparation	Bulk Density (g/cc)	Tapped Density (g/cc)	Angle of Repose (°)	Carr's Index (%)	Hausner Ratio
FD-01	0.96	1.15	29	19.80	1.20
FD-02	0.96	1.13	30	17.71	1.18
FD-03	0.94	1.15	29	18.26	1.22
FD-04	0.97	1.17	29	20.62	1.21
FD-05	0.96	1.14	29	18.75	1.19

All obtained data was calculated as mean average± n= 3

The obtained results for hardness come in the range of 3.40Kg/cm^3-5.00Kg/cm^3. Friability was under the limit of 0.5%. Disintegration time the orodispersible portion of all produced formulations obtained in the range of 18-60sec [23]. The obtained results confirm that the formulation FD-05 was within the specified limits according to USP, 2017 and showed in Tables 5 and 6.

3.2.2 Assay content of API

Assay content was measured to quantify the drug in finally compressed tablets. The obtained result for sustained release core of all formulations falls in range of 97.83% to 99.95% while in case of orodispersible coat obtained result falls in between 91.20% to 99.33% [24]. Result of assay content is mentioned in Tables 5 and 6.

3.2.3 Dissolution studies

In-vitro dissolution studies are performed to predict *in-vivo* activity of prepared dosage form. Result of *in-vitro* dissolution studies is shown in Table 7, obtained results elaborate that drug release from all formulation matrixes become zero at start of dissolution in simulated dissolution media. Further by starting the process of dissolution release of API start and proceed according to predetermined parameter. The results of release profile founded in good agreement with study conducted by Kramar, et al., 2003 [25,26]. The obtained percent amount of drug release is listed Table 7. Variation in HPMC K15 percent concentration in all formulations FD-01 - FD-05 imparts profound effect on release of drug form matrix.

3.3 Release Kinetics of Drug

The Correlation coefficient values after using different release kinetic models [27,28] are showed in following table i.e. Table 8. While Fig. 3A-3E representing the drug release pattern for selected formulation (FD-05).

Table 5. Physical characterization and assay result of diclofenac potassium SR core

Preparation	Average weight (mg)	Thickness (mm)	Hardness (Kg)	Friability (%)	Assay (%)
FD-01	104	3.12	4.50	0.30	97.83
FD-02	106	3.15	3.75	0.25	98.10
FD-03	105	3.10	3.40	0.32	99.28
FD-04	105	3.21	4.50	0.38	99.02
FD-05	106	3.19	4.20	0.22	99.95

All obtained data was calculated as mean average± n= 3

Table 6. Final tablet characterization results

Preparation	Average Weight	Thickness (mm)	Hardness (Kg)	Friability (%)	Disintegration Time of Orodispersible layer (Sec)	Assay of Orodispersible layer (%)
FD-01	490.8	5.15	4.70	0.42	60	91.20
FD-02	491.4	5.10	4.30	0.48	60	90.46
FD-03	490.2	5.15	4.70	0.39	50	93.08
FD-04	491.1	5.10	4.90	0.50	35	95.45
FD-05	490.3	5.15	5.00	0.40	18	99.33

