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SUSTAIN RELEASE FORMULATION, AND EVALUATION OF CIPROFLOXACIN SUSTAIN RELEASE TABLET AND ITS COMPARISON WITH MARKET PRODUCT

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ABSTRACT: In this study, an attempt was made to design and evaluate oral sustained release matrix tablets of ciprofloxacin using methocel K4M CR, HPMC 15 cps, avicel PH 101 as the retardant polymer. Tablets were prepared by conventional wet granulation technique. Tablets were evaluated for parameters such as weight variation, hardness, friability, and drug content. All the formulations showed compliance with pharmacopeial standards. In vitro release studies were performed using USP type II apparatus (paddle method) in 900 ml of 0.1N HCl at 50 rpm for 8 h. The release kinetics was analyzed using the zero-order, first order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas equations to explore and explain the mechanism of drug release from the matrix tablets. In vitro release studies revealed that percent drug release decreased with increase of polymer loading. Based on the dissolution data comparison with innovator brand F-5 formulation (16% Methocel K4M CR w/w of drug) was elected as the best formulation. The drug release profile of the best formulation was well controlled and uniform throughout the dissolution studies.

Keywords: Sustain release, Ciprofloxacin HCl, Formulation and Evaluation, *In-vitro* release study, Drug release kinetics

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INTRODUCTION: In the last two decades, sustained-release dosage forms have made significant progress in terms of clinical efficacy and patient compliance [1]. Conventional tablets are the most popular and available oral solid formulations that are preferred by physicians and patients [2]. But conventional tablet formulations are not ideally suited to some drugs having high solubility in low pH and short plasma half-life [3].

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The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve the desired drug concentration. That is, the drug-delivery system should deliver the drug at a rate dictated by the needs of the body throughout treatment [4]. This idealized objective points to the two aspects most important to drug delivery, namely, spatial placement and temporal delivery of a drug. Spatial placement relates to targeting a drug to a specific organ or tissue, while temporal delivery refers to controlling the rate of drug delivery to the target tissue [5].

The bulk of research has been directed at oral dosage forms that satisfy the temporal aspect of drug delivery, but many of the newer approaches under investigation may allow for spatial placement

as well as [6, 7]. Modern drugs are rarely administered in pure chemical form. Rather, they are prepared in a vehicle called a drug delivery system [8]. Thus, depending on the route of administration and therapeutic objectives, the drug delivery systems can be categorized as [9]-

A) Conventional Drug Delivery Systems:

- Solids
- Liquids
- Semisolids

B) Controlled-Release Drug Delivery Systems:

- Sustained release
- Prolonged release
- Pulse-release
- Constant release

C) Novel Drug Delivery Systems:

- Targeted
- Self-regulated
- Biofeedback
- Biological carriers

Most conventional dosage forms function merely to place a drug at the site of administration and pay no regard to the regulation of release and absorption or the duration and targeting of drug in the body [10]. With many drugs, the basic goal of therapy to achieve a steady-state blood level or tissue level that is therapeutically effective and nontoxic for an extended period. The design of proper dosage regimens is an important element in accomplishing this goal. A basic objective in dosage form design is to optimize the delivery of medication to achieve a measure of control of the therapeutic effect in the face of the uncertain fluctuations in the *in-vivo* environment in which drug release takes place 11.

So nowadays one of the most active areas of research and development in drug delivery involves -controlled release products rather than develop new drug entities at great cost; as some drug therapies already on the market can be improved simply by controlling the rate at which they enter the bloodstream. The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians alike [12]. In long term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses and therefore, have several disadvantages. Controlled release (CR) tablet formulations are preferred for such therapy because they offer better patient compliance, maintain uniform drug levels, reduce dose and side effects, and increase the safety margin for high-potency drugs [13].

Joseph R. Robinson has claimed in the book 'Sustained and controlled release drug delivery systems, "Drug delivery must be continued at a rate such that the condition in question is cured or controlled in minimum time with the fewest side effects. Thus, an appropriate definition of controlled drug release is as follows: It is the phasing of drug administration to the needs of the condition at hand so that an optimal amount of drug is used to cure or control the condition in a minimum time [14].

In some situations, this might mean that drug is delivered more promptly for short periods, and in other cases, it would mean prolongation of drug levels. In the latter category we employ the terms 'sustained release' and 'prolonged-release' interchangeably this designates only one aspect of controlled release, namely, to produce protracted levels of the drug in the body" [15, 16, 17].

