Section A-Research paper
ISSN 2063-5346

FORMULATION AND EVLUATION OF SUSTAINED RELEASE GLICLAZIDE MATRIX TABLET BY USING NATURAL ANDSYNTHETIC POLYMER

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ABSTRACT

The study's objective was to develop a matrix tablet formulation of Gliclazide. The new formulation will provide the benefit of SR formulations of gliclazide, an anti-diabetic medication that stimulates insulin production through the beta cell sulfonylurea receptor. Matrix tablets containing Gliclazide were made using the wet granulation technique, and their drug release characteristics were studied. Natural polymers like pectin were used into the formulation. Polymers in pectin are hydrophilic and can slow or speed things up. There was evidence that all of the formulations met pharmacopeial requirements. There are six distinct formulations, each with a unique drug:polymer concentration. HPMC K100M-F1 (1:1), F2 (1:2), F3 (1:3), F4 (1:1), F5 (1:2), and F6 (1:3) all include the medicine in a polysaccharide form of pectin, while the remaining three formulations all have the drug in a polymer combination of pectin. After 12 hours, F6 is the only formulation that exhibits any sign of sustained release. The optimized formulation F6 containing (pectin and HPMC K100M) is superior to other formulations in terms of sustained efficacy over a 12-hour period. Increasing the polymer concentration resulted in a noticeable change in the drug's release kinetics. To assess the mechanism of drug release, the data was fitted to several (mathematical) models, including the higuchi, first-order, and zero-order. The best formulation, f6, is governed by zero-order kinetics.

Key words: Matrix Tablet, Diabetes, Sustain Released,

INTRODUCTION

The oral route of drug delivery system is one amongst for most appropriate suggests that to administer drug to the human body to get the therapeutic result. Although it's a convenient route it give varied challenges to the formulator to design to improvement such it provides the in associate optimum concentration need to achieves a plasma level of the drug which is able to move among the therapeutic window to obtained the required effect. SR, this system involves any DDS that get slow release of drug over a larger duration of time. The structure of regular dosage regimens essential part completes this goal

[1].

Sustained Release Drug Delivery System

Sustained release dose forms are style to get induce a chronic therapeutic result within continued releasing medicament over a large period of time when administration of one dose. Most focus of manufacturing sustained unharnessed dosage form was arranging to modification & enhances the drug showing by grow the time of drug action, lowering [2].

Limitation of Sustained Release Formulation

- Administration of SR Dose not permits cause termination of medical aid. Fast amendment within the drug if required through medical aid once important adverse result is noted can't be accommodated.
- The physician has low flexibility in managing dosing program, because it fastened by dosage type design.
- Sustained release dosage form is structured for traditional population i.e. on basis of average biological half-life.
- Higher prise able process and equipment are concerned in producing several SRDF.
- Dose dumping
- Unpredictable & less in vitro and in vivo relationship
- Effective drug unharness duration is influenced & restricted by gastrointestinal residence time. Need advance patient qualification (like not to break the dosage form before consume).

Materials and Method

Preformulation Study
Standardization of drug

UV Spectrophotometric method for Gliclazide

The drug Gliclazide was analyzed by using LAB INDIA UV-1800 spectrophotometer having double beam detector configuration. Standard curve was plotted in 0.1N HCL at the maximum wavelength of 273nm [3].

Micrometry Study

Angle of repose powder

Mostly funnel is used in this method, firstly weight of the powder and it taken in a funnel, the height (h) funnel is place in a stand, after the powder is place in the funnel to freely flow,

Then the angle of repose of the powder is find out. Range of repose can zero degree. The angle of repose of the powder is found out the following formula **[4].**

Tan θ= h/r (1).....(1)

Therefore, θ = tan height/ radiosHere,

θ = angle of repose

h = height of the pile

r = radius of the pile base

Bulk density

Bulk density is calculated by adding a known mass powder to a cylinder. The density is calculated as mass.

Tapped density in this method firstly we have to weigh the known powder and then the known powder transfer in a 10 ml mechanically tapping cylinder. The tapping is started until the little further volume changed is observed [5].

Calculated by following equation

Loosen bulk density = total mass of powder /volume of powder

Tapped bulk density = powder wt. / tapped volume

Carr's index

Carr's index help in measuring the power need to breakdown the friction into the particle & the hopper. Carr's index > 25 % is carefully to be a sign of low flow capability, and under 15,of good flow property It can be calculated by following equation [6, 7].