All obtained data was calculated as mean average± n= 3

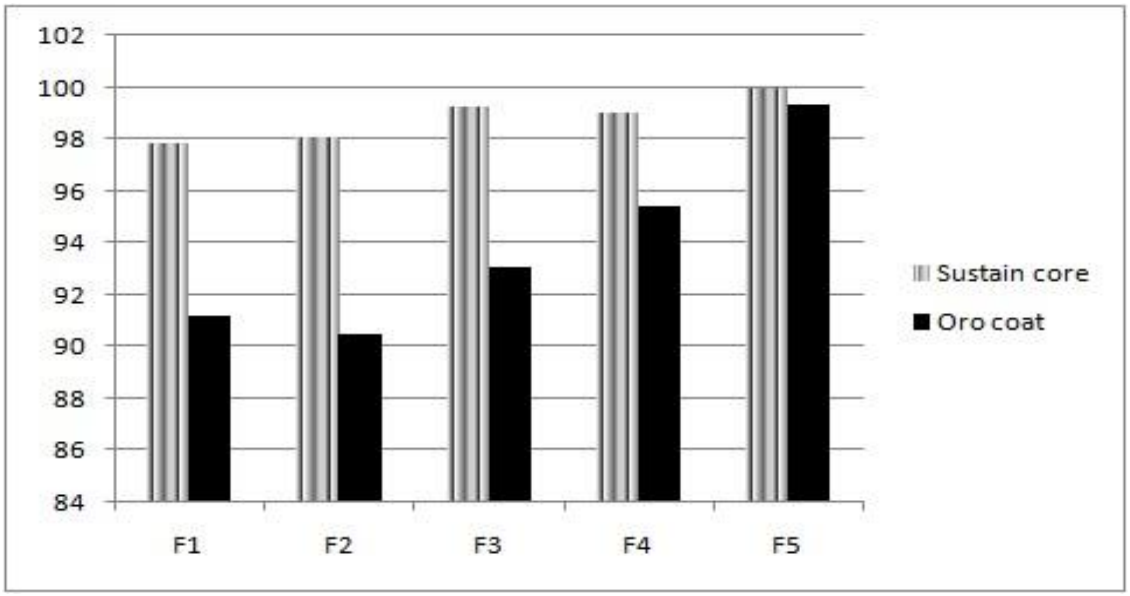


Fig. 1. Assay result of Diclofenac Potassium Orodispersible coat and Sustained release core)

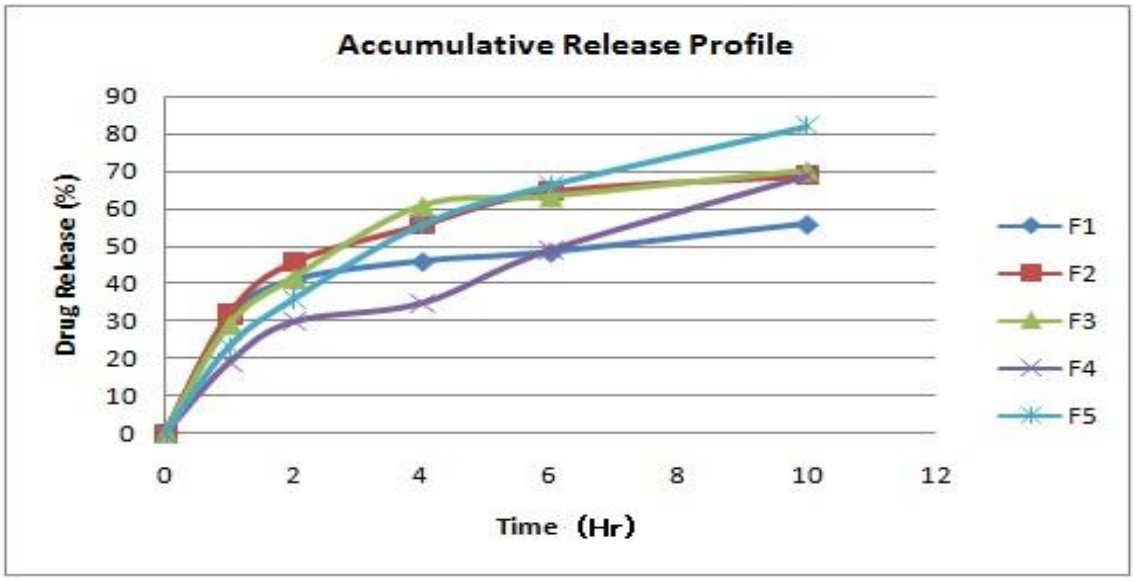


Fig. 2. Combined drug release profile of all formulations from FD-01 to FD-05

Table 7. Combined dissolution result of SR core

Preparation	Drug release %					
	0 hr	1st hr	2nd hr	4th hr	6th hr	10th hr
FD-01	0%	30.89	40.81	45.86	48.31	55.8
FD-02	0%	31.84	45.73	55.78	64.69	68.92
FD-03	0%	29.05	41.55	60.79	63.31	70.23
FD-04	0%	18.93	29.84	34.81	49.01	68.84
FD-05	0%	23.15	35.79	55.63	66.20	81.93