MATERIALS AND METHODS:

TABLE 1: REAGENTS AND SOLVENTS USED, WHICH WERE USED IN THE EXPERIMENT ARE AS FOLLOWS:

S. no.	Name	Source
1	Ciprofloxacin HCl	Incepta Pharmaceuticals Limited, Bangladesh
2	Methocel K15 M CR	Incepta Pharmaceuticals Limited, Bangladesh
3	Avicel PH 101	Veer Pharma Chem, Ahmedabad, India
4	Magnesium Stearate	Chemical Management Co. Germany
5	Hydrochloric acid	Merck, Germany.
6	HPMC 15 CPS	Eskayef Bangladesh Ltd.
7	Purified Talc	Wilfrid Smith Ltd, UK

Methodology:

Preparation of Sustained Release Granules: For tablet preparation, we have to make the sustain release granules. Ciprofloxacin hydrochloride, HPMC 15 CPS, Mithocel K 15 M CR & Lactose has been used to make granules.

TABLE 2: LIST OF APPARATUS USED IN THIS EXPERIMENT ARE AS FOLLOWS

S. no.	Name	Source	Country of origin
1	Electronic Balance	Shimadzu Corporation	Japan
2	Single Punch Compression Machine	Manesty	England
3	Tablet Dissolution Appararus	Veego	Japan
4	UV-Vis Spectrophotometer	Shimadzu	Japan
5	PH meter	Eutech Instrument	Singapore
6	Digital Veneer Caliper	SDK	China
7	Sonicator	Hwashin Technology	Korea

TABLE 3: COMPOSITION OF SUSTAINED RELEASE GRANULES

S. no.	Ingredients (mg/tablet)	Sustained release granules 1	Sustained release granules 2
1	Ciprofloxacin Hydrochloride	2.5 gm	2.5 gm
2	HPMC 15 CPS	2 gm	-
3	Mithocel K 15 MCR	-	2 gm
4	Lactose	0.5	0.5

Evaluation of Granules:

Bulk Density: LBD (Loose bulk density) and TBD (Tapped bulk density) were determined by placing 2 g of powder from each formula (previously lightly shaken to break any agglomerates formed) into a 10-ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its weight onto a hard surface from the height of 2.5 cm at 2-second intervals. The reading of tapping was continued until no further change in volume was noted. Using the following equation, LBD and TBD was calculated:

LBD = Weight of the powder/volume of the packing

TBD = Weight of the powder/Tapping volume of the packing

Compressibility Index: The compressibility index of the granules was determined by Carr's compressibility index:

Carr's index (%) = {(TBD – LBD) × 100}/ TBD

The Angle of Repose: The angle of repose is the maximum angle that can be obtained between the freestanding surface of a powder heap and the horizontal plane. Such a measurement gives a qualitative assessment of the internal cohesive and frictional effects under low levels of external loading, as might in powder mixing, or tablet die or capsule shell filling operations. It was measured by fixed funnel and freestanding cone method as reported by Raghuram *et al.,* Accurately weighed powders of each formulation (excluding talc and magnesium stearate) were carefully poured through the funnel stationed on a clamp with its tip at 2 cm height, H from the base, until the apex of the conical heap so formed just reached the tip of the funnel. The mean diameter, 2R, of the base of the powder cone was measured, and the angle of repose (θ) was calculated using the following equation:

$$\tan \theta = H/R$$

TABLE 4: U.S PHARMACOPOEIA HAS CLASSIFIED FLOW PROPERTIES OF POWDER BASED ON ANGLE OF REPOSE

Flow property	Angle of repose (degree)
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable-may hang up	41-45
Poor- must agitate, vibrate	46-55
Very poor	56-65
Very, very poor	>66

The values for the angle of repose were found to range from 30^{o}-35^{o}. This indicates fairly good flow properties of powders, through the feed hopper into the die cavity of the tablet punch machine. However, it is advisable to use glidants and lubricants to facilitate its passage through the hopper without any hindrance.

Studies of Bulk and Tapped Densities: The US Pharmacopoeia (USP) makes the following comments on powder density: "The bulk density often is the bulk density of the powder 'as poured' or as passively filled into a measuring vessel. The tapped density is a limiting density attained after 'tapping down' usually in a device that lifts and drops a volumetric measuring cylinder containing the powder a fixed distance". Both poured (or fluff) bulk (Do) and tapped densities (Df) was determined using a tensiometer, using USP-2 method.

Accurately weighed powders from each formulation, previously lightly shaken to break any agglomerates formed, were introduced into a 10 ml measuring cylinder. After the initial volume, Va was recorded, the initial tappings of 500 taps were allowed to begin.