Carr's index (%) = [(total bulk density –loosen bulk density) ×100]/TBD

Where TBD = tapped bulk density..... (2**)**

Fourier transformation infra –red analysis

Drug- excipients compatibility studies the infra red absorption spectra of unmixed drug & with unalike ingredient were hold in the scale of four hundred thousand to four hundred **cm-1** using KBr dise procedure**,** 1-2 milligram of material to be analyse was mixed with 300-400 mg, specified quantity of minute powder & dried KBr these sum are mainly enough to give a circle of 10-15 diameter and pellet of right strength by a hydraulic press [8].

Preparation of Gliclazide Matrix Tablets

Method of preparation

Gliclazide 80 mg tablets were formulated using various polymers, including pectin and HPMC, at different concentrations (50, 100, 150, 25, and 75 mg). Different formulations were created by varying

ratio of polymers used. drug & polymer were thoroughly mixed in a mortar & pestle & then sieved through a number 40 sieve. A starch solution was employed as a binding agent in conjunction with water. Granules were dried at a temperature of 50°C for duration of 30 minutes. Subsequently, granules were transferred through sieve 22-25 and magnesium stearate was added. Granules were then compressed using a 16-station rotary tablet machine. **[9].**

Evaluation Parameters of Matrix Tablet

Physiological parameter or postcompressional parameters of all formulations

Tablet hardness

Tablet hardness refers to a set of laboratory techniques. This technique involves assessing hardness of tablets prior to their use, specifically in relation to storage & handling. tablet hardness that we can achieve.

Hardness of tablets was determined using a Monsanto hardness tester. In each batch, six tablets were crushed & their weight in kg/cm2 was recorded. average weight of crushed tablets was then calculated. [10].

Tablet thickness

Thickness of tablets is determined to ensure uniformity in tablet size. Tablet thickness will be controlled within a 5% deviation from standard value. Twenty tablets were randomly selected from the batch, & thickness of each tablet was measured using a digital vernier. [11].

Friability of tablets

Friability refers to the ability of a solid material to break into smaller pieces during transportation. Friability is determined using following procedure. First, accurately weigh 20 tablets & place them in a plastic chamber. Set chamber at a rotation speed of 25 rpm for a duration of 4 minutes. After the 4-minute period & completion of 100 revolutions, stop Roche apparatus & reweigh 20 tablets. Tablet weight loss can be determined using following formula. [12].

%weight loss = initial of tablet – final weights of tablets/ final weights ×10…… (3)

Weight variation

Weight variation is a parameter used to ensure that each tablet contains correct amount of drug. This method involves weighing 20 tablets individually using an analytical balance. average weight of tablets is then calculated, & weight of each tablet is compared to average weight. [72].

% of weight Variation = average wt–average wt individual wt / average wt× **100 ……** (4)

Uniformity of drug content

We ground 10 tablets into a fine powder using a mortar. We then measured out a portion of this powder that weighed 50mg, and transferred it to a 100ml volumetric flask. The flask already contained 70ml of a 0.1N HCL solution. The mixture was mechanically shaken for one hour, followed by filtration using a Whatman filter paper. The resulting solution was then diluted to a final volume of 100 mL. A 1 ml sample

of the solution was diluted with 50 ml of 0.1N buffers. The absorbance at 273nm was measured against a blank at the same wavelength. [13].

Dissolution studies

Drug release was assessed using a dissolution test, employing the United States Pharmacopoeia type 2 dissolution equipment (paddle method) at a speed of 50 rpm. The test was conducted in 900 millilitres of 0.1N hydrochloric acid, maintained at a temperature of 37±0.5°C for a duration of 1 to 12 hours. A 5 millilitre hole was created for sampling purposes.

sample was subjected to a fresh dissolution method at a temperature of 37°C ± 0.5°C. After a specified time interval, sample was analysed using a UV-visible spectrophotometer at a wavelength of 273nm. [14,15].

Kinetic Parameters of All Formulations

Dissolution view of main acceptable preparation is provide to zero order, 1st order & higuchi model to know mechanism modelling of liberate model was adopted for determining proper model.

Zero order

Zero-order response in certain reactions can be measured by reactant concentration, as the rate of a zero-order reaction does not vary with changes in reactant concentration. This implies that rate remains constant, denoted as (k), throughout reaction..

