PREPARATION AND *IN-VITRO* EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF ZIDOVUDINE

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ABSTRACT
The sustained release matrix tablet used in this study contains eudragit and ethyl cellulose and was created using a direct compression technique. It also contains one grade of eudragit (RS100), three viscosity grades of HPMC (K100M, K15M, and K4M).Each of these manufactured tablets is examined for weight variation, friability, hardness, diameter, drug content, and drug release pattern. The study of drug-excipient interactions using FTIR Spectroscopy and ocular inspection (by keeping drug-excipient mixture for one month at room temperature). Comparative analyses of the dissolution profiles show that Non-Fickian diffusion or unusual drug release patterns are present in all formulations.

KEYWORDS- Sustained Release, Matrix Tablet, *In-Vitro* Evaluation, Drug-Excipient compatibility study, Dissolution Profile.

INTRODUCTION

Sustained release dosage forms:-

The term "Sustained Release" has long been used in medical and pharmaceutical literature, as is common knowledge. In order to extend the plasma profile of the therapeutic drug and ensure its constant presence in the circulation, its release has continuously been delayed via sustained release. Although its therapeutic effect lasts for a long time, its pharmacological action typically takes time to start.

Due to its improved patient compliance and decreased frequency of adverse drug responses, sustained release (SR) dose forms have attracted continuous interest in recent years[1].

Sustained release, sustained action, prolonged action, and extended action are terms used to describe drug delivery methods that aim to produce a substantial therapeutic impact by continuously releasing medication over a lengthy period of time following administration of a single dose[2].

Given the novelty of sustained release technology, research has been quite fruitful and has produced a number of advancements. New, more sophisticated controlled release/sustained release delivery devices are still being developed and tested.

The following advantages of controlled or sustained pharmaceutical delivery systems over conventional dose forms[3]:

[1] Greater patient comfort and compliance due to less frequent treatment administration.

[2] Reducing fluctuations in steady state levels, which improves illness management and mitigates severe local or systemic side effects. greater safety margin for drugs with high potencies due to better control of plasma levels.

[3] The maximum amount of drug intake permits a reduction in the total dose given.

[4] Decrease in healthcare expenses as a result of improved treatment, a shorter course of therapy, less frequent dosing, and a reduction in the amount of staff time required to administer and monitor patients[4].

Nevertheless, there are a number of disadvantages to using controlled or continuous release dosage formulations. Here are those:

1. There is weak in vitro-in vivo connection.

2. When compared to quick release conventional dosage forms, higher first pass metabolism, increased instability, insufficient residence time for complete release, site-specific absorption, pH dependent solubility, etc. may all have a negative impact on systemic availability[5].

3. The risk of toxicity may be increased by patients chewing or grinding oral formulations or by the potential for dose dumping into food physiologic or formulation variables.

4.There is less likelihood of adjusting the dosage of drugs that are normally administered in various strengths.

5.Retrieving drugs in cases of toxicity, poisoning, or hypersensitivity reactions can be difficult.

6. Exorbitant formulation expenses[6].

Objectives of sustained release drug delivery systems:-

Maintaining the therapeutic level of the drug in the blood or tissues for an extended period of time is the main goal of sustained release dosing. The most common method for accomplishing this is to aim for "zero order" release from the dosage form. No matter how much of a drug is in the delivery mechanism, zero order release refers to the dosage from which the drug is released. Sustained release systems often fail to achieve this type of release, opting to distribute the drug slowly in a "first order" way in an effort to mimic zero order release[7] (i.e. concentration dependent).

As a result, a sustained release dosage form consists of two parts:

[1] A dose that is easily accessible and that can be used to quickly establish blood levels in an amount adequate to cause the desired pharmacological effect, i.e. (Loading dose).

[2] The remaining portion of the full dose (maintenance dose) is then gradually released to maintain a constant medicine level in the blood[8].

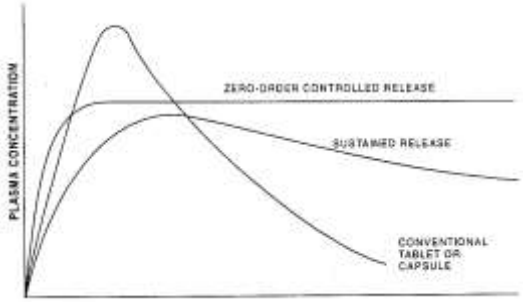

Figure -1. Plasma drug concentration profiles for conventional tablet or capsule formulation, a sustained release formulation and a zero order controlled release formulation[9].

Matrix systems for sustained release:-

The method most frequently employed to regulate the release of drugs from a pharmaceutical dosage form is called the matrix system. Compressing combinations of the medication, the retardant, and the additives results in a tablet with the medication embedded within the matrix core of the retardant. The oral route is the most common for matrix systems, while other routes are equally effective. The Higuchi equation is followed by the release kinetics. These have a linear release rate that is square-root time dependant[10].

MATERIALS AND METHODS

Free zidovudine samples were provided by Mumbai-based Macleods Pharma Pvt. Ltd. The polymers, including HPMC K4M, K15M, and K100M, were supplied by Dr. Reddy's Lab in Hyderabad. The polymers, eudragit and ethylcellulose, were given by the CDH Pvt. Ltd., a New Delhi-based business. Lobachem, Pvt. Ltd. in Mumbai provided the magnesium stearate (MCC) that was acquired. Conc. HCl was bought from SD Fine-Chem Ltd. in Mumbai, and all other chemicals were of analytical purity. To make matrix tablets, polymers and polymers that spread medication were squeezed together. The components and medication were weighed in accordance with the method indicated in Tables 1, 2, 3, 4 and 5 then mixed for 15 minutes in a polythene bag. The slurry was then mixed with magnesium stearate for an additional 4 minutes after passing through a 20 mesh filter. The mixture was then fed into a die on an eight-station tablet punching machine (Rimek Minipress-I, India) to make tablets with punches with biconcave blades that were 12 mm in diameter.

Table –1:Formulation of Zidovudine SR Tablets using HPMC K100M:

Ingredients	Quantity of Ingredient / Tablet (mg)		
	Batch Number (Drug : Polymer ratio)		
	F1 (1.0:0.183)	F2 (1.0:0.36)	F3 (1.0:0.55)
Zidovudine	300	300	300
HPMC K100M	55	110	165
MCC	189	134	79
Magnesium stearate	6	6	6
Total Weight	550	550	550

Table –2:Formulation of Zidovudine SR Tablets using HPMC K15M:

Ingredients	Quantity of Ingredient / Tablet (mg)		
	Batch Number (Drug : Polymer ratio)		
	F4 (1.0:0.183)	F5 (1.0:0.36)	F6 (1.0:0.55)
Zidovudine	300	300	300
HPMC K15M	55	110	165
MCC	189	134	79
Magnesium stearate	6	6	6
Total Weight	550	550	550

Table –3: Formulation of Zidovudine SR Tablets using HPMC K4M:

Ingredients	Quantity of Ingredient / Tablet (mg)		
	Batch Number (Drug : Polymer ratio)		
	F7 (1.0:0.183)	F8 (1.0:0.36)	F9 (1.0:0.55)
Zidovudine	300	300m	300
HPMC K4M	55	110	165
MCC	189	134	79
Magnesium stearate	6	6	6
Total Weight	550	550	550

Table –4: Formulation of Zidovudine SR Tablets using Eudragit RS100:

Ingredients	Quantity of Ingredient / Tablet (mg)			
	Batch Number (Drug : Polymer ratio)			
	F10 (1.0:0.183)	F11 (1.0:0.36)	F12 (1.0:0.55)	F13 (1.0:0.73)
Zidovudine	300	300	300	300
Eudragit RS100	55	110	165	220
MCC	189	134	79	24
Magnesium stearate	6	6	6	6
Total Weight	550	550	550	550

Table –5: Formulation of Zidovudine SR Tablets using combination of Eudragit RS100 & Ethyl cellulose:

Ingredients	Quantity of Ingredient / Tablet (mg)	
	Batch Number (Drug : Polymer ratio)	
	F14 (1.0:0.36:0.183)	F15 (1.0:0.458:0.091)
Zidovudine	300	300
Eudragit RS100	110	137.5
Ethyl cellulose	55	27.5
MCC	79	79
Magnesium stearate	6	6
Total Weight	550	550

PHYSICO-CHEMICAL EVALUATION OF POWDERED-MIXTURES:

The features of the resultant powdered mixes were subjected to the following characterisation prior to compression because they would be essential to the ideal formulation of the tablets[11]. All the physico-chemical properties, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio are shown in Table-6.