After an initial of 500 taps, the volume, Vb, was noted. Then after, the second round of tapping of 750 taps started. The volume, Vf was again noted. If the difference between the last two volumes was equal or greater than 2%, then a final tapping of 1250 times was allowed until the difference remained less than 2%. Bulk and tapped densities were estimated using the following formula:

Bulk density= M/ Va

Tapped density= M/Vf

Where, Va= poured volume Vf= final volume after tapping M= mass of the powder blend

Preparation of Sustain Release Tablet: For the preparation of tablet, we sieve the excipients and active material and make the granules and dry it by the oven. Then compressed the granules by single punch machine. After that, we got the double-layered tablet. In this research work, the drug release pattern from various formulations (based on hydrophilic matrix system) was observed to identify the probability of certain hydrophilic polymer as sustaining agents for drug release. With a view to this, 5 probable formulations were designed. Here ciprofloxacin was taken as a model drug.

Formulation:

TABLE 5: COMPOSITION OF IMMEDIATE LAYER

S. no.	Ingredients	Amount (mg/tablet)
1	Ciprofloxacin hydrochloride	2.5 gm
2	Avicel PH 101	2 gm

TABLE 6: COMPOSITION OF SUSTAINED LAYER

S. no.	Ingredients (mg/tablet)	F1	F2
1	Ciprofloxacin hydrochloride	2.5 gm	2.5 gm
2	HPMC 15 CPS	2 gm	-
3	Mithocel K 15 M CR	-	2 gm
4	Lactose	0.5	0.5

TABLE 7: DIFFERENT TYPES OF FORMULATIONS USING DIFFERENT TYPES OF POLYMERS

Granules	F1	F2	F3	F4	F5
Immediate release	450	450	450	450	450
HPMC 15 CPS	516	-	258	172	344
Mithocel K 15 M CR	-	516	258	344	172

FIG. 1: DIFFERENT TYPES OF DIFFERENT FORMULATED TABLETS OF F1, F2, F3, F4 AND F5

For the preparation of tablet, we sieve the excipients and active material and make the granules and dry it by the oven. Then compressed the granules by single punch machine. After that, we got the double-layered tablet.

Measurement of Some Physical Parameters Matrix Tablets: The tablets of each formulation were tested for certain physical parameters, *e.g.* hardness and tensile strength, thickness, diameter, friability, etc. Before compression of the tablets, the powders were examined for their angle of repose to gather knowledge about the flow properties of the powder.

Thickness Measurement: Five tablets of each of the formulations were taken, and thickness was measured by digital Vernier Caliper. The values were reported in millimeter (mm). Mean was calculated.

Diameter Measurement: Similarly, six tablets of each of the formulations were taken, and their diameters were measured by Vernier Caliper. The

values were reported in millimeter (mm). Mean was calculated.

The Average Weight of the Dosage Unit: 10 tablets of each formulation were weighed using an electronic balance. Weight values were reported in mg. Mean values were calculated.

Preparation of Dissolution Media: After preparation a tablet then we prepare a dissolution media. Dissolution media was 0.1 N HCl, PH was 1.2.

***In-vitro* Dissolution Test:**

***In-vitro* Release Studies:** For dissolution simulated gastric medium (pH 1.2) prepared by mixing 8.6 ml of hydrochloric acid (37% w/v) with sufficient water to produce 1000 ml was used. The release rates of ciprofloxacin sustain release tablet was determined using US FDA Dissolution Guideline. Dissolution Testing Apparatus was apparatus 2 (paddle method). The dissolution test was performed using 900 ml medium at 37 ±0.5 °C and 50 rpm. The medium was preheated to 37 °C, added to the vessels and was allowed to equilibrate for 15 min. Six tablets from each formulation were weighed and placed in the baskets. The operation was carried out for 8 h. After every 2 h, 10 ml of sample solution was withdrawn and filtered. The released drug was assayed by using UV spectrophotometer (Shimadzu, Model UV-160A, Kyoto, Japan) at 276 nm after suitable dilution. The amount of drug present in the samples was calculated from calibration curves constructed from the standard solution of the reference standard.

Drug Release Kinetics: To study the release kinetics, data obtained from in vitro drug release study were tested with the following mathematical model.

Zero-Order Equation: The equation assumes that the cumulative amount of drug release is directly related to time. The equation may be as follows:

$$C = K_0 t \quad (1)$$

Where, K_0 is the zero order rate constant expressed in unit concentration/time, and t is the time an hour. A graph of concentration vs. time would yield a straight line with a slope equal to K_0 and intercept the origin of the axes.

First Order Equation: The release behaviour of first-order equation is expressed as the log cumulative percentage of drug remaining vs. time. The equation may be as follows (Wagner, 1969):

$$Log\ C = Log\ C_0 - kt / 2.303 \quad (2)$$

Where, C = The amount of drug un-dissolved at t time, C_0 = Drug concentration at t =0, k = Corresponding release rate constant.