First order reaction

A first-order reaction is characterised by a linear relationship between the rate of reaction & concentration of a single reactant**.**

Higuchi model

Many modified release formulations utilise a limited number of matrix systems. In these cases, active ingredient dissolves from matrix,& drug's dissolution pattern is determined by water permeation. Higuchi method is commonly used to analyse this process, where a linear relationship is observed between cumulative percentage of active ingredient released & square root of time..

$$Ft=Kht1/2$$

Krosmeyer - peppas model

Krosmeyer peppas model empirical related function of time for diffusion controlled mechanism; it is given as followed:

ISSN 2063-5346

$$Mt / M\infty = ktn \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(5)$$

Stability Studies

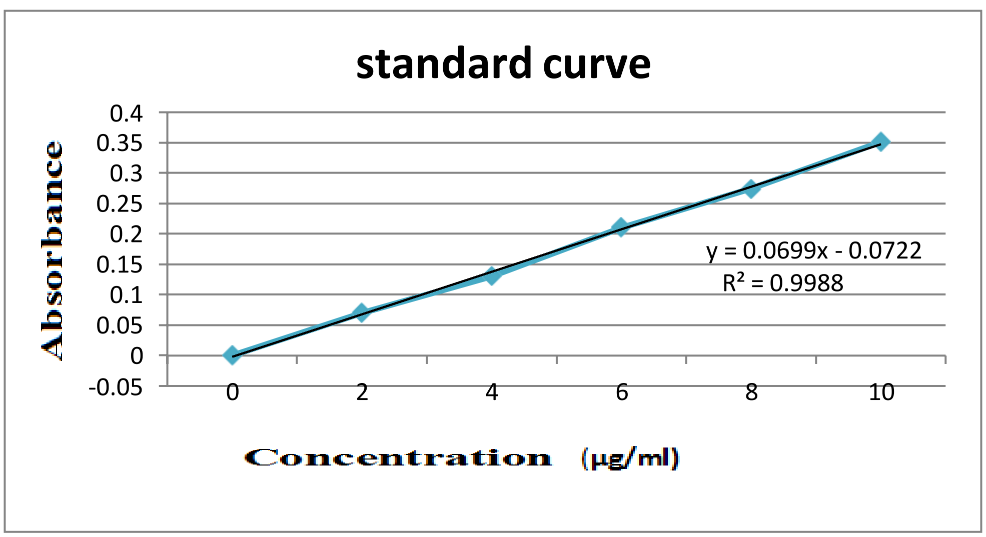
Stability studies play a crucial role in enhancing the lifespan of pharmaceutical dosage forms. APIs can be evaluated. Drug product stability studies involve determining appropriate preparation method according to guidelines set by International Conference of Harmonisation. These studies are conducted at a temperature of 40±2°C & a humidity level of 75±5%. physical & chemical properties of formulation F6 tablets remained stable over a period of 3 months, as indicated in Table 5.8 which presents the parameters measured at different time intervals. [16].

RESULT AND DISCUSSION

PREFORMULATION STUDIES

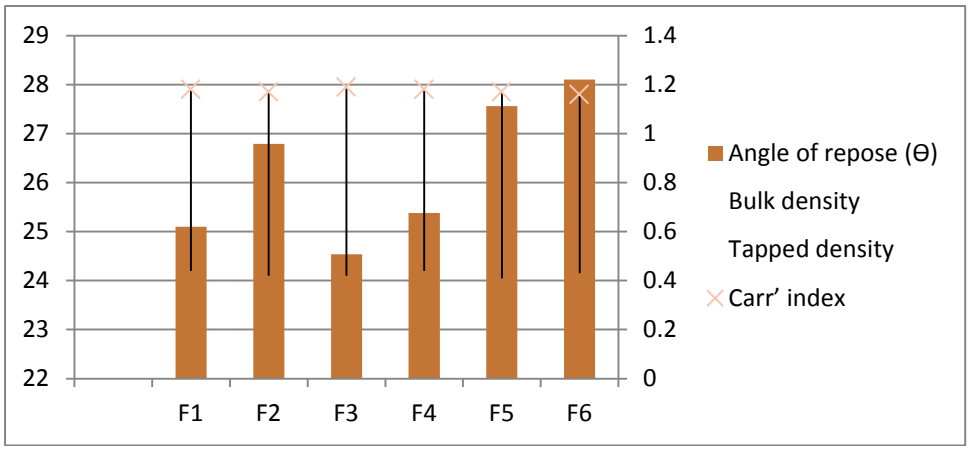
UV Spectrophotometric Method for Gliclazide