Table –6. Physico-chemical Properties of Powered Mixtures:

Formulation No.	Bulk density n = 3	Tapped density n = 3	Carr's Index %	Hausner's ratio	Angle of repose n = 3
F1	0.361 ± 0.007	0.394 ± 0.008	8.45	1.09	22.23 ± 0.24
F2	0.357 ± 0.008	0.408 ± 0.008	12.25	1.13	22.63 ± 0.28
F3	0.335 ± 0.001	0.363±0.0007	7.71	1.082	21.66 ±0.25
F4	0.303 ± 0.004	0.333 ± 0.011	9.30	0.90	21.91 ± 0.22
F5	0.297 ± 0.013	0.312 ± 0.009	3.42	1.035	20.95 ± 0.88
F6	0.353 ± 0.067	0.384 ± 0.014	9.54	1.105	22.42 ± 0.10
F7	0.361 ± 0.007	0.379 ± 0.008	4.41	1.04	21.88 ± 0.33
F8	0.333 ± 0.011	0.357 ± 0.012	6.77	1.07	21.64 ± 0.33
F9	0.329 ± 0.006	0.361 ± 0.007	8.90	1.09	22.99 ± 0.40
F10	0.357 ± 0.012	0.405 ± 0.009	7.05	1.07	21.65 ± 0.29
F11	0.365 ± 0.007	0.405 ± 0.009	9.42	1.104	22.39 ± 0.26
F12	0.394 ± 0.008	0.416 ± 0.009	5.41	1.057	22.39 ± 0.26
F13	0.357 ± 0. 007	0.379 ± 0.008	5.16	1.05	22.18 ± 0.25
F14	0.361 ± 0.007	0.379 ± 0.008	4.90	1.05	22.42 ± 0.37
F15	0.345 ± 0.011	0.379 ± 0.008	8.01	1.08	21.60± 0.05

EVALUATION OF MATRIX TABLETS

We examined the compressed tablets for important elements that affect the medication release. Some of the criteria include weight variation, thickness, hardness, friability, tablet disintegration, drug content, and in-vitro drug release pattern[12].

1. Weight variation [13]:

The average weight of each batch of 20 tablets was calculated, then it was compared to the weight of each tablet. Weight variation tolerance was allowed, as per USP XXVI. The average weight of tablets for each formulation is shown in Table -7.

2. Diameter[14]:

For user acceptance, it is essential to have control over a tablet's physical characteristics, such as its diameter and uniformity amongst tablets. The first variable parameter may be the tablet's diameter. Ten tablets from each batch were measured using Vernier callipers, and every effort was taken to keep the deviation from the standard value to within 5%. The usual tablet diameter for each formulation is listed in Table -7.

3. Hardness Test[15]:

Pfizer's hardness tester was used to evaluate the hardness of 10 tablets from each batch. It measures the force required to break a matrix tablet that is placed in a different way. Data on the hardness of all formulations are provided in Table -7.

4. Friability Test[16]:

Roche weighed and placed 10 tablets into the friabilator test apparatus. The tablets experienced rolling and repeated shocks as a result of the free falls inside the apparatus. After 100 revolutions, the tablets were lowered and weighed once more. The % weight loss of the pills was used to compute the friability using the formula below. $\%\ \text{friability} = \left[1 - \frac{\text{weight of tablets after test}}{\text{weight of tablets before test}}\right] \times 100$

The ideal value is less than 1%. The results are displayed in Table -7.

5. Drug content estimation:

Each tablet's medication content was determined using the traditional spectrophotometric method. The entire assay procedure is as follows:

Preparation of standard drug solution in 0.1N HCl:

ZIDOVUDINE (AZT), accurately weighed at 1 mg, was added to a 10 ml volumetric flask and briefly dissolved in 0.1 N HCl. Then, using 0.1 N HCl, volume was added after the drug's solubility. A solution containing 10 mcg/ml was produced by carefully pipetting 0.1 ml from this into a second volumetric flask with a volume of 10 ml. The volume was then filled with 0.1N HCl[17].

Sample preparation:

In a mortar and pestle, 10 tablets from each batch were precisely weighed, crushed, and pulverised. Three samples, each weighing the same as 100 mg of the drug, were transferred to a volumetric flask of 1000 ml. 500ml of 0.1N Hcl were initially added, and they were agitated for an hour. The volume was then filled with 0.1N Hcl. A portion of the solution was then filtered using Whatmann filter paper, and 10 ml of the filtrate was then diluted to a volume of 100 ml using 0.1 N HCl[18].

Elico 164 double beam UV/Vis spectrophotometer was used to measure the samples' drug content for zidovudine and compare it to a calibration curve made with standard zidovudine in the same medium[19]. (0.1N HCl)

The Table -07 lists all formulations' % medication contents.

Table -07. Physico-Chemical Properties of Prepared Tablets:

Formulation No.	Avg. Wt. (mg) n = 20	Hardness (kg/cm2) n = 10	Diameter(cm) n = 10	Drug Content (%)* n = 10	Friability(%) n=10
D1	557.947±6.210	7.11±0.324	11.93±0.053	99.314±2.024	0.553
D2	558.547±5.891	7.24±0.356	11.945±0.05	99.64±2.055	0.545
D3	558.091±6.113	7.43±0.405	11.958±0.044	100.04±2.271	0.573
D4	557.342±6.035	6.89±0.398	11.937±0.049	99.025±2.054	0.534
D5	558.341±6.148	7.01±0.28	11.932±0.051	99.145±2.144	0.562
D6	558.298±6.349	7.13±0.336	11.938±0.044	99.37±1.991	0.579
D7	556.822±6.413	6.48±0.225	11.950±0.047	98.774±2.191	0.575
D8	555.773±6.717	6.7±0.278	11.947±0.047	98.73±2.12	0.568
D9	556.047±6.601	6.83±0.356	11.936±0.049	98.83±2.053	0.574
D10	546.25±6.257	5.84±0.337	11.963±0.045	97.292±2.282	0.587
D11	557.79±6.63	5.79±0.288	11.955±0.045	97.654±2.246	0.571

D12	557.79±6.63	5.88±0.265	11.947±0.052	97.932±2.064	0.582
D13	557.55±6.634	6.11±0.188	11.452±0.0.55	99.051±2.102	0.566
D14	556.768±5.491	6.29±0.219	11.943±0.53	98.83±2.21	0.549
D15	557.648±6.943	6.41±0.223	11.952±0.048	99.07±2.12	0.578

* Triplicate

6. *In-vitro* Dissolution Study:

In-vitro dissolution studies were developed with the goal of imitating in vivo conditions. The in-vitro release study was designed to provide a rapid, easy, and inexpensive approach that correlates with the dosage form's efficacy when given to healthy participants[20]. The in-vitro dissolving test conditions were precisely defined, standardised, and permitted comparison of a range of outcomes. It was decided to conduct out the dissolving at two physiological pH values for the in-vitro dissolution experiment, namely for the first two hours in 0.1 N HCl (1.2 pH Buffer) and for the remaining period in 7.0 pH distilled water[21].

Dissolution Parameters:

Apparatus : USP XX Apparatus I (Rotary basket)

Medium : 900 ml of 0.1 N HCl (1^{st} two hrs)

: 900 ml 7.0 pH distilled-water (rest of period)

RPM : 50

Temperature: 37 ± 0.5^0C

Sample collection volume: 1 ml

Replacement : 1 ml of respective dissolution medium was added.

Sampling intervals : 0.5^{th}, 1^{st}, 2^{nd}, 3^{rd}, 4^{th}, 5^{th}, 6^{th}, 7^{th}, 8^{th}, 9^{th}, 10^{th}, 11^{th} and 12^{th} hr.

Sample dilution : Directly 1ml sample was pipetted out, filtered and diluted to 25ml with respective dissolution medium and absorbance seen directly against the blank.

Absorbance measurement at λmax: I) for 0.1 N HCl – 265.6nm.

II) For 7.0 pH distilled-water – 269 nm.

Standard Preparation:

The same preparation guidelines that were previously indicated for determining medicine content also applied to the dissolving study[22].

Sampling and estimation:

In order to conduct dissolution studies (in both media), one millilitre of sample was obtained, filtered using Whatmann's filter paper, diluted to a volume of twenty-five millilitres using the proper dissolving medium, and then tested for UV absorbance. Each time, 1ml of the proper dissolving agent was used[23].

Calculation:

Cumulative amount and percent drug release was calculated by the following formula:

$$\text{Amount of drug release} = \frac{\text{Sample Abs}}{\text{Std. Abs.}} \times \frac{\text{Std. dilution}}{\text{Sample dilution}} \times \frac{\%\ \text{Purity}}{100} \times \text{Factor}$$

$$\%\ \text{Drug released} = \frac{\textit{Amount of drug released}}{\textit{Amount of claimed drug}\,(300mg)} \times 100$$

N. B.: Preparation of 0.1 N HCl :

8.5 ml of concentrated HCl (35.5% V/V) was taken and volume was made up to 1000 ml in distilled-water[24].

❖ **Mechanism of drug release:**

To find out the mechanism of drug release from hydrophilic matrices, the dissolution data of tablets of each batch was treated with different kinetic equations, namely zero order, 1st order, Higuchi, Hixon-crowell, Korsemeyer and Peppas etc[25].

- **Zero order Kinetic Model :**

According to this model, under standard conditions of temperature and agitation in the dissolution medium, the dissolution rate model can be described by the following equation[26].

$dQ/dt = K_0$

or in an integral form

$Q = K_0 t$

Where Q = amount of drug released / unit surface area.

K_0 = Zero-order release rate constant

T = Time

The percent of drug released with respect to different time intervals of different formulations and pure drug are given[27] in the Tables-09 to 13.

The plots of percentage of drug released Vs time of different formulations are given in the Figures –02 to 05 . The R^2 (regression) values & rate constant values of all formulations are given[28] in the Table-29.

- **First order Kinetic Model :**

According to Noyes Whitney, under standard condition of agitation and temperature the dissolution rate process for solids can be described by the following equation[29].

$Dq/dt = K_1 (C_s - C_t)$

Under sink condition, i.e. when $C_t < 0.15\ C_s$, the equation becomes

$Dq / dt = K_1 C_s$

Or an integrated form

$\text{Ln}\ q_0/q_t = k_1 t$

where, q_t = amount drug released per unit surface area

k_1 = 1st order release rate constant

q_0 = Initial amount

Cs = Saturation stability

Ct = concentration at time 't'

The Log % amount remaining to be released in different time intervals of different formulations are given in the Tables-14 to 17. The plots of log % amount remaining to be released vs time of different formulations are given the Figures 06-09. The R^2 (regression) values and rate constants of all the formulations are depicted[30] in the Table-29.

