Research Article

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## Sustained release of glipizide monolithic matrix tablets formulation & evaluation

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**Abstract**

Glipizide showed maximum absorbance at 276nm.Glipizide was prepared at different concentrations and absorbance was observed at 276nm.A calibration curve was plotted, and the curve observed is linear. Flow properties of the drugBulk density of all formulations range from 0.505 to 0.515. Tapped density of all formulations range from the 0.591 to0.602.Hausner's ratio of all formulations range varied from1.16 to 1.18. Compressibility Index of all formulations was found to be 13.84% to 15.81% Angle of repose of all formulations was found to be 26.28 to29.75.Hence by the above values, it is confirmed that all the formulation prepared showed good flow properties. Tablet evaluation studiesThe results of the weight variation tests showed values in the desired range varying from 120mg to 123 mg.The thickness of tablets prepared for allformulation'srangesbetween 4.1mm to4.9mm.The hardness of the tablets for the prepared formulations varied between 5.1kg/cm$^2$ to 6.0kg/cm$^2$.

***Keywords:*** Glipizide, ablet evaluation studies.



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### Introduction

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such *immediate- release products* result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. After absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached, another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms. In recent years, various modified- release drug products have been developed to control the release rate of the drug and/or the time for drugrelease.

The term *modified-release drug product* is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions or promptly dissolving dosage forms as presently recognized". Several types of modified-release drug products are recognized [1].

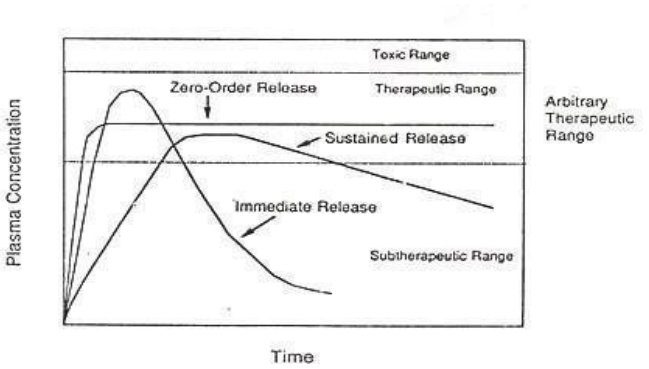
### SUSTAINED RELEASESYSTEMS

These systems include any drug delivery system that achieves slow release of drug over a prolonged period of time are known as sustainreleasesystems.

The goal of sustained –release dosage form is to maintain therapeutic blood or tissue levels of the drug for an extended period. This is usually accomplished by attempting to obtain zero order release from the dosage form. Zero order release constituents drug release from the dosage form that is independent of the amount of drug in the delivery system (a constant release rate).

Sustained release system generally do not attain this type of release and usually try to mimic Zero order release by providing drug in a slow first order fashion (concentration dependent) as shown in figure 1.4.1. Systems that are designated as prolonged release can also be considered as

attempts at achieving sustained release delivery. Repeat – action tablets are an alternative method of sustained release




in which multiple doses of the drug are contained within a dosage form, and each dose is released at a periodicinterval. Delayed release system in contrast, may not be sustaining, since often the function of these dosage forms is to maintain the drug within the dosage form for sometime before release.

Commonly, the release rate of drug is not altered and does not result in sustained delivery once drug release has begun

**Graphical diagram of sustained drug release form**

Advantages of sustained release products:

- Decreased local and systemic sideeffects
- Reduced gastro intestinalirritation.
- Better drugutilization
- Reduction in the total amount of drugused.
- Minimum drug accumulation on chronicdosing.
- Optimized therapy.

Disadvantages of sustained release products

- Dose dumping may occur either as a release of more than the usual fraction of drug or as the release of drug at a greaterrate.
- Removal of drug from the system is difficult in case of any toxicity, adverse drug reaction are accidentally becomesintoxicated.
- Orally administered sustained release products may yield erratic or variable drug absorption as a result of various drug interactions with the content of GI tract and changes in GImotility.
- Sustained release may not be practicable for drugs that are usually given in large doses in conventional dosageforms.
- Higher cost of medication has compared to conventional drugproduct

ORAL SUSTAINED DRUG DELIVERYSYSTEMS:

- Oral sustained release drug delivery is a system that provides continuous oral delivery of drugs at predictable and reproducible kinetics for a determined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemicaction.