Higuchi Square Root Law: The Higuchi release model describes the cumulative percentage of drug release vs. square root of time. The equation may be as follows (Higuchi, 1961):

$$Q = K\sqrt{t} \quad (3)$$

Where, Q = the amount of drug dissolved at time t. K is the constant reflecting the design variables of the system. Hence, the drug release rate is proportional to the reciprocal of the square root of time.

Hixson-Crowell Cube Root Law: It is the law that represents the idea about the evaluation of drug release pattern changes with the surface area and the diameter of the particles/tablets (Hixon *et al.*, 1931). It is mentioned as the cube root of the percentage of drug remaining in the matrix *vs.* time. The equation may be as follows

$$Q_0\ 1/3 - Q_t\ 1/3 = k_{HC} \times t \quad (4)$$

Where Q_0 = Initial amount of the drug in the tablets. Q_t = the amount of drug release in time 't.' k_{HC} = The rate constant for the Hixson-Crowell cube root law.

Korsmeyer–Peppas Equation: Korsmeyer *et al.*, developed a simple, semi-empirical model relating exponentially the drug release to the elapsed time. The equation may be as follows:

$$Q/Q_0 = Kt^n \quad (5)$$

Where Q/Q_0 = The fraction of drug released at time_t'. k = Constant comprising the structural geometric characteristics. N = The diffusion exponent that depends on the release mechanism.

If $n \leq 0.5$, the release mechanism follows a Fickian diffusion, and if $0.5 < n < 1$, the release follows a non-Fickian diffusion or anomalous transport

(Peppas, 1985). The drug release follows zero order drug release and case II transport if n=1. But when n>1, then the release mechanism is super case II transport. This model is used in the polymeric dosage form when the release mechanism is unknown or more than one release phenomena is present in the preparation.

Swelling Index: Tablets composed of polymeric matrices form a gel layer around the tablet core when they come in contact with water. This gel layer governs the drug release. The kinetics of swelling is important because the gel barrier is formed by water penetration. Swelling indices of tablets of each formulation were determined at the time intervals of 1, 3, and 7 h. 3 tablets of each formulation were initially weighed and carefully placed on Petri dishes, labelled 1, 3 and 7 respectively, all containing pH 6.8 phosphate buffers. The temperature is maintained at about 37°C. At every assigned time intervals, the tablets were removed from the Petri dishes, the surface liquid was carefully removed by tissue paper and reweighed to assess weight gain of the swollen tablets. Swelling index for each tablet is then determined by using the formula:

$$\% \text{ Swelling} = S/R \times 100$$

Where, S= weight of the matrix after swelling, R= weight of the eroded tablet

The visual demonstration of the swelling process of the different formulations at different times of the investigation aid to get a proper understanding of the process.

Initial Weight:

1. 900 mg
2. 910 mg
3. 933 mg
4. 892 mg

Weight after Swelling:

S 1 =1.130 gm
S 3 = 1.296 gm
S 7= 1.300 gm

Weight of Eroded Tablet:

R 1= 0.905 gm
R 3= 0.977 gm

% swelling = S/R × 100

= 124.862 (after 1 h)
=132.650 (after 3 h)

Erosion Index: Similarly, the erosion indices of the tablets of each formulation were determined in the above set up, only this time the tablets were dried in a vacuum oven at 40°C for 2.5 h and reweighed after drying. Erosion index is calculated using the formula:

$$\% \text{ erosion} = (T-R/T) \times 100$$

Where, T= initial weight of the tablet, R=weight of the eroded tablet

The visual demonstrations of erosion of polymer matrix observed in different formulations during different times of the investigation are provided as follows.

FIG. 2: DISPERSION OF F-1 MATRIX TABLET IMMEDIATELY AFTER BEING PLACED IN THE AQUEOUS FLUID

FIG. 3: DISPERSION OF F-2 MATRIX TABLET IMMEDIATELY AFTER BEING PLACED IN THE AQUEOUS FLUID

FIG. 4: F-3 TABLET AFTER 1 h OF SWELLING

FIG. 5: F-3 TABLET AFTER 3 h OF SWELLING

FIG. 6: F-3 TABLET AFTER 7 h OF SWELLING

FIG. 7: F-1 TABLET DEPICTING EROSION AFTER 1 h OF STUDY

FIG. 8: F-2 TABLET DEPICTING EROSION AFTER 1 h OF STUDY

FIG. 9: F-3 TABLET DEPICTING EROSION AFTER 1 h OF STUDY

FIG. 10: F-4 TABLET DEPICTING EROSION AFTER 3 h OF STUDY

FIG. 11: F-5 TABLET DEPICTING EROSION AFTER 3 h OF STUDY

FIG. 12: F-6 TABLET DEPICTING EROSION AFTER 3 h OF STUDY

FIG. 13: F-3 TABLET DEPICTING EROSION AFTER 7 h OF STUDY

RESULTS AND DISCUSSION:

Characterization of Granules: The granules of different proposed formulations (F-1 to F-5) were evaluated for LBD, TBD, compressibility index, and angle of repose **Table 8**. The results of LBD ranged from 0.200 to 0.620 g/cm^3 and TBD ranged from 0.313 to 0.911 g/cm^3 respectively. The bulk densities of granules of the proposed formulation were quite higher than those of other granules. This may be due to the presence of more fine granules.

TABLE 8: PHYSICAL PROPERTIES OF GRANULES

Parameters	Starch	Avicel pH 101	Lactose	HPMC 15 cps	Talc	Mg. Stearate	Methocel K 15 MCR
LBD (g/cm^3)	0.456	0.361	0.620	0.440	0.510	0.200	0.300
TBD (g/cm^3)	0.589	0.451	0.721	0.564	0.911	0.313	0.469
Compresibility Index %	22.5	20	14	22	44	36	36
Angle of Repose	33.69	45	48.01	33.69	37.56	37.56	35.53

The results of compressibility index (%) ranged from 14 to 44 generally, compressibility index values up to 15% result in good to excellent flow properties. So the granules showed good flow properties than other granules. The results of the angle of repose ranged from 33 to 48. The results of the angle of repose (<30) indicate good flow properties of granules, which was supported the results found from compressibility index. All these results indicate that the granules possessed satisfactory flow properties and compressibility.

Physicochemical Evaluation of Matrix Tablets: The results of physical parameters (weight, hardness, thickness, and friability) and drug content of the prepared matrix tablets are shown in this study. The thickness of the tablets was found between 5.42 mm to 5.23, the hardness of the tablets ranged from 382 N to 379 N and diameter 13.02 mm to 12.82 mm.

The weight variations of prepared tablets complied with the pharmacopoeial specifications. The drug content of every formulation was found about 100% of the labelled content. So it can be said that physical properties and drug content of the compressed matrix tablets were satisfactory.

TABLE 9: COMPARISON OF HAUSNER RATIO AND COMPRESSIBILITY INDEX (IN PERCENT) OF DIFFERENT FORMULATIONS

Comparison of Hausner Ratio and Compressibility Index (in percent) of Different Formulations		
Material	**Hausner Ratio**	**Compressibility Index (in percent)**
Starch	1.290	22.5
Avicel pH 101	1.250	20
Lactose	1.163	14
HPMC 15 cps	1.282	22
Talc	1.786	44
Mg Stearate	1.563	36
Methocel K 15 MCR	1.563	36