- **Hixon – Crowell Kinetic Model**[31-35] **:**

As solid dissolved, the surface area changed with time. The Hixon-Crowell cube root equation for dissolution kinetics is based on the assumption that:

a) Dissolution occurs normal to the surface area of the particles.

b) Agitation is uniform on overall exposed surface and there is no stagnation.

c) The particles of solute retain its geometric shape.

For a non-dispersible powder with spherical particles a bit mathematical derivation leads to the kinetics equation.

$$W_o^{1/3} - W_t^{1/3} = K_{Hc}t$$

Where, W_o = Initial weight of the particles

W_t = Weight of the particle at 't'

K_{HC} = Hixon – Crowell release rate constant

t = time

The changes in weight ($W_o^{1/3} - W_t^{1/3}$) in different time intervals of different formulations are given in the Tables18 to 21. The plots of change in weight ($W_o^{1/3} - W_t^{1/3}$) Vs time (t) of different formulations are illustrated in the Figures -10 to 13. The R^2 values (regression) and rate constants of all formulations are shown in the Table-29.

- **Higuch kinetic Model** [36-40]**:**

For a coated or matrix type dosage form, the dissolution medium enters the dosage form in order the drug to be released by diffusion.

In such cases, the dissolution follows the equation by Higuchi.

$$Q = [DE(2A-EC_S)C_St]^{0.5}$$

Or $Q = K_{HG}\, t^{0.5}$

Where, Q = Amount of drug released per unit area of the dosage form.

D = Diffusion coefficient of the drug.

E = Porosity of the matrix

A = Area

C_s = Saturation solubility of the drug in the surrounding liquid.

K_{HG} = Higuchi Release rate constant.

t = time

The cumulative % amounts of drug released with respect to square root of time of various formulations are given in the Tables -22 to 25. The plots of cumulative % amount of drug released vs square root of time of various formulations are shown in the Figures 14 to 17 . The R^2 values and rate constant (K_{HG}) of different formulations are provided in the Table –29 .

- **Korsemeyer – Peppas kinetic Model[41-45] :**

Korsmeyer developed a simple Semi emphereal model, relating exponentially the drug release to the elapsed time, which was verified by Peppas & Franson, Peppas & Sahlin.

The model relates the fractional release with potency time and described as.

$M_t / M_\alpha = K_m t^n$

$\text{Log } M_t/M_\alpha = \log k_m + n \log t.$

Where, M_t/M_α = Fraction release of drug.

t = Release time.

K_m = Constant incorporating geometric and structural characteristics of release device.

n = release exponent indicative of release mechanism.

If one plot the logarithm of the fractional release Vs the logarithm time then the slope of the graph gives the values of 'n'. An analysis of diffusional drug release using Korsemeyer – Peppas is shown in the Figure 18-21 and Table 26-28 .

Table -08. Interpretation of diffusional drug release from hydrophilic matrix- tablets:

Release Exponent (n)	Drug transport mechanism	Rate at function of time
≤ 0.5	Fickian diffusion	$t^{0.5}$
0.5 < n < 1	Non Fickian diffusion/Anomolus transport	t^{n-1}
1.0	Case II transport	Zero order release
Higher than 1.0	Super case – II transport	t^{n-1}

Log % amount of drug released with respect to the log time of different formulation are given in the Tables – 09 to 28 .

The Plot of log % amount of drug released with respect to log time of different formulations are shown in the Figures 02 to 21 .

The n (release exponent) values and rate constant (km) are given in the table -29.

COMPARATIVE EVALUATION OF DISSOLUTION PROFILES:

Table -09. Cumulative % amount of drug released from the formulations using HPMC K100M:

Sl.No.	Time (hr)	%CDR of F1	%CDR of F2	%CDR of F3
1	0	0	0	0
2	0.5	18.18182	15.15152	12.12121
3	1	25.77777	22.74411	19.71044
4	2	31.876003	30.1936	28.09596
5	3	43.876003	39.1936	35.29596

6	4	51.380337	46.7036	43.10396
7	5	55.902003	51.97194	48.52063
8	6	61.765337	58.4361	53.03529
9	7	67.961837	63.72744	60.72096
10	8	74.001837	68.7146	65.10713
11	9	78.548503	74.75727	71.44813
12	10	82.35017	77.0566	74.04613
13	11	87.656003	81.45844	75.59696
14	12	95.21767	87.5151	79.09946

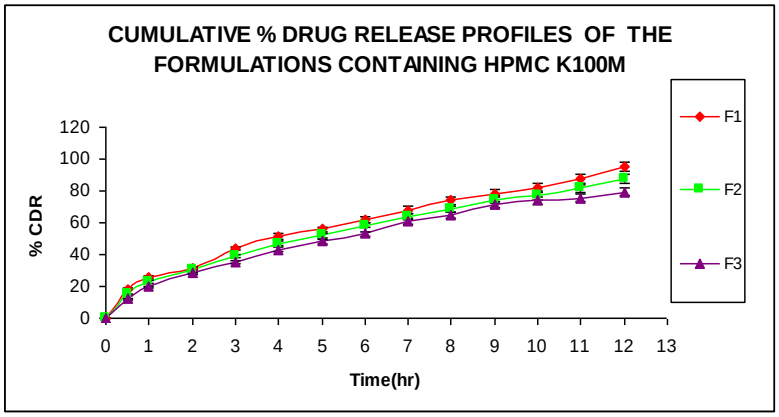

Figure -02. Zero order release of formulations using HPMC K100M

Table -10. Cumulative % amount of drug released from the formulations using HPMC K15M:

Sl.No.	Time (hr)	%CDR 0f F4	%CDR of F5	%CDR of F6
1	0	0	0	0
2	0.5	21.21212	19.69697	16.66667
3	1	28.81145	25.1734	21.98822
4	2	34.90404	30.35286	30.34596
5	3	51.40404	42.35286	39.34596
6	4	57.42237	48.3662	46.85596
7	5	63.14737	54.3862	52.12429
8	6	67.96037	60.39953	58.58846
9	7	75.51537	66.4462	61.92979
10	8	80.06037	69.4862	67.96479
11	9	87.61037	76.27953	74.00646
12	10	95.01871	80.08036	77.05479
13	11	…..	86.88536	83.85646
14	12	…..	92.34786	88.56563

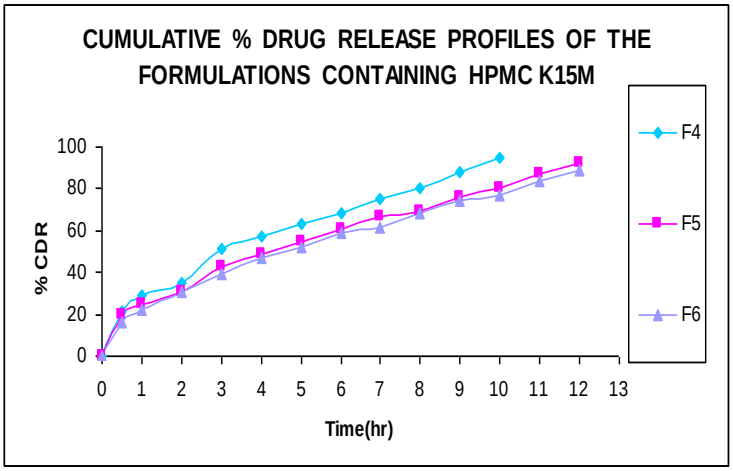

Figure -03. Zero order release of formulations using HPMC K15M

Table -11. Cumulative % amount of drug released from the formulations using HPMC K4M:

Sl.No.	Time (hr)	%CDR 0f F7	%CDR 0f F8	%CDR 0f F9
1	0	0	0	0
2	0.5	24.24242	25.15152	19.69697
3	1	31.84512	30.17946	25.02189
4	2	43.39562	38.84933	34.14057
5	3	60.94562	58.79933	48.09057
6	4	68.91512	63.62149	55.30607
7	5	73.44346	68.89899	60.12957
8	6	80.95729	74.76016	65.84291
9	7	87.01846	82.17216	70.39357
10	8	96.06679	85.52016	74.93374
11	9	…..	90.67183	82.47891
12	10	…..	97.62916	86.13241
13	11	…..	…..	90.68991
14	12	…..	…..	97.50241

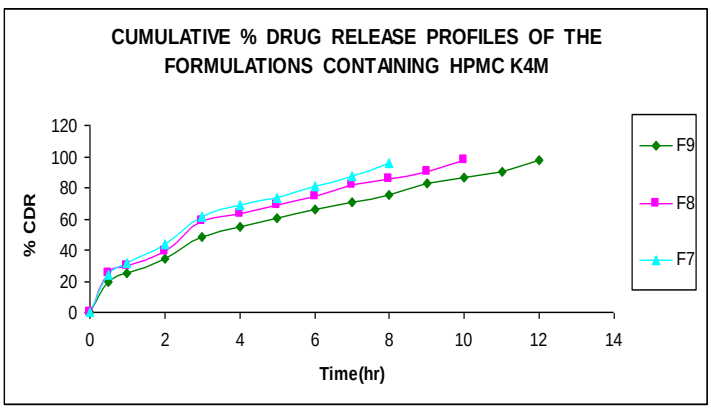

Figure -04. Zero order release of formulations using HPMC K4M

Table -12. Cumulative % amount of drug released from the formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Sl.No.	Time (hr)	%CDR 0f F10	%CDR 0f F11	%CDR 0f F12	%CDR 0f F13	%CDR 0f F14	%CDR 0f F13
1	0	0	0	0	0	0	0
2	0.5	26.9697	22.72727	17.72727	12.57576	10.60606	16.66667
3	1	36.3936	30.32828	24.56515	20.317	19.70875	22.74579
4	2	50.69798	41.8771	34.28939	29.88502	28.51852	33.3771
5	3	68.69798	57.3	46.28939	35.58502	33.91852	42.3771
6	4	77.71798	69.29714	56.65273	45.04135	43.37452	54.2371
7	5	84.04798	77.99108	63.27756	53.00818	50.74102	59.36027
8	6	90.51498	83.98852	68.69639	58.27752	55.11569	64.9391
9	7	94.02915	88.3797	75.34789	62.96535	60.09519	70.5241
10	8	…..	94.37489	80.79339	68.10202	65.98019	75.81527
11	9	…..	97.07085	87.29489	72.94435	69.92169	82.16227
12	10	…..	…..	92.77827	75.84202	73.56752	84.01627
13	11	…..	…..	94.76823	78.89285	75.26735	88.57227
14	12	…..	…..	…..	83.44702	78.31902	92.23327