Preparation of Calibration Curve in 0.1N Hydrochloric acid



Graph 1- Gliclazide in 0.1N HCL

Micrometry Study



Mean± SD (n=3)

Graph 2: Micrometrics Charactertics of Gliclazide

Fourier transformation infra –red (FTIR) analysis

Table No. 1- FTIR Spectrum Analysis

S. No	**Frequency ,cm ▪1**	**Bond**	**Functiona lgroup**	**Pure dru g (Glicliazide)**	**Drug +pectin**
1	3300-3500	=CH- stretch	Alcohol	3356.6	3423.4
2	1680-1620	C=O	Alkenyl	1639.53	1637.4
3	920-675	C-H	Aromatics	917.5	946.44

Evaluation Parameters

Post compression or physical parameters as of vildagliptin tablet performed and found therelevant data shown in below table.

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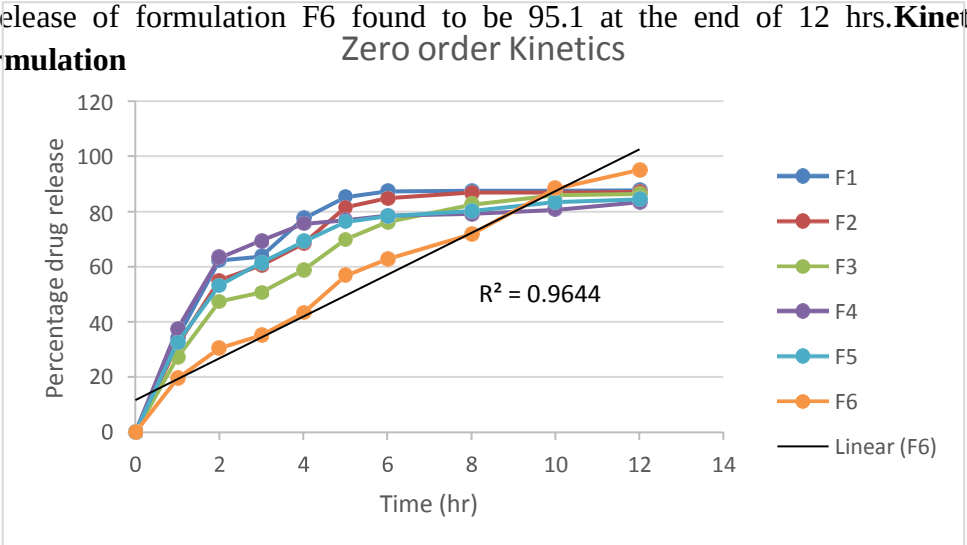
Table No 2: Evaluation Parameters

Formulation code (F)	Hardness (kg/cm2)	Thickness (mm)	Friability (%w/w)	Drug uniformity (%)	Weight variation (mg)
F1	**4.2**±0.08	3.82±0.02	0.26±0.03	99.6±0.25	248±4.1
F2	4.0±0.05	4.15±0.08	0.35±0.02	99.0±0.30	249±7.2
F3	4.3±0.07	4.20±0.02	0.28±0.02	99.4±0.25	252±4.1
F4	4.7±0.03	3.99±0.05	0.28±0.04	99.2±0.47	247±3.6
F5	4.5±0.03	3.97±0.06	0.33±0.03	99.3±0.37	249±2.7
F6	4.9±0.09	4.20±0.14	0.5±0.03	99.5±0.31	252±6.9

Mean± SD, n = 3

Dissolution Study:

In vitro, the percentage drug released study of gliclazide tablet was performed with different polymers concentration at different intervals (1 to 12 hrs) & found the relevant data showing below. The maximum Percent drug release of formulation F6 found to be 95.1 at the end of 12 hrs.**Kinetic Parameters of Optimized Formulation**