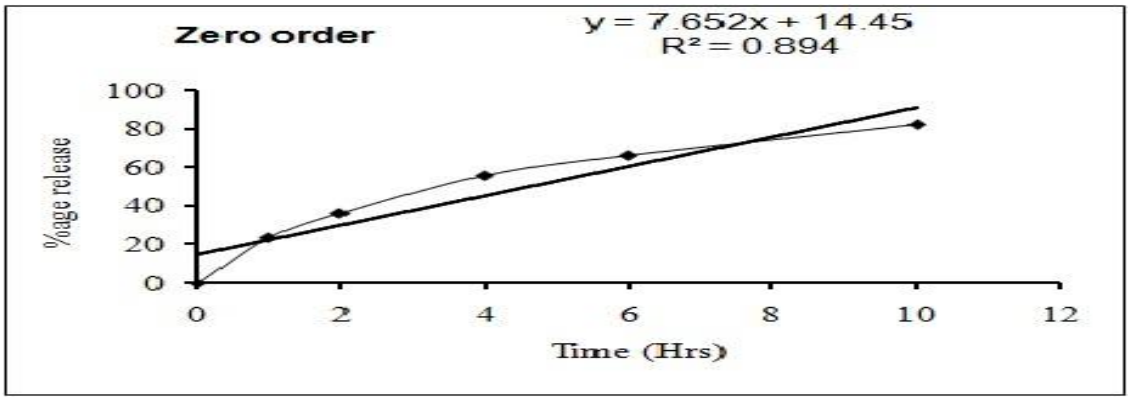
All obtained data was calculated as mean average± n= 3

Table 8. Different drug release kinetic models

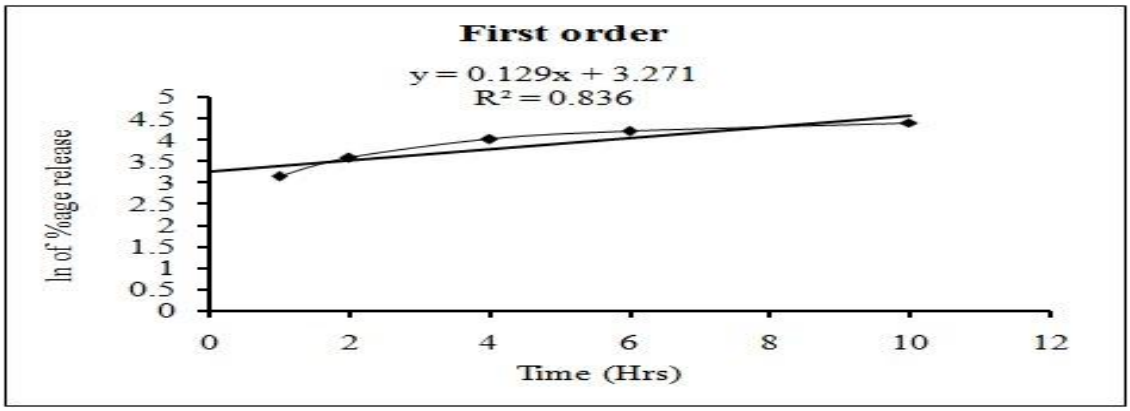
Preparation	Zero order Model		First order Model		Higuchi Model		Hixson-Crowell Model		Korsmeyer Peppas Model	
	Y	R^2	Y	R^2	Y	R^2	Y	R^2	Y	R^2
FD-01	4.272	0.634	0.131	0.068	16.762	0.886	0.014	0.015	0.728	0.121
FD-02	5.817	0.711	0.076	0.759	22.153	0.937	0.134	0.802	0.337	0.960
FD-03	6.129	0.737	0.088	0.73	23.03	0.944	0.142	0.817	0.393	0.946
FD-04	6.220	0.938	0.132	0.925	21.116	0.981	0.138	0.974	0.533	0.971
FD-05	7.652	0.895	0.129	0.836	26.782	0.995	0.195	0.973	0.557	0.991

All obtained data was calculated as mean average± n= 3

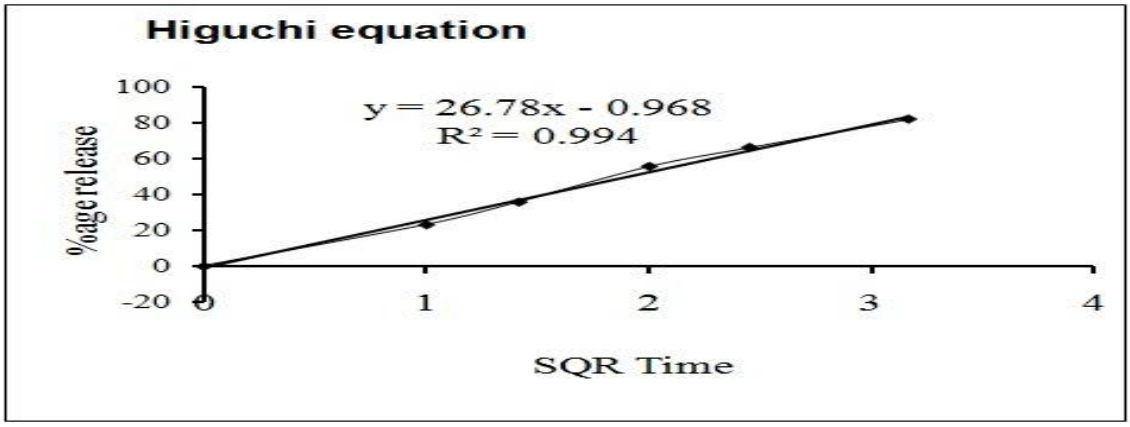
Release kinetic models of optimized formulation (FD-05)