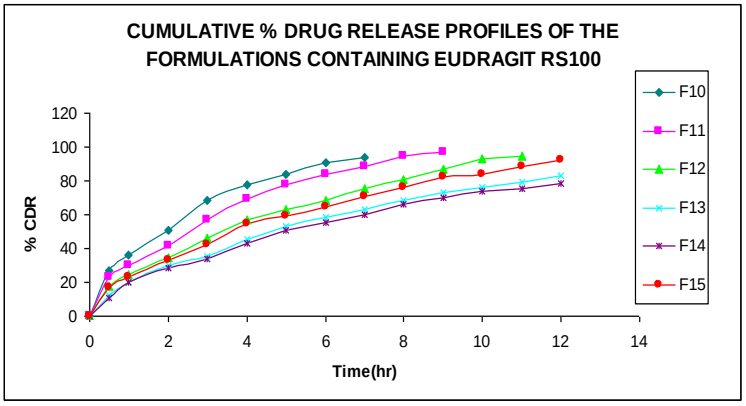

Figure -05. Zero order release of the formulations using EUDRAGIT RS100, & its combination with ETHYLCELLULOSE

Table -13. Cumulative log % amount of drug remain unreleased from the formulations using HPMC K100M:

Sl.No.	Time (hr)	Cumulative log % ADR of F1	Cumulative log % ADR of F2	Cumulative log % ADR of F3
1	0	2	2	2
2	0.5	1.91285	1.928644	1.943884
3	1	1.87142	1.887932	1.904659
4	2	1.835286	1.843895	1.856753
5	3	1.75271	1.783949	1.810931
6	4	1.682804	1.726698	1.755082

7	5	1.644444	1.681495	1.711633
8	6	1.590916	1.618716	1.671772
9	7	1.507733	1.559578	1.594161
10	8	1.414985	1.495342	1.542737
11	9	1.306504	1.402136	1.455635
12	10	1.227896	1.360658	1.414202
13	11	0.970503	1.268146	1.387444
14	12	0.473929	1.096385	1.320158

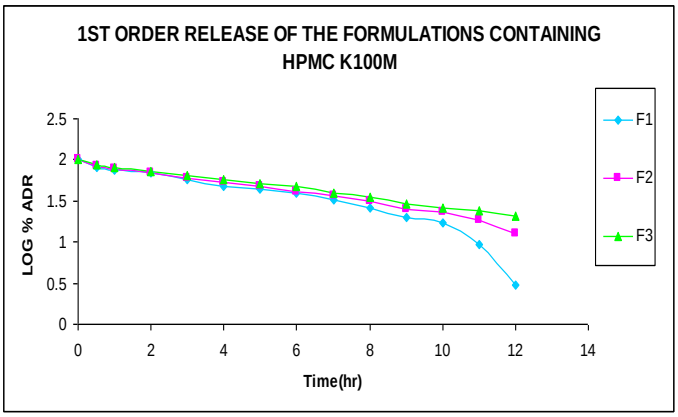

Figure -06. 1st order release of formulations using HPMC K100M

Table -14. Cumulative log % amount of drug remain unreleased from the formulations using HPMC K15M:

Sl.No.	Time (hr)	Cumulative log %ADR of F4	Cumulative log %ADR of F5	Cumulative log %ADR of F6
1	0	2	2	2
2	0.5	1.896459	1.904732	1.920819
3	1	1.85241	1.874056	1.89216
4	2	1.813554	1.842903	1.842946
5	3	1.6866	1.760778	1.78286
6	4	1.629181	1.712934	1.725455
7	5	1.566468	1.659096	1.680115
8	6	1.505687	1.5977	1.617121
9	7	1.388893	1.525742	1.580585
10	8	1.299717	1.484496	1.505628
11	9	1.093058	1.375123	1.414865
12	10	0.697342	1.299281	1.360692
13	11	…..	1.117756	1.207999
14	12	…..	0.883783	1.058212

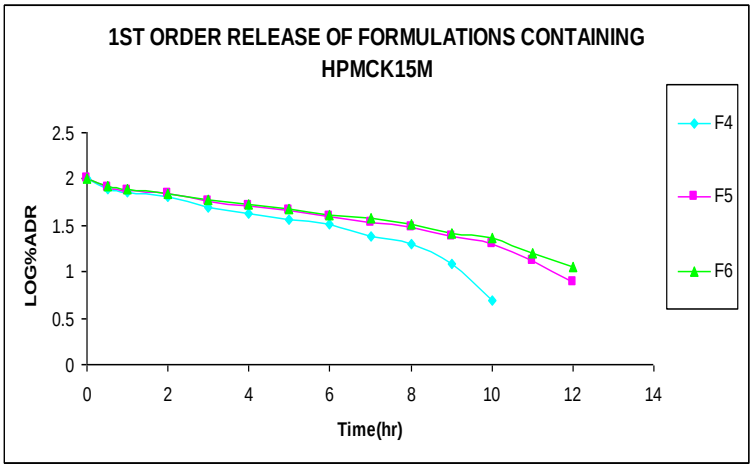

Figure -07. 1st order release of formulations using HPMC K15M

Table -15. Cumulative log % amount of drug remain unreleased of formulations using HPMC K4M:

Sl.No.	Time (hr)	Cumulative log %ADR of F7	Cumulative log %ADR of F8	Cumulative log %ADR of F9
1	0	2	2	2
2	0.5	1.879426	1.874183	1.904732
3	1	1.833497	1.843983	1.874935
4	2	1.75285	1.786401	1.818618
5	3	1.59167	1.614904	1.715246
6	4	1.492549	1.560845	1.650249
7	5	1.424172	1.492774	1.600651
8	6	1.279729	1.402087	1.533481
9	7	1.113326	1.251099	1.471386
10	8	0.594747	1.160764	1.39909
11	9	-----	0.969797	1.243561
12	10	-----	0.374902	1.142001
13	11	-----	-----	0.968954
14	12	-----	-----	0.397522

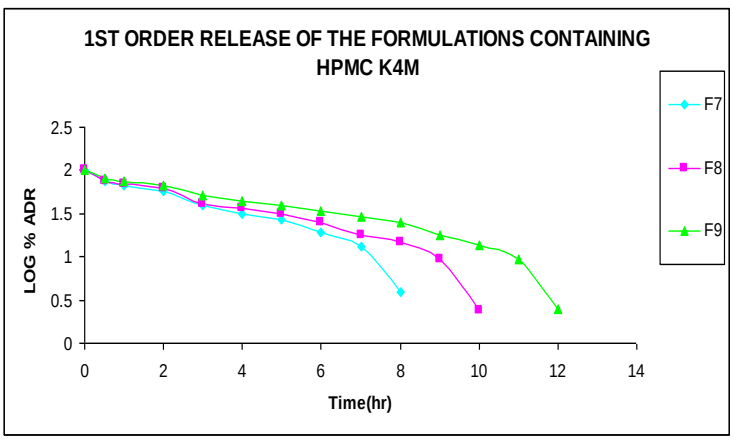

Figure -08. 1st order release of formulations using HPMC K4M

Table -16. Cumulative log % amount of drug remain unreleased of formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Sl.No.	Time (hr)	Cumulative log %ADR of F10	Cumulative log %ADR of F11	Cumulative log %ADR of F12	Cumulative log %ADR of F13	Cumulative log %ADR of F14	Cumulative log %ADR of F15
1	0	2	2	2	2	2	0
2	0.5	1.863503	1.888026	1.915256	1.941632	1.951308	16.66667
3	1	1.803501	1.843057	1.877572	1.901366	1.904668	22.74579
4	2	1.692865	1.764347	1.817635	1.845811	1.854194	33.3771
5	3	1.495572	1.630428	1.73006	1.808987	1.82008	42.3771
6	4	1.347955	1.487179	1.636962	1.740036	1.753012	54.2371
7	5	1.202816	1.342599	1.564932	1.672022	1.692485	59.36027
8	6	0.977038	1.204431	1.495594	1.62037	1.652095	64.9391
9	7	0.776036	1.065217	1.391854	1.568608	1.601025	70.5241
10	8	-----	0.750131	1.283451	1.503763	1.531732	75.81527
11	9	-----	0.466742	1.103978	1.432258	1.478254	82.16227
12	10	-----	-----	0.858641	1.383061	1.422138	84.01627
13	11	-----	-----	0.718649	1.32443	1.393271	88.57227
14	12	-----	-----	1.238421	1.218876	1.336079	92.23327