Graph 3–zero Order Release Kinetics

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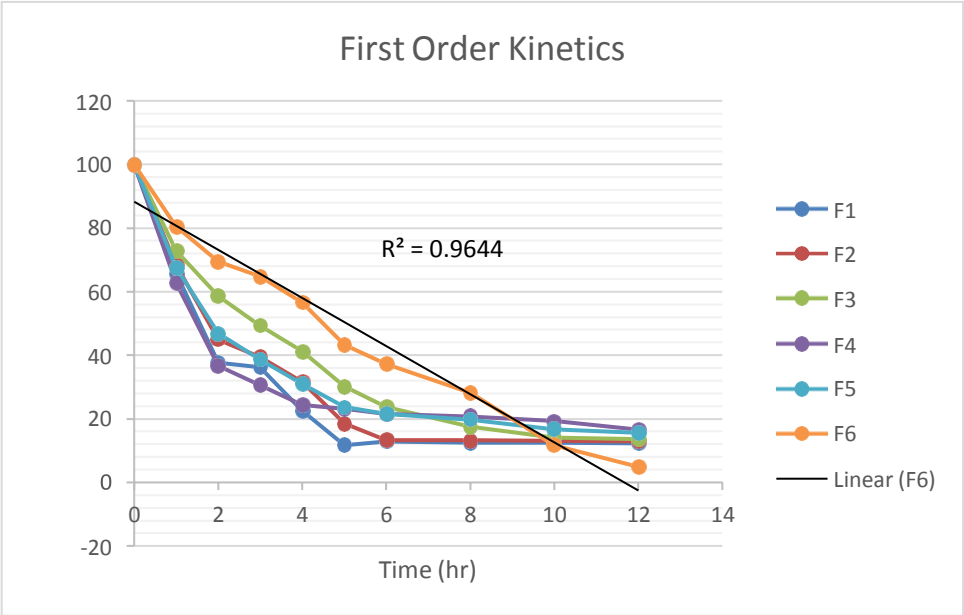
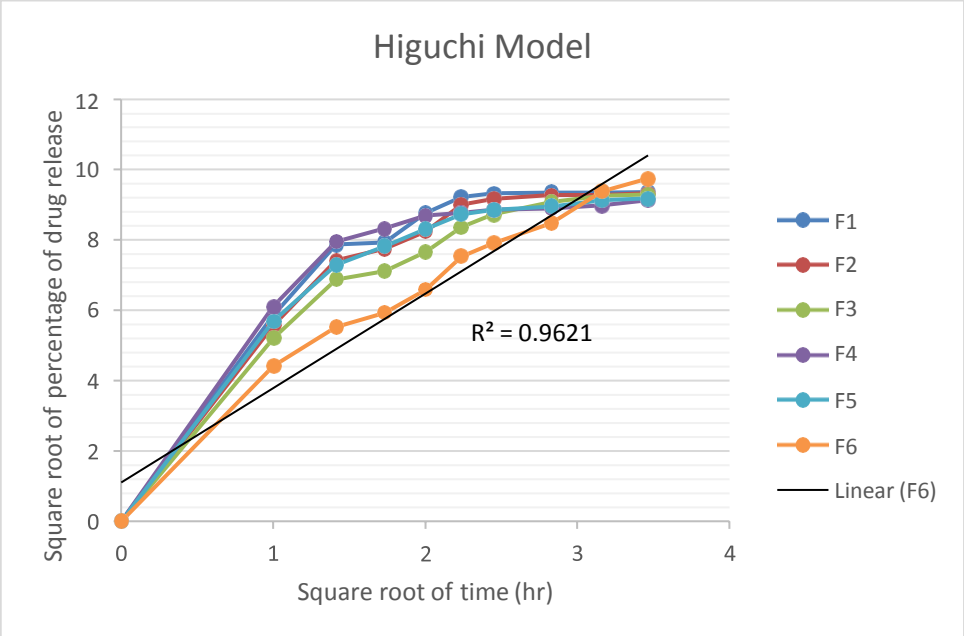
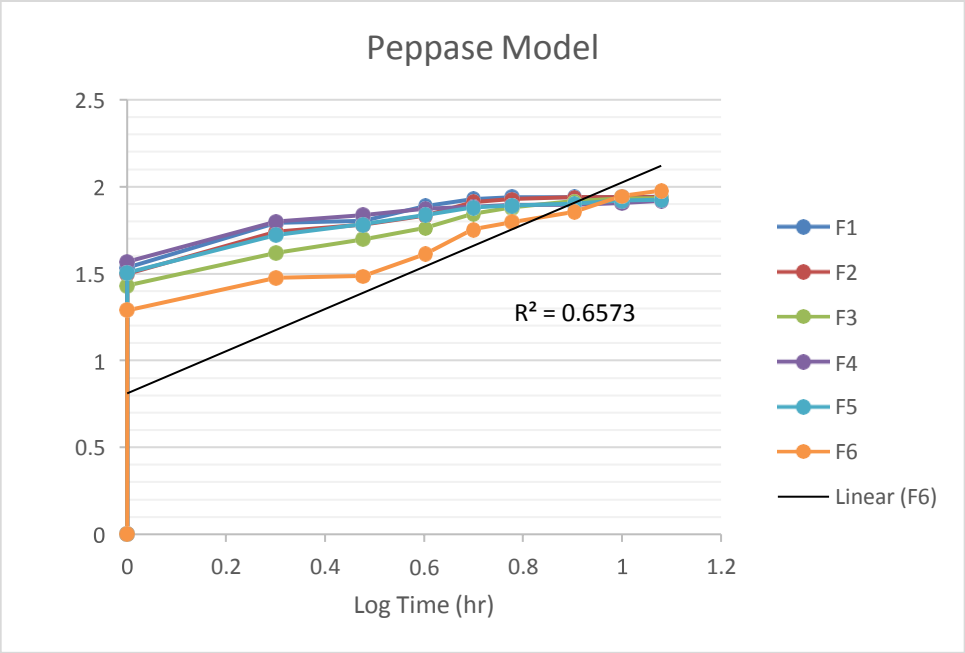