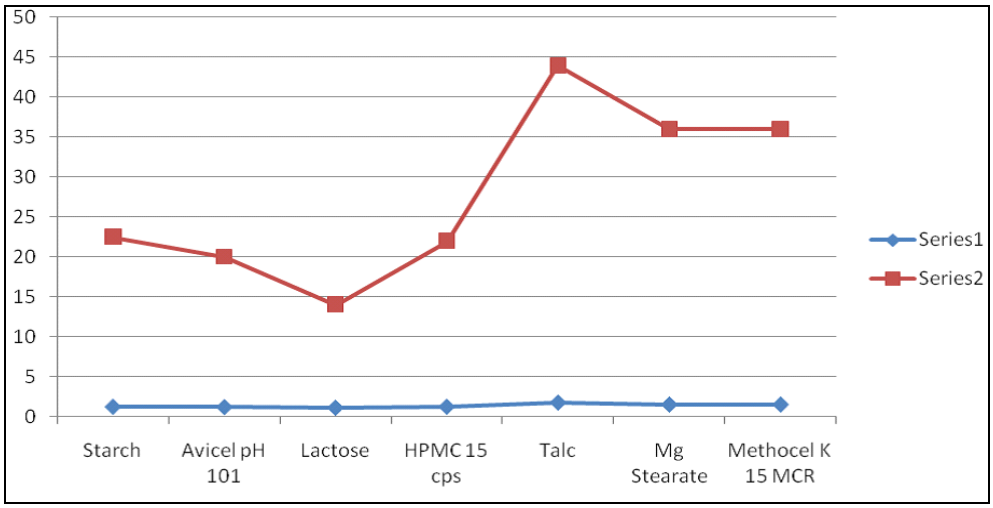

FIG. 14: COMPARISON OF HAUSNER RATIO AND COMPRESSIBILITY INDEX (IN PERCENT) OF DIFFERENT FORMULATIONS

TABLE 10: COMPARISON OF BULK DENSITY (gm/cm^3) AND COMPRESSIBILITY INDEX (IN PERCENT) OF DIFFERENT FORMULATIONS

Comparison of Bulk Density (gm/cm^3) and Compressibility Index (in percent) of Different Formulations		
Material	**Bulk Density**	**Compressibility Index (in percent)**
Starch	0.456	22.5
Avicel pH 101	0.361	20
Lactose	0.620	14
HPMC 15 cps	0.440	22
Talc	0.510	44
Mg Stearate	0.200	36
Methocel K 15 MCR	0.300	36

TABLE 11: PREPARATION OF CIPROFLOXACIN STANDARD CURVE

Conc.(mcg/ml)	Absorbance
0	0.000
1	0.129
2	0.258
3	0.387
4	0.516
5	0.645
6	0.774
7	0.903
8	1.032

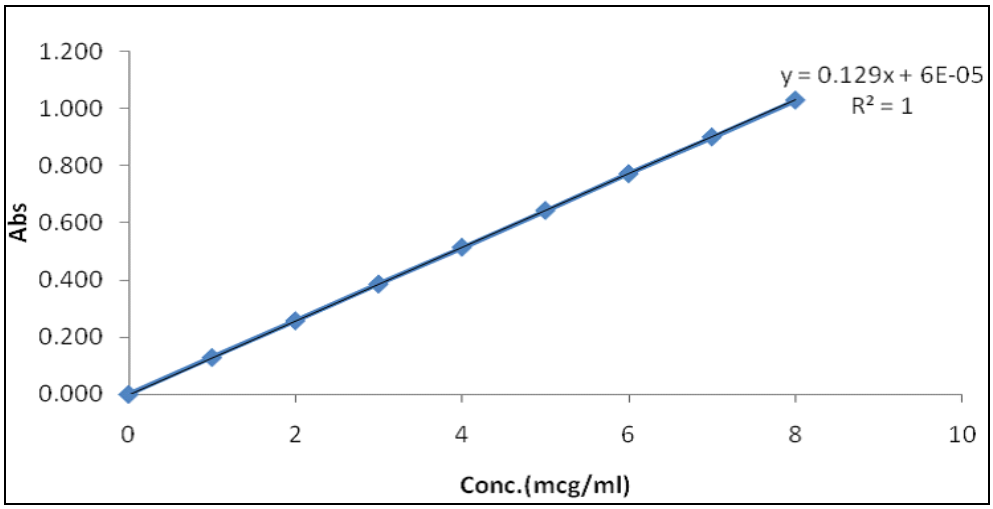

FIG. 15: CIPROFLOXACIN STANDARD CURVE

Dissolution Study of Market Product: First of all, I have studied market products of different pharmaceutical companies. I have collected the ciprofloxacin 1000 mg sustain release tablet and shown the dissolution profile. I have shown the % release of different brands. I observed the release is 71% at 7 h. To compare the release pattern, I studied the innovator brand of ciprofloxacin tablet. The % release is about 100 % at 2 h, but the tablet was 500 mg.

TABLE 12: DISSOLUTION PROFILE (% RELEASE) OF BRAND PRODUCT A, B & C

	% Release		
Time (min)	**A**	**B**	**C**
0	0	0	0
15	2.675	1.7	2.1875
30	4.55	3.7	4.125
60	9.75	10.955	10.3525
90	11.985	16.415	14.2
120	19.675	21.445	20.56
180	26.075	31.46	28.7675
240	35.78	38.125	36.9525
300	44.63	59.365	51.9975
360	49.645	61.125	55.385
420	71.600	68.545	70.0725