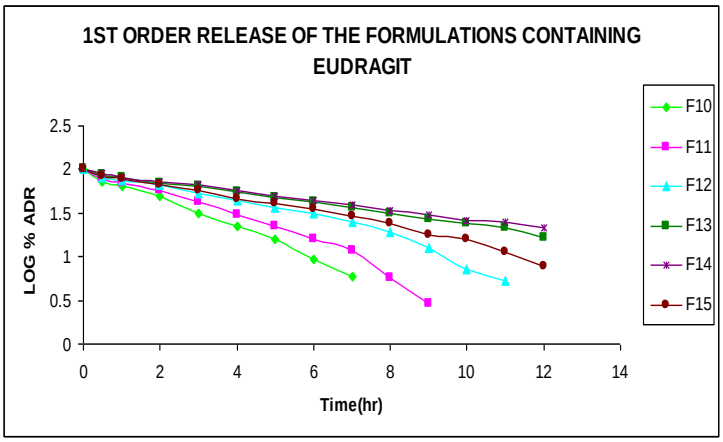

Figure -09. 1st order release of formulations using EUDRAGIT RS100, & its combination with ETHYLCELLULOSE

Table -17. Change in weight ($W_0^{1/3}$-$W_t^{1/3}$) in different time intervals of formulations using HPMC K100M:

Sl.No.	Time (hr)	$W_0⅓ - W_t⅓$ of F1	$W_0⅓ - W_t⅓$ of F2	$W_0⅓ - W_t⅓$ of F3
1	0	0	0	0
2	0.5	0.300321	0.247373	0.1956712
3	1	0.436196	0.38256	0.327527
4	2	0.551225	0.524107	0.48327
5	3	0.802423	0.709261	0.626975
6	4	1.002986	0.878314	0.795429
7	5	1.108554	1.00664	0.921576

8	6	1.250763	1.177635	1.033666
9	7	1.460487	1.331349	1.242309
10	8	1.679066	1.490597	1.373863
11	9	1.915742	1.708138	1.585179
12	10	2.075340	1.800057	1.680845
13	11	2.53538	1.994823	1.741032
14	12	3.202869	2.321729	1.887027

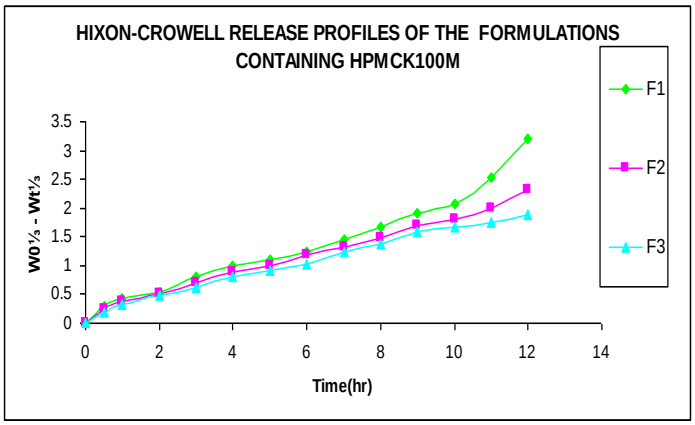

Figure -10. Hixon-Crowell release of formulations using HPMC K100M

Table -18. Change in weight ($W_0^{1/3} - W_t^{1/3}$) in different time intervals of formulations using HPMC K15M:

Sl.No.	Time (hr)	$W_0^{1/3} - W_t^{1/3}$ of F4	$W_0^{1/3} - W_t^{1/3}$ of F5	$W_0^{1/3} - W_t^{1/3}$ of F6
1	0	0	0	0
2	0.5	0.354592	0.327286	0.273687
3	1	0.4971089	0.427678	0.368715
4	2	0.618885	0.52724	0.527104
5	3	0.9923689	0.778578	0.712548
6	4	1.149699	0.91786	0.881903
7	5	1.313797	1.068596	1.010487
8	6	1.465477	1.233061	1.181873
9	7	1.737804	1.416211	1.277544
10	8	1.929905	1.516718	1.465623
11	9	2.327645	1.768332	1.679338
12	10	2.933748	1.930812	1.799982
13	11	…..	2.283363	2.114234
14	12	…..	2.671008	2.388712

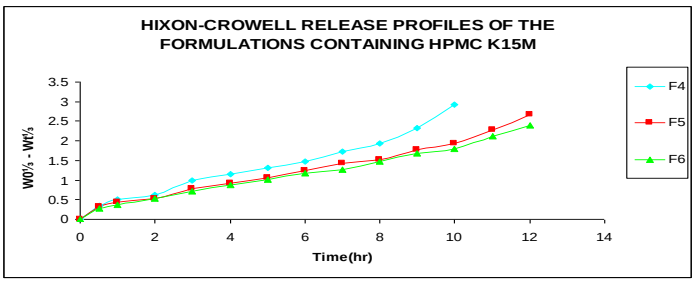

Figure -11. Hixon-Crowell release of formulations using HPMC K15M

Table -19. Change in weight ($W_0^{1/3} - W_t^{1/3}$) in different time intervals of formulations using HPMC K4M:

Sl.No.	Time (hr)	$W_0^{1/3} - W_t^{1/3}$ of F7	$W_0^{1/3} - W_t^{1/3}$ of F8	$W_0^{1/3} - W_t^{1/3}$ of F9
1	0	0	0	0
2	0.5	0.410274	0.427267	0.327286
3	1	0.556837	0.523829	0.424836
4	2	0.802012	0.701853	0.60322
5	3	1.248802	1.187755	0.911246
6	4	1.497344	1.32813	1.092778
7	5	1.658104	1.4968	1.225334
8	6	1.971189	1.70825	1.396995
9	7	2.291367	2.02923	1.548004
10	8	3.063073	2.20422	1.71499
11	9	…..	2.536524	2.044299
12	10	…..	3.308167	2.239069
13	11	…..	…..	2.537885
14	12	…..	-----	3.284816

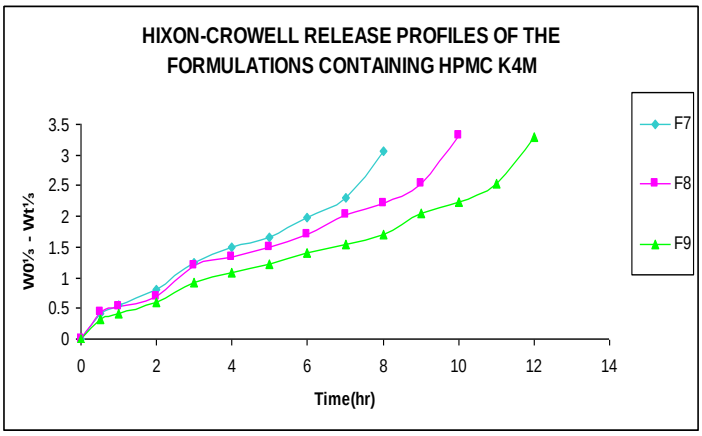

Figure -12. Hixon-Crowell release of formulations using HPMC K4M

Table -20. Change in weight ($W_0^{1/3} - W_t^{1/3}$) in different time intervals of formulations using EUDRAGIT RS100 & its combination ETHYLCELLULOSE:

Sl. No.	Time (hr)	$W_0^{1/3}$ - $W_t^{1/3}$ of F10	$W_0^{1/3}$ - $W_t^{1/3}$ of F11	$W_0^{1/3}$ - $W_t^{1/3}$ of F12	$W_0^{1/3}$ - $W_t^{1/3}$ of F13	$W_0^{1/3}$ - $W_t^{1/3}$ of F14	$W_0^{1/3}$ - $W_t^{1/3}$ of F15
1	0	0	0	0	0	0	0
2	0.5	0.461671	0.382251	0.292296179	0.20335	0.170266	0.273687
3	1	0.649806	0.526756	0.416290866	0.338418	0.327497	0.382591
4	2	0.97478	0.76798	0.606264085	0.5180482	0.491432	0.587675
5	3	1.490039	1.146357	0.868589884	0.632962	0.598686	0.77912
6	4	1.827627	1.510277	1.128784773	0.839589	0.801535	1.064708
7	5	2.124268	1.839171	1.317720279	1.032972	0.975848	1.203501
8	6	2.524791	2.121144	1.489986187	1.173235	1.087746	1.368627
9	7	2.827415	2.376567	1.731197808	1.308327	1.224352	1.552557
10	8	…..	2.863131	1.963549963	1.470164	1.401348	1.749708
11	9	…..	3.210783	2.308169645	1.639529	1.531655	2.028747
12	10	…..	…..	2.708669809	1.750774	1.662757	2.122601
13	11	…..	…..	2.905589224	1.87798	1.728031	2.389148
14	12	…..	…..	…..	2.093045	1.853159	2.66122

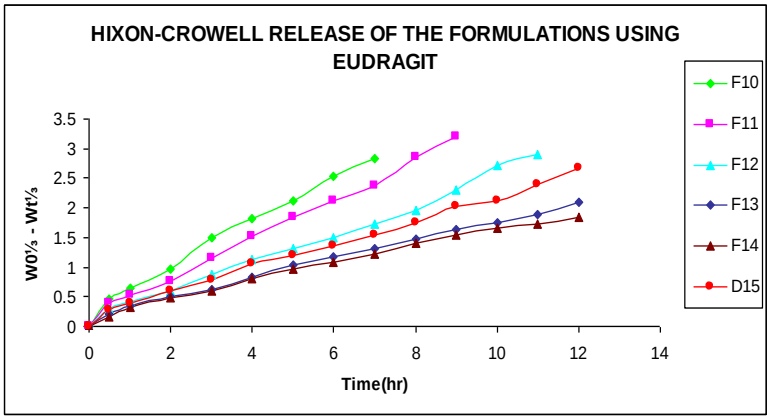

Figure -13. Hixon-Crowell release of formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Table -21. Cumulative %amount of drug released at different square root of time intervals of formulations using HPMC K100M:

Sl.No.	Sqt	%CDR of F1	%CDR of F2	%CDR of F3
1	0	0	0	0
2	0.707107	18.18182	15.15152	12.12121
3	1.0000	25.77778	22.74411	19.71044
4	1.414214	31.867	30.1936	28.09596
5	1.732051	43.867	39.1936	35.29596
6	2.0000	51.38034	46.7036	43.10396
7	2.236068	55.902	51.97194	48.52063
8	2.44949	61.76534	58.4361	53.03529

9	2.645751	67.96184	63.72744	60.72096
10	2.828427	74.00184	68.7146	65.10713
11	3.0000	78.5485	74.75727	71.44813
12	3.162278	82.35017	77.0566	74.04613
13	3.316625	87.656	81.45844	75.59696
14	3.464102	95.21767	87.5151	79.09946

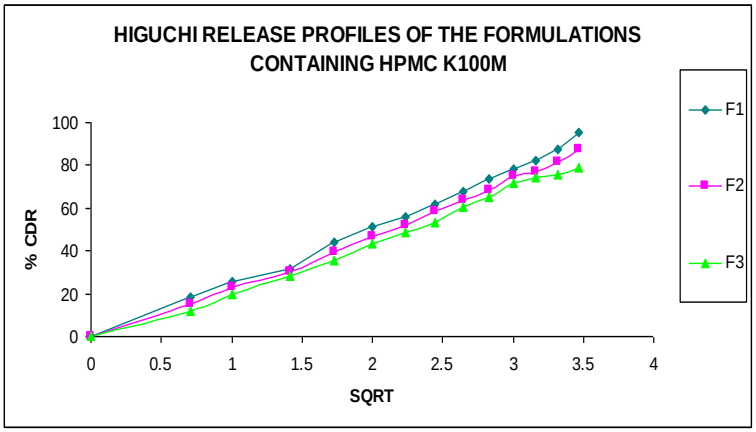

Figure -14. Higuchi release of formulations using HPMC K100M

Table -22. Cumulative %amount of drug released at different square root of time intervals of formulations using HPMC K15M:

Sl.No.	Sqrt	%CDR 0f F4	%CDR of F5	%CDR of F6
1	0	0	0	0
2	0.707107	21.21212	19.69697	16.66667
3	1.0000	28.81145	25.1734	21.98822
4	1.414214	34.90404	30.35286	30.34596
5	1.732051	51.40404	42.35286	39.34596
6	2.0000	57.42237	48.3662	46.85596
7	2.236068	63.14737	54.3862	52.12429
8	2.44949	67.96037	60.39953	58.58846
9	2.645751	75.51537	66.4462	61.92979
10	2.828427	80.06037	69.4862	67.96479
11	3.0000	87.61037	76.27953	74.00646
12	3.162278	95.01871	80.08036	77.05479
13	3.316625	…..	86.88536	83.85646
14	3.464102	…..	92.34786	88.56563

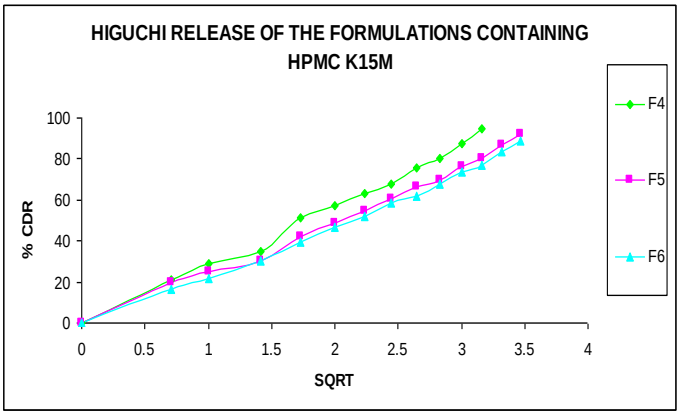

Figure -15. Higuchi release of formulations using HPMC K15M

Table -23. Cumulative %amount of drug released at different square root of time intervals of formulations using HPMC K4M:

Sl.No.	Sqt	%CDR 0f F7	%CDR 0f F8	%CDR 0f F9
1	0	0	0	0
2	0.707107	24.24242	25.15152	19.69697
3	1.0000	31.84512	30.17946	25.02189
4	1.414214	43.39562	38.84933	34.14057
5	1.732051	60.94562	58.79933	48.09057
6	2.0000	68.91512	63.62149	55.30607
7	2.236068	73.44346	68.89899	60.12957
8	2.44949	80.95729	74.76016	65.84291
9	2.645751	87.01846	82.17216	70.39357
10	2.828427	96.06679	85.52016	74.93374
11	3.0000	…..	90.67183	82.47891
12	3.162278	…..	97.62916	86.13241
13	3.316625	…..	…..	90.68991
14	3.464102	…..	-----	97.50241

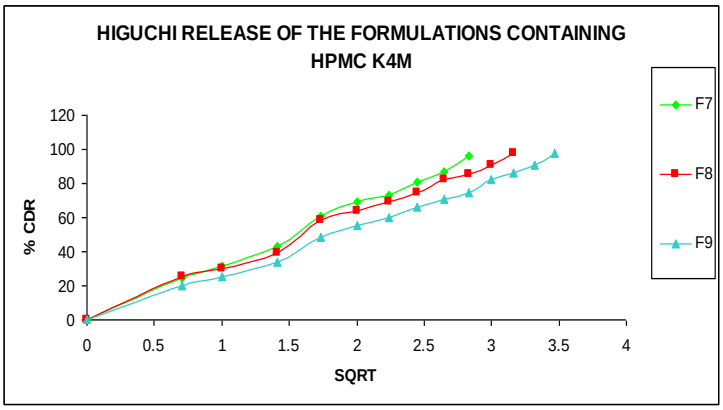

Figure -16. Higuchi release of formulations using HPMC K4M:

Table -24. Cumulative %amount of drug released at different square root of time intervals of formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Sl. No.	Sqt	%CDR 0f F10	%CDR 0f F11	%CDR 0f F12	%CDR 0f F13	%CDR 0f F14	%CDR 0f F15
1	0	0	0	0	0	0	0
2	0.707107	26.9697	22.72727	17.72727	12.57576	10.60606	16.66667
3	1.0000	36.3936	30.32828	24.56515	20.317	19.70875	22.74579
4	1.414214	50.69798	41.8771	34.28939	29.88502	28.51852	33.3771
5	1.732051	68.69798	57.3	46.28939	35.58502	33.91852	42.3771
6	2.0000	77.71798	69.29714	56.65273	45.04135	43.37452	54.2371
7	2.236068	84.04798	77.99108	63.27756	53.00818	50.74102	59.36027
8	2.44949	90.51498	83.98852	68.69639	58.27752	55.11569	64.9391
9	2.645751	94.02915	88.3797	75.34789	62.96535	60.09519	70.5241
10	2.828427	…..	94.37489	80.79339	68.10202	65.98019	75.81527
11	3.0000	…..	97.07085	87.29489	72.94435	69.92169	82.16227
12	3.162278	…..	…..	92.77827	75.84202	73.56752	84.01627
13	3.316625	…..	…..	94.76823	78.89285	75.26735	88.57227
14	3.464102	…..	…..	…..	83.44702	78.31902	92.23327

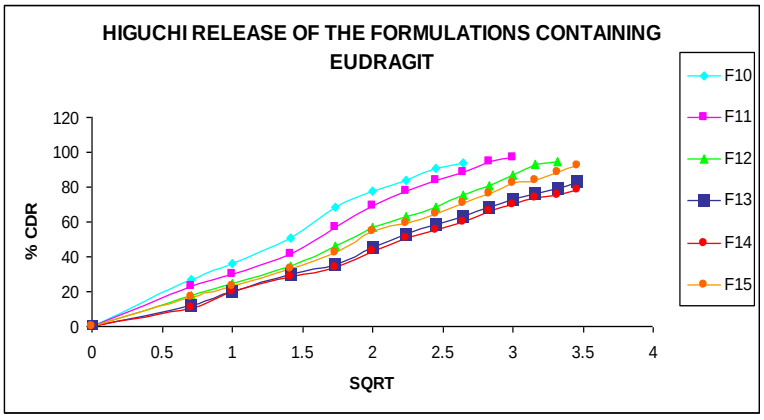

Figure -17. Higuchi release of formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE

Table -25. : Logarithm of the fractional release Vs the logarithm time of various formulations using HPMC K100M:

Sl.No.	Log time(hr)	Log m_t/m_0 of F1	Log m_t/m_0 of F2	Log m_t/m_0 of F3
1	…..	…..	…..	…..
2	-0.30103	1.259637	1.180456	1.083546
3	0	1.11245	1.356869	1.294696
4	0.30103	1.503341	1.479915	1.448644
5	0.477121	1.642148	1.593215	1.547725

6	0.60206	1.710797	1.66935	1.634517
7	0.69897	1.747427	1.715769	1.685926
8	0.778151	1.790745	1.766681	1.724565
90	0.845098	1.832265	1.804326	1.783339
10	0.90309	1.869242	1.837049	1.813629
11	0.954243	1.895138	1.873653	1.853991
12	1.0000	1.915665	1.88681	1.869502
13	1.041393	1.942782	1.910936	1.878504
14	1.079181	1.978718	1.942083	1.898174