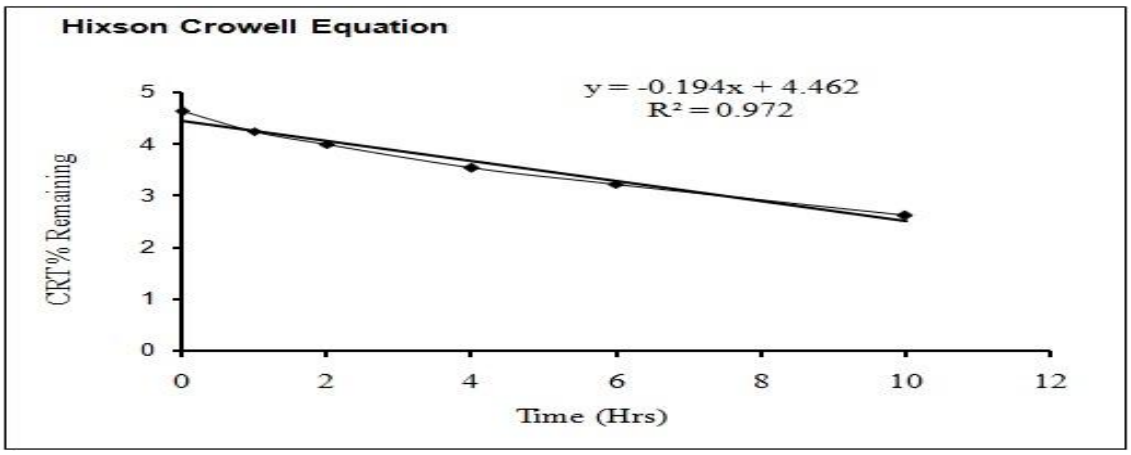
3(A). Formulation Zero order release kinetic



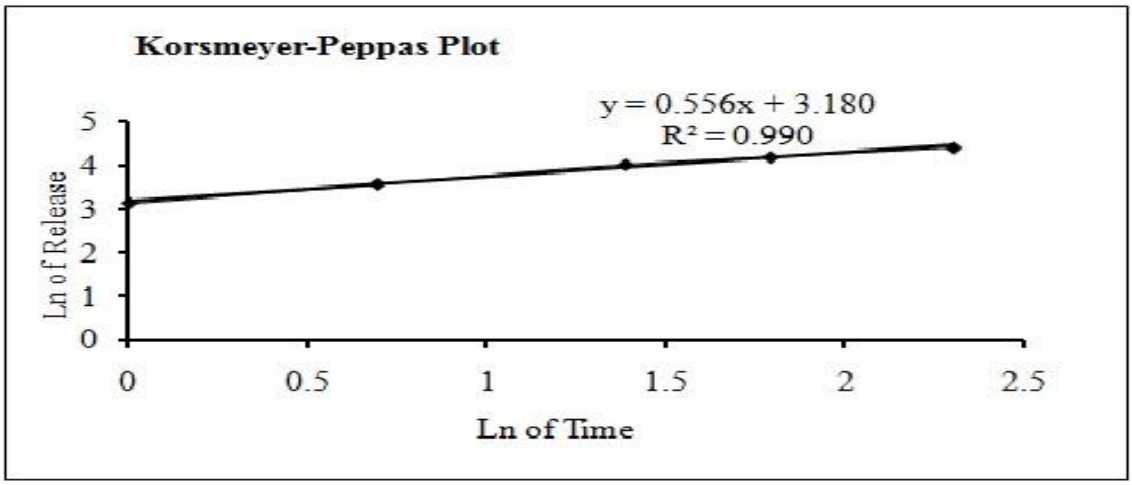
3(B). Formulation first order release kinetic



3(C). Formulation Higuchi release kinetic



3(D). Formulation Hixson Crowell release kinetic



3(E). Formulation Korsmeyer-Peppas release kinetic

Fig. 3A-E.