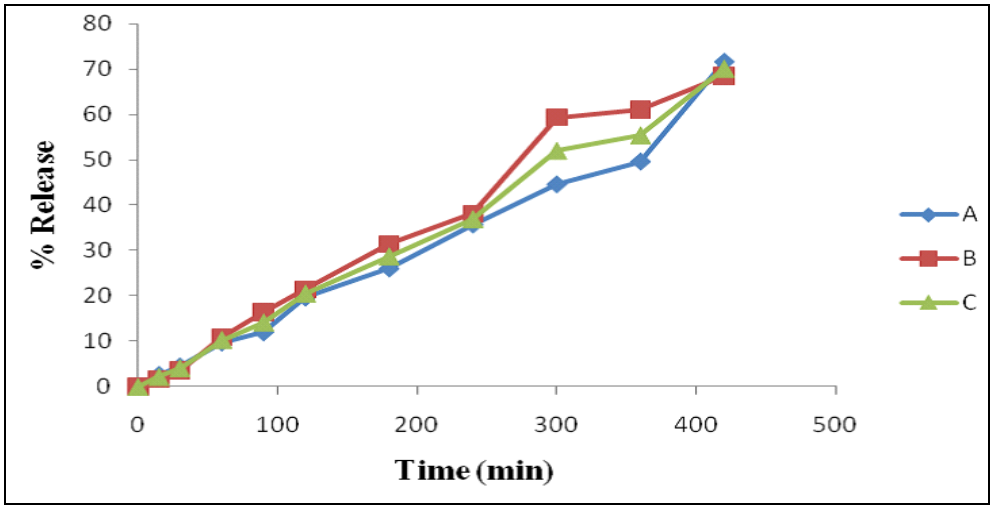

FIG. 16: DISSOLUTION PROFILE (% RELEASE) OF BRAND PRODUCT A, B & C

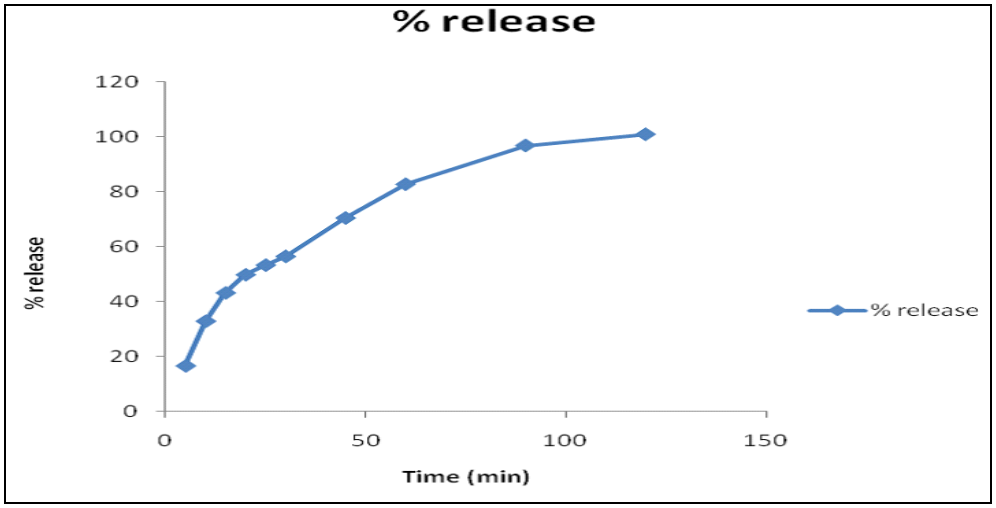

FIG. 17: DISSOLUTION PROFILE OF INNOVATOR BRAND

TABLE 13: DISSOLUTION PROFILE OF INNOVATOR BRAND

Time (min)	% release
5	16.6
10	32.9
15	43.2
20	49.8
25	53.3
30	56.5
45	70.5
60	82.8
90	96.9
120	101

Dissolution Study of New Formulation: Finally, I have prepared 5 different formulations by using different polymers with ciprofloxacin for comparison with the market product (dissolution profile).

TABLE 14: DISSOLUTION STUDY FOR DIFFERENT FOMULATION (% DRUG RELEASE)

Time (min)	F1	F2	F3	F4	F5
0	0	0	0	0	0
15	5.065116279	10.213953	4.2	3.516279	4.339534884
30	5.902790698	10.369302	7.73503876	12.68093	9.145891473
60	11.60496124	30.227442	26.9227907	12.38884	20.66093023
90	19.92325581	29.723566	39.49953488	24.45473	36.3772093
120	32.00232558	51.396434	52.49178295	55.56016	58.12604651
180	71.7848062	51.425581	61.66992248	61.5738	59.69178295
240	72.9275969	58.984496	66.02170543	61.68605	66.23875969
300	74.98914729	58.728682	67.55193798	61.10078	69.37674419
360	78.6496124	56.80155	68.95813953	67.62636	87.72093023
420	84.02635659	58.379845	68.5627907	68.9938	85.2372093
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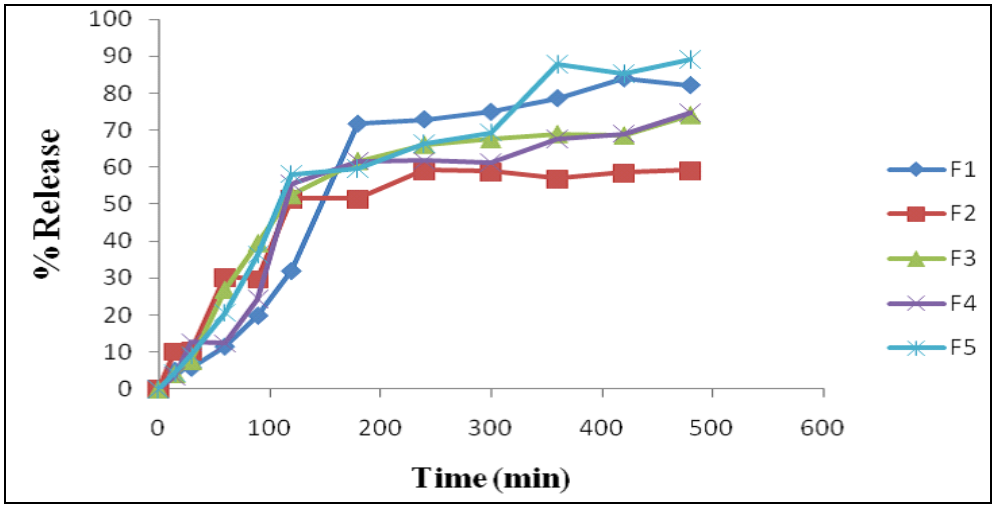