Graph 4- First Order Release Kinetics



Graph 5- Higuchi Model



Graph 6- Peppas Model

Stability Study

Table No. 3 Stability Study of Best Formulation F6

S.No	Parameter	Initial	1st month	2nd month	3rd month
1	Appearance	White	No change	No change	No change
3	Drug content	99.5	99.5	99.2	99
4	Hardness	4.9	4.9	4.7	4.5
5	Friability	0.5	0.5	0.6	0.8

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SUMMARY AND CONCLUSION

Summary

The primary focus of this study was to formulate and evaluate a tablet matrix containing gliclazide using both natural and synthetic polymers. Several types of research, including preformulation, kinetics, and stability investigations, were conducted using the wet granulation technique. Knowing which polymer gave the tablets the superior matrix form necessary for prolonged release is useful. Pectin (100), HPMC K100M (50), and Sodium Polyacrylate (75) were used in various medication rations to construct the formulation.

The angle of repose for gliclazide tablets ranges from 25.100.13 to 28.1038, the Bulk density ranges from 0.440.002 to 0.430.003, the Tapped density ranges from 0.500.004 to 1.180.002, and the Carr's index ranges from 1.180.002 to 1.160.011. The scheme's most vital component is the characterization and assessment stage, which allows researchers to examine the tablet's physical qualities such its hardness, friability, weight variation, and thickness. The empirical information for several formulations (F1-F6), including hardness (4.20.08 to 4.90.09), thickness (3.820.02 to 4.200.14), and friability (4.20.08 to 4.90.09).

Change in mass (from 248.4 to 252.6) per centimeter squared (0.260.03 to 0.50.03) Pectin-100,50mg 50,50mg 150,50mg 25,50mg 75,50mg HPMC- K100M 50,50mg 25,50mg 75,50mg were used in the in vitro gliclazide drug release research at various release times ranging from 1 to 12 hours. After 12 hours, the formulation (F6) that included pectin 75 mg and HPMC 75 mg showed the best sustained release of the medication (95,1 0.03), but the percentage varied across the intervals. Discovering the composition of the tablet formulation required the use of the kinetic property. "In vitro" The kinetics models were applied to the drug release data of (F6).

Conclusion

It was concluded that the matrix tablets of gliclazide were successfully developed in order to sustain the drug release rate by using pectin as release retardant. The present work, “Formulation and Evaluation of gliclazide SR Tablets” was taken on with an aim to formulate gliclazide SR tablets. In this work investigation so many factors which likely to affect the performance of the sustained release was studied. Wet granulation method was formulated. Preformulation study was done before punched tablet, after that the evaluation parameter of the tablet like weight variation, thickness and friability, in-vitro dissolution test were performed & % drug release was studied. Dissolution tests were performed and % drug release was found out. Dissolution profile of Formulation – F6 was optimized based on evaluation parameters. In the dissolution modelling all the developed formulations followed higuchi-peppas drug release. The optimized formulation F6 followed zero order drug release. The developed formulation was tested for its stability for three month & found to be stable at different type’s temperature and humidity. In this research, pectin was found to play a most important role in controlling release of drug from the matrix system. Accordingly, it can conclude that the formulation is strong in the performance, is less likely to be affected by the various factors studied.

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