4. DISCUSSION

In the administration of extended-release dosage forms, rapid onset of action is a great problem, because these types of dosage units are dissolved by taking time due to the presence of hydrophobic entities. In present research an effort has been made to prepare a tablet having a combination of sustained effect and produce immediate effect also. This may be possible by preparing a dosage device which having sustained release and rapid release properties simultaneously. Dosage forms design to administer orally must be prepared by focusing on the solubility of the drug in various regions of GIT, based upon pH and gastric motility every portion of GIT having different solubility. Weakly acidic drug in their salt forms shows profound solubility in comparison to free acidic form. Three form of Diclofenac is available which includes potassium and sodium salts as well as in free acid form also. Now a day's commonly available forms of diclofenac are potassium or sodium salt, due to their excellent solubility as compare to free acid forms. The usually available dosage form of diclofenac is sustained release, delayed-release (Potassium and sodium salts), and rapid release (Potassium salt). Diclofenac with potassium salt is considered to have greater solubility then sodium salt that is why it is proffered to use in rapid-release formulation. A newly prepared novel tablet of diclofenac potassium is prepared having an orodispersible coat to give fast release in mouth and to provide repeated action it is also formulated as sustained release core. Presently researchers are focusing on the development of dosage forms that disintegrate and dissolve in the mouth, as it has advantaged that mouth having spongier and porous membrane which allow permeating drug more rapidly and efficiently, rest of drug pass into GIT. Super-disintegrants including cross povidone and primogel are an integral part of rapid release preparations, numerous studies are available on the capability of an agent to disintegrate and affect drug release. Polymers such as HPMC frequently used to sustained or extend the release of API from dosage unit, both hydrophilic and hydrophobic polymers are effectively used and imparts great effect on drug release [29].

Commonly there are two possible mechanisms for the breakdown of tablets imparted by super disintegrant swelling and capillary action. Sodium starch glycolate and crosspovidone are mostly used as a super disintegrant for rapid release dosage forms, having a certain advantage over the others, like nontoxic, inner, and very short disintegration time. The combination of supper disintegrants *i.e.* crosspovidone and sodium starch glycolate was used in the present work showed promising super-disintegrant qualities permitting the tablet to break within a short period in seconds without incorporation of any solvent. The incorporated amount of super-disintegrants showed a profound effect on disintegration time, change in time was observed with little variation in the amount of disintegrants. From results, it was concluded that formulation FD-05 is optimized preparation because it showed promising results in comparison to other formulations. The result of formulation FD-05 showed that as the amount of super disintegrant primogel was increase to 25.5 mg/tablet it reduces the disintegration time to 18 seconds, while formulations with less amount of Primogel (FD-01 to FD-04) showed an increase in disintegration time. HPMC is a unique polymer it shows gelling properties when coming in contact with intestinal fluid, this phenomenon proves helpful in the sustained effect of drug molecule from the polymeric matrix. The obtained results regarding in-vitro evaluations revealed that HPMC K15 should be used as the polymer of choice in preparation of diclofenac potassium sustained-release tablets. The results of FD-05 formulation are in good acceptable range of USP 2017 that is drug should not be released less than 65% after 10 hours' dissolution study [30]. The amount of polymer concerning the amount of drug showed great importance to sustain the drug release from the polymeric matrix. During the development of tablets, the direct compression method proved to be an effective method for the preparation of orodispersible tablets.

5. CONCLUSION

In the present project, a multilayered dosage device with a dual release pattern i.e. rapid and sustain release was developed in form of solid tablets. The sustained release formulation having a major disadvantage of delayed onset of action, to overcome this problem in the present formulation a rapid release orodispersible coat was constructed on the outermost portion of the tablet. Prepared tablets were evaluated for physicochemical and in-vitro studies, finding revealed that sustaining effect of the drug was successfully achieved by using the optimum concentration of hydroxypropylmethyl cellulose while rapid release effect of the drug from the

outer core was successfully achieved by the combination of cross povidone and primogel.

In the future, the prepared formulation can effectively use to relieve the pain in a rapid manner for a prolonged period. Further In-vivo evaluations with pharmacokinetic parameters and stability studies are recommended to conduct. Finally, before the market, clinical studies are also needed to conduct of newly formulated novel dosage device. This unique idea of dual release pattern will provide a new window in dosage form sciences.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/63169