I. CLASSIFICATION OF ORAL SUSTAINED RELEASE SYSTEMS:

A. Diffusion Sustained Systems Reservoir Devices. A core of drug (the reservoir) surrounded by a polymeric membrane characterizes them. The nature of the membrane determines the rate of drug release. The characteristics of reservoir diffusion systems are Zero order drug release ispossible. The drug release rate is dependent on the type ofpolymer. High molecular weight compounds are difficult to deliver through the device.
Coatingandmicroencapsulationtechniquecanbe usedtopreparesubdevices.

B. MatrixDevices.
It consists of drug dispersed homogeneously in a matrix. The characteristics of the matrix diffusion system is Zero order release cannot beobtained.

C. Easy to produce than reservoirdevices. High molecule weight compounds are delivered through thedevices.

**Dissolution controlled systems**

**I.Matrix Dissolution ControlledSystem**

Aqueous dispersions, congealing, spherical agglomeration etc. can be used.

**II.Encapsulation Dissolution Control**

Particles, seeds or granules can be coated by technique such as microencapsulation.

**Diffusion and Dissolution ControlledSystem.**

In a bio-erodible matrix, the drug is homogenously dispersed in a matrix and it is released either by swelling controlled mechanism or by hydrolysis or by enzymaticattack.

**MONOLITHIC MATRIXSYSTEM:**

In pharmaceutical CRDDS, matrix-based systems are the most commonly used type of release controlling methodology owing to their simple manufacturing process. The preparation of a tablet with the matrix involves the direct compression of the blends of drug, release retardant and other additives.The drug is uniformly distributed throughout the matrix core of the release retardant. Alternatively, drug-release retardant blends may be granulated to make the mix suitable for the preparation of tablets by wet granulation or beads [11].

1. To characterize and define the matrix systems the following properties of the matrix are considered.
2. Chemical nature of thesupport.
3. The physical state of thedrug.
4. The matrix and alteration in volume as the function of thetime.

5. The routes ofadministration.

The release kinetics model (in accordance with Higuchi's equation,thesesystem considered to release the drug as a function of square root of time).

The classification of the matrix-based systems is based on the following criteria.

- Matrix structure
- Releasekinetics
- Controlled release properties (diffusion, erosion andswelling).
- Chemical nature and the properties of the applied releaseretardant(s).

**MATERIALS & METHODS**

**LIST OFMATERIALS**

The materials used in the formulation area given

| S.No | Name of the material | Laboratory |
|---|---|---|
| 1. | Glipizide | Natco Pharma Limited |
| **2.** | Hydroxy Propyl Methyl Cellulose K100 CR | Natco Pharma Limited |
| **3.** | Eudragit L100 | Natco Pharma Limited |
| **4.** | Aero sil | Natco Pharma Limited |
| **5.** | Microcrystalline cellulose 102 | Natco Pharma Limited |
| **6.** | Polyvinyl pyrrolidine | Natco Pharma Limited |

**METHODOLOGY FOR GLIPIZIDEMONOLITHIC MATRIXTABLETS:**

Based on preformulation data following strategy it is used for developing matrix type drug release i.e.

1) DirectCompression [2].
   - Lesstime
   - MoreEconomic
   - Low cost ofLabour.

**STEP 1. WEIGHING**

Weighed the required quantities of Glipizide, HPMC, Eudragit, Micro crystalline cellulose, PVP and Magnesium stearate and other dry mix materials as per table given separately .

**STEP 2. SIFTING**

Sifted the drug , HPMC, Eudragit, Micro crystalline cellulose, PVP through #20 mesh and mixed the blend in a poly bag for uniform distribution of API.

**STEP 3. LUBRICATION**

Required amount of colloidal silica was weighed, passed through #80 meshand blended with aboveblend