FIG. 18: DRUG RELEASE FROM DIFFERENT FORMULATIONS (F-1 TO F-5)

***In-vitro* Release Study:** The release profiles of different formulations (F-1 to F-5) of ciprofloxacin matrix tablets. All dissolution data are based on the actual drug content of the test tablets as calculated from the assay results. As per the results of dissolution study formulations F1, F2, F3, F4, F5, showed 82%, 59%, 74%, 74% and 89%, drug release in 8 h respectively. This showed that the drug release from the tablet was sustained for 8 hr. Drug release decreased with an increase of polymer loading as HPMC 15 cps polymers form a viscous gelatinous layer (gel layer) upon exposure to the

aqueous medium by undergoing rapid hydration and chain relaxation and this gel layer acts as the barrier to release of drug and as a result drug release are prolonged.

TABLE 15: Y-EQUATION (Y = aX+b) AND CORRELATION CO-EFFICIENT (R^2) FROM DIFFERENT PLOTS OF FORMULATION F-1 TO F-5

Formula	Zero Order Y equation	R^2	1st order Y equation	R^2	Higuchi Model Y equation	R^2	Hixson-Crowell Model Y equation	R^2
F1	y = 11.70x + 7.600	R^2 = 0.859	y = -0.110x + 1.994	R^2 = 0.915	y = 36.87x - 12.65	R^2 = 0.905	y = 0.434x + 1.719	R^2 = 0.719
F2	y = 6.811x + 17.90	R^2 = 0.711	y = -0.048x + 1.908	R^2 = 0.758	y = 23.20x + 3.376	R^2 = 0.876	y = 0.297x + 2.168	R^2 = 0.494
F3	y = 8.923x + 16.36	R^2 = 0.775	y = -0.072x + 1.923	R^2 = 0.866	y = 29.72x - 1.604	R^2 = 0.913	y = 0.36x + 2.035	R^2 = 0.569
F4	y = 9.251x + 12.53	R^2 = 0.799	y = -0.073x + 1.947	R^2 = 0.872	y = 30.05x - 4.916	R^2 = 0.896	y = 0.375x + 1.897	R^2 = 0.620
F5	y = 11.29x + 12.83	R^2 = 0.879	y = -0.123x + 1.991	R^2 = 0.955	y = 36.08x - 7.507	R^2 = 0.953	y = 0.403x + 1.965	R^2 = 0.650

Drug Release Kinetics: The data from **Table 15** shows that most of the formulations of all the formulations were found to follow the 1st order and Higuchi release model. F-1 was best fitted in terms of 1st order release kinetics (R^2 = 0.915), F-2, F-3, F-4 follows Higuchi model (R^2 = 0.876), (R^2 = 0.913), (R^2 = 0.896) respectively. F-5 follows 1st order release R^2 = 0.955).

C**ONCLUSION:** The present study was undertaken to design oral sustained-release tablets of ciprofloxacin. It can be concluded that the present study indicates that the oral sustained-release tablets of ciprofloxacin provide a better option for therapy. The success of the *in-vitro* drug release studies recommends the product for further in vivo studies. We can see that from dissolution data, the release pattern of ciprofloxacin is much better than market product ciprofloxacin sustain release. So if we can manufacture ciprofloxacin sustain release tablet by using new formulation (F1, F2, F3, F4, F5), we will get a good result than an existing market product.

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CONFLICT OF INTEREST: Nil

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