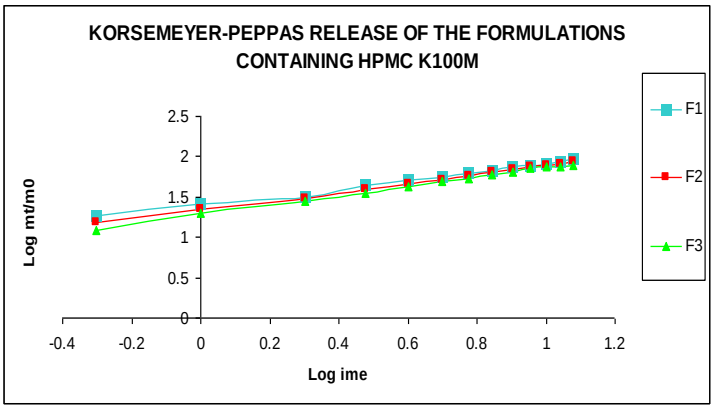

Figure-18. Korsemeyer-Peppas release of formulations using HPMC K100M

Table -26. Logarithm of the fractional release Vs the logarithm time of various formulations using HPMC K15M:

Sl.No.	log time(hrs)	log m_t/m_0 of F4	log m_t/m_0 of F5	log m_t/m_0 of F6
1	…..	…..	…..	…..
2	-0.30103	1.326584	1.294399	1.221849
3	0	1.459565	1.400942	1.34219
4	0.30103	1.542876	1.4822	1.482101
5	0.477121	1.710997	1.626883	1.5949
6	0.60206	1.759081	1.684542	1.670765
7	0.69897	1.800355	1.735489	1.71704
8	0.778151	1.832256	1.781034	1.767812
9	0.845098	1.878035	1.82247	1.7919
10	0.90309	1.903418	1.841899	1.832284
11	0.954243	1.942556	1.882408	1.86927
12	1.0000	1.977809	1.903526	1.8868
13	1.041393	…..	1.938947	1.923537
14	1.079181	…..	1.965427	1.947265

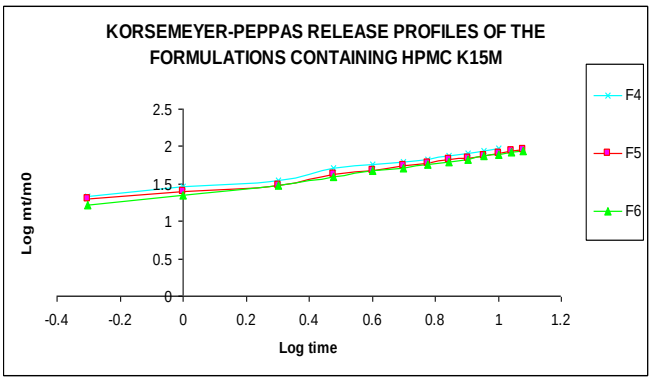

Figure -19. Korsemeyer-Peppas release of formulations using HPMC K15M

Table -27. Logarithm of the fractional release Vs the logarithm time of various formulations using HPMC K4M:

Sl.No.	log time(hrs)	log m_t/m_0 of F7	log m_t/m_0 of F8	log m_t/m_0 of F9
1	-----	-----	-----	-----
2	-0.30103	1.384576	1.400564	1.294399
3	0	1.503043	1.479711	1.39832
4	0.30103	1.637446	1.589383	1.533271
5	0.477121	1.784943	1.769372	1.68206
6	0.60206	1.838315	1.803604	1.742773
7	0.69897	1.865953	1.838213	1.779088
8	0.778151	1.908256	1.87367	1.818509
9	0.845098	1.939611	1.914725	1.847533
10	0.90309	1.982573	1.932069	1.874677
11	0.954243	…..	1.957472	1.916343
12	1.0000	…..	1.98958	1.935167
13	1.041393	…..	…..	1.957559
14	1.079181	…..	…..	1.989015

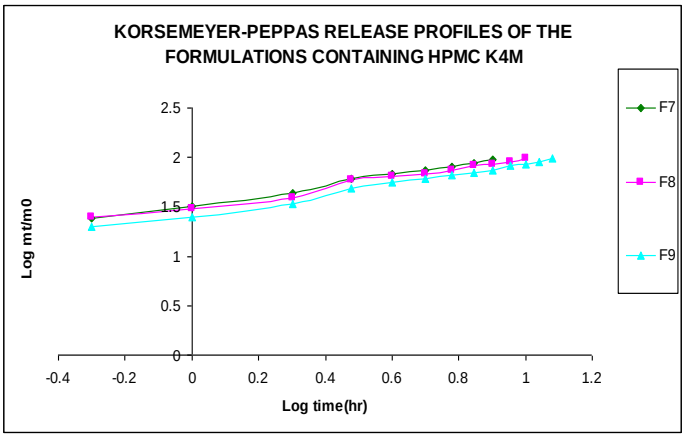

Figure -20. Korsemeyer-Peppas release of formulations using HPMC K4M

Table -28. Logarithm of the fractional release Vs the logarithm time of various formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Sl.no.	log time(hr)	log m_t/m_0 of F10	log m_t/m_0 of F11	log m_t/m_0 of F12	log m_t/m_0 of F13	log m_t/m_0 of F14	log m_t/m_0 of F15
1	…..	…..	…..	…..	…..	…..	…..
2	-0.30103	1.430876	1.356547	1.248642	1.099534	1.025554	1.221849
3	0	1.561025	1.481848	1.390319	1.30786	1.294659	1.356901
4	0.30103	1.704991	1.621977	1.53516	1.475454	1.455127	1.523449
5	0.477121	1.836944	1.758155	1.665481	1.551267	1.530437	1.627131
6	0.60206	1.890522	1.840715	1.753221	1.653611	1.637235	1.734296
7	0.69897	1.924527	1.892045	1.80125	1.724343	1.705359	1.773496
8	0.778151	1.95672	1.92422	1.836934	1.765501	1.741275	1.812506
9	0.845098	1.973262	1.946353	1.877071	1.799102	1.77884	1.848338
10	0.90309	…..	1.974856	1.907376	1.83316	1.819414	1.879757
11	0.954243	…..	1.987089	1.940989	1.862992	1.844612	1.914672
12	1.0000	…..	…..	1.967446	1.87991	1.866686	1.924363
13	1.041393	…..	…..	1.976663	1.897038	1.876607	1.947298
14	1.079181	…..	…..	…..	1.921411	1.893867	1.964888

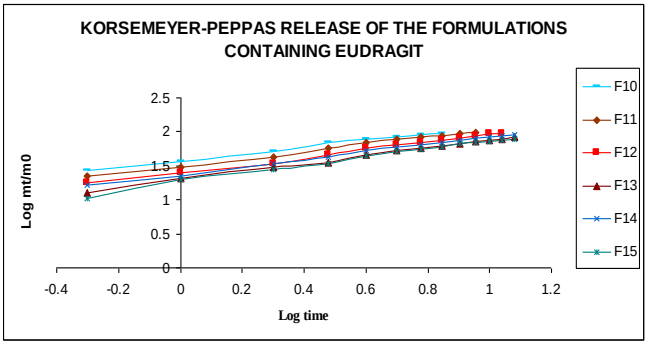

Figure -21. Korsemeyer-Peppas release of formulations using EUDRAGIT RS100 & its combination with ETHYLCELLULOSE:

Table -29. **Regression analysis of different release kinetics:**

Formulations	Zero-order	First-order	Higuchi	Korsemeyer-Peppas	Release exponent (n) values	Hixon-crowell
F1	0.9538	0.9165	0.9967	0.9935	0.52	0.9743
F2	0.9556	0.9819	0.9963	0.998	0.54	0.992
F3	0.953	0.9956	0.9941	0.998	0.59	0.9906
F4	0.9436	0.916	0.9933	0.9876	0.50	0.9707
F5	0.9572	0.9449	0.9925	0.9846	0.5	0.9806
F6	0.9603	0.9696	0.9945	0.9952	0.53	0.9897
F7	0.9267	0.9217	0.9956	0.9922	0.50	0.9751
F8	0.9181	0.8993	0.9937	0.9837	0.48	0.8359
F9	0.9428	0.8821	0.9965	0.9933	0.51	0.9672
F10	0.901	0.9938	0.9959	0.994	0.49	0.9897
F11	0.9225	0.9677	0.9938	0.9921	0.53	0.9957
F12	0.9496	0.9607	0.996	0.9968	0.56	0.9923
F13	0.9494	0.9965	0.9953	0.9975	0.59	0.993
F14	0.9454	0.9969	0.994	0.9929	0.61	0.9882
F15	0.9408	0.9838	0.9967	0.9969	0.55	0.9947

7. FTIR Study:

An FTIR investigation was carried out to identify the drug sample and establish its suitability for use with polymers and other excipients. The sample was converted into a KBr pellet using a KBr press, and the analysis was carried out at BIT, Mesra, Ranchi using a PARKIN-ELMER FTIR. The IR spectrum of the pure drug sample was obtained by first identifying the sample by comparing it to a reference standard. The sample is in its purest form and can be used with various polymers and excipients because it produced exact absorbance peaks when compared to the standard. The FTIR study graphs are shown[46-48] in Figures 22 to 27.

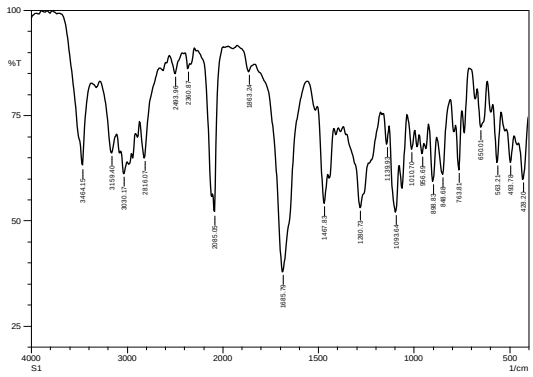

Figure-22. Illustration of the IR spectrum of Zidovudine

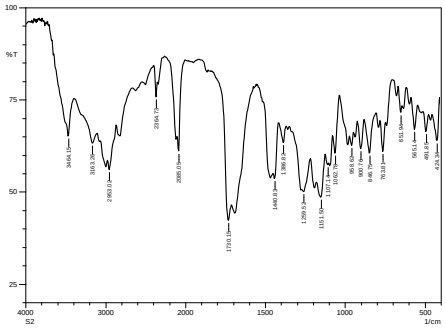

Figure -23. Illustration of the IR spectrum of Zidovudine & Eudragit RS100

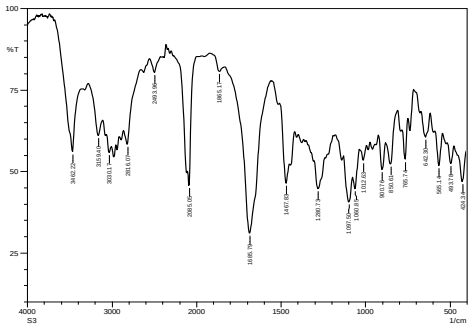

Figure -24. Illustration of the IR spectrum of Zidovudine & Ethyl Cellulose

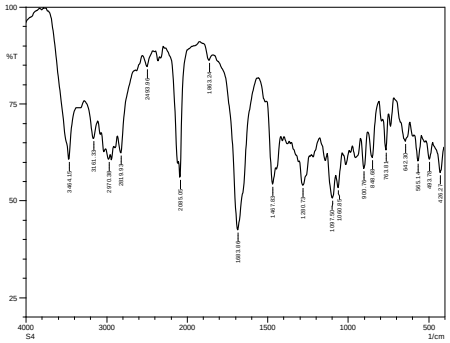

Figure -25. Illustration of the IR spectrum of Zidovudine & HPMC

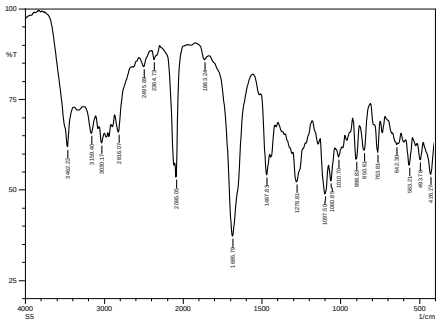

Figure -26. Illustration of the IR spectrum of Zidovudine & MCC

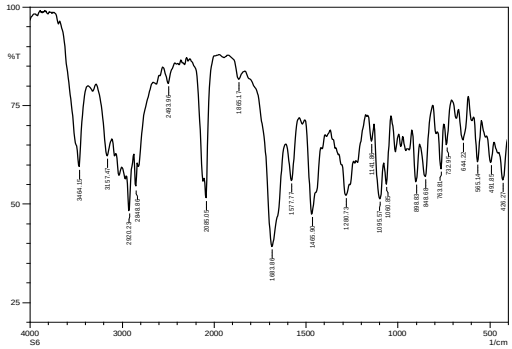

Figure -27. Illustration of the IR spectrum of Zidovudine & Mg.stearate

RESULTS AND DISCUSSION

The current study focuses on creating hydrophilic matrix tablets using direct compression technology and a variety of pH-independent hydrophilic polymers, such as hydroxypropylmethylcellulose (HPMC K100M, K15M, and K4M) and eudragit, either by themselves or in combination with hydrophobic ethyl cellulose. By adding 10 to 30 percent more of each viscosity grade of polymer to the polymer mix, 15 formulations were created, and they were then tested to see which ones had the desired release rate and physical features.

The designed tablets' physical characteristics are as follows:

According to the protocol outlined in the Indian Pharmacopoeia, the tablets of various formulations were subjected to several evaluation tests, including physical appearance, weight-variation, friability, hardness, and drug content consistency. According to the information in Table -07, all formulations are deemed to be satisfactory and repeatable.

Tablet hardness was found to be good (between 5-7 kg/cm2) based on compression force applied, and friability was less than 0.5 percent (wt/wt). The produced tablets showed low weight variation (less than 3%) and strong drug content homogeneity across multiple batches of tablets (more than 97%).

The kinetic parameters for each formulation are presented in Table -29, Figure 02 shows a plot of cumulative percent released versus time for zidovudine embedded matrix sustained release tablets made using various HPMC ratios (100,000 cps). The initial percentage released for the first hour for all formulations ranged from 19 to 25%. However, it was later found that the tablets with more polymer had a slower and more regulated release. The medicine release lasted longer when the polymer fraction was increased from 10% to 30%. Formulations F1, F2, and F3 with different quantities of polymer (10%, 20%, and 30%) have release rates of 95.21%, 87.51%, and 79.09%, respectively.

Zidovuvine matrix embedded SR-tablet formulations made with HPMC 15000 cps and 4000 cps as the retarding polymer showed a similar pattern. As the polymer proportion grew, the release rate reduced and the amount of medication released increased. According to the polymer proportions, the initial

release for the first hour in the case of HPMC 15000 cps ranged from 21 to 29 percent, but the release was discovered to be more regulated in subsequent stages in the tablets with larger proportions of polymer (Figure 17). When the drug was released, it took longer—10 hours in the case of 10% (F4) and 12 hours in the case of 30%. (F6). In formulations F4 and F5, the drug is delivered in 10 hours, but in F6 and F5, the medication is released in 12 hours. Initial release rates in formulations including HPMC K4M range from 25% to 31% depending on the amount of polymers present; however, later phases of release rates were discovered to be more controlled in formulations with higher amounts of polymers (Figure-13). When using a 30% polymer, drug release is prolonged from 8 hours for 10% (F7) to 11 hours (F9).

The release rate of the drug from the matrix tablets decreased as the polymer proportion rose because of increasing gel strength and the formation of a gel layer with a longer diffusion path. This could have led to a decrease in the drug's effective diffusion coefficient and, as a result, a decrease in the rate of release.

The effect of various concentrations of Eudragit RS100 (10%, 20%, 30%, and 40% wt/wt of medication) on zidovudine release rate is depicted in Figure 17. In the first hour, it ranges from 26 to 36 percent, and as the polymer concentration rises, it gradually falls. Initial burst effects were observed during the first hour with formulations F10 and F11; this phenomenon may be attributed to matrix tablet surface erosion or initial disaggregation before the gel layer formed around the tablet core.

For formulations F12 and F13, a rise in the concentration of eudragit resulted in a fall in the drug release pattern. Ethyl cellulose was added to the formulations F14 and F15, which contained 20 and 25% of Eudragit, resulting in stronger retarding qualities and a release of just 19 to 22% of the medicine during the first hour.

Zidovudine has a pH-independent solubility and is continuously absorbed throughout the GIT. Zidovudine must be released from the upper GIT and continue for 10 to 12 hours up to the lower GIT in order for a sustained-release formulation to be effective. This release must be pH-independent. The structure of Eudragit RS100 contains quaternary ammonium groups, which when dissolved lead to the formation of pores in the matrix and the release of zidovudine at an acidic pH. Ethyl cellulose may have a propensity to partially obscure the quaternary ammonium groups, altering the pattern of drug release. .. According to reports, even at lower compression strengths, ethyl cellulose exhibits higher rates of fragmentation and plasticity, producing tougher tablets with low porosity and longer lasting action. The tablet also experiences significant plastic deformation as a result of this process, making it harder. This prevents the burst impact of formulations F14 and F15 as well as the potential for dose dumping.

The release kinetic information for each formulation is shown in Table -29. According to the 'n' values for all formulations ranging from 0.48 to 0.61, the release mechanism for all formulations was non-Fickian or anomalous. It is obvious that the release required both drug diffusion and polymer relaxation. Although polymer relaxation is one of the causes of drug release, diffusion is the primary mechanism, as evidenced by the poor correlation-coefficient (R2values) between kinetic parameters based on Zero-order release and the Higuchi equation.

From FTIR study of drug and drug with the combination of different polymers showed no deviation of graph and hence it can be concluded that, there was no interaction between drug and polymer.

CONCLUSION

The direct compression method, three viscosity classes of HPMC (K100M, K15M, and K4M), one grade of Eudragit (Eudragit RS100), and a mixture of Eudragit and Ethyl cellulose are used in the formulation of Matrix SR tablets. There were 15 formulas altogether (5 with HPMC and 6 with Eudragit).

Each of these manufactured tablets is examined for weight fluctuation, friability, hardness, diameter, drug content, and drug release pattern. There was no obvious breach of I.P. restrictions.

The study of drug-excipient interactions using FTIR Spectroscopy and ocular inspection (by keeping drug-excipient mixture for one month at room temperature). The excipient and the drug did not appear to interact in any obvious way.

Comparisons and evaluations of the dissolution profiles were made. The optimal formulation is "F9," and all formulations display Non-Fickian diffusion, or an atypical pattern of drug release, as a result of this.

All formulations follow the sustained-release model of medication release, according to the facts previously mentioned.

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