**STEP 5. COMPRESSION**

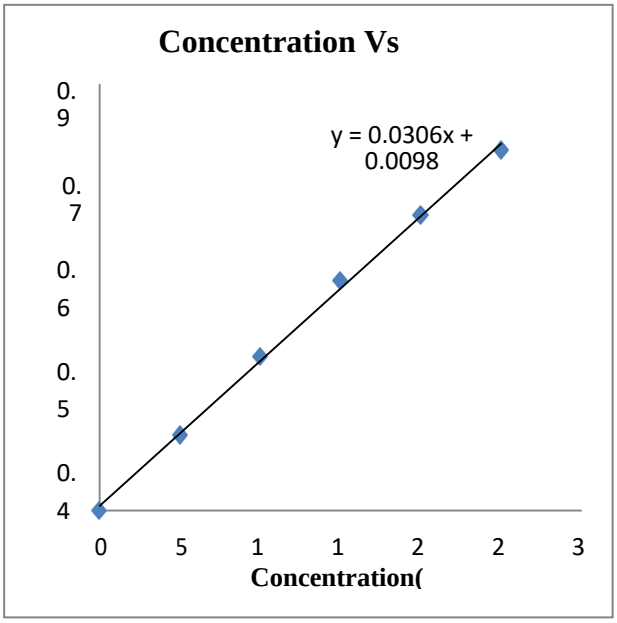
The Blend was compressed using 8.0mm Round shaped standard concave punches using 10 station compression machine.

**RESULTS & DISCUSSION**

**CHARACTERIZATION OF PURE DRUGSAMPLE:**

**IDENTIFICATION OFDRUG:**

The drug was identified by physical observation, melting point, ultra- violet spectroscopy and FTIR Spectroscopystudies.




**PHYSICALOBSERVATION**

The color and powder forms of the drug were observed and identified as per the Indian Pharmocopoeia. The colour of the Glipizide was found to be White to off-white crystallinepowder.

**MELTING POINTDETERMINATION**

The melting point of the bulk drug was determined in a melting point apparatus and compared with the value available Indian Pharmocopoeia. The melting point of the Glipizide was found to be 209 $^{O}$C.

**ULTRAVIOLETSPECTROPHOTOMETER:**

The UV –spectrum of the pure drug sample was analyzed in phosphate buffer of p$^{H}$ 6.8 in the range of 200 to 400 nm and $\lambda_{max}$ determined. The obtained $\lambda_{max}$ at 276 nm was compared and same was used for the quantitative analysis of thesample.

**STANDARD SOLUTION AND CALIBRATION CURVE OFGLIPIZIDE**

The UV scanning of drug sample was carried out using a solution of drug dissolved in methanolic 6.8ph phosphate buffer solutions at concentration of 100 µg/ ml. The $\lambda$max was observed at276nm.The calibration curve of Glipizide was obtained by dissolving the drug in buffer solutions and absorbance was measured at 276nm in methanolic buffer solution used as blank. Beer's law was obeyed the concentration range of 5-25 µg in 0.1 N HCLsolution.

**STANDARDGRAPHOF GLIPIZIDE**

| S.No | Concentration in µg/ml | Absorbance at 276nm |
|---|---|---|
| 1 | 0 | 0.0 |
| 2 | 5 | 0.159 |
| 3 | 10 | 0.326 |
| 4 | 15 | 0.486 |
| 5 | 20 | 0.624 |
| 6 | 25 | 0.761 |

**Standard Plot of Glipizide drug**

**PREPARATION OFTABLETS**

Glipizide tablets are prepared by direct compression method. The following steps are involved in the direct compression method.

**Step 1:** Weighing and Blending - the active ingredient, disintegration agents are Weighed and mixed.

**Step 2:** Sieving of the all mixture

**Step3:** Lubricate with Aerosil

**Step4:** Compression in 6mm concave punch

**MASTER FORMULATION FORGLIPIZIDE**

**Master formulation**

| Ingredients | F1 (3%) | F2 (6%) | F3 (9%) | F4 (12%) | F5 (3%) | F6 (6%) | F7 (9%) | F8 (12%) | F9 (1:1) |
|---|---|---|---|---|---|---|---|---|---|
| **Glipizide(mg)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **MCC 102(mg)** | 98 | 94.4 | 90.8 | 87.2 | 98 | 94.4 | 90.8 | 87.2 | 94.4 |
| **HPMCK100CR(mg)** | 3.6 | 7.2 | 10.8 | 14.4 | - | - | - | - | 3.6 |
| **EudragitL-100(mg)** | - | - | - | - | 3.6 | 7.2 | 10.8 | 14.4 | 3.6 |
| **PVPK-30(5%)** | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| **Aerosil (2%)** | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 |
| **Total tab wt(mg)** | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 |

In the above total 9 formulations were made by changing the polymers ratio's. In the first four formulations only HPMC polymer is used in different ratios along with other excipients except Eudragit. In the remaining four formulations only Eudragit –L is used along with other excipients other than HPMC.In the final final formulation that is ninth formulation both HPMC &Eutragit-L is used. The nine formulations were sent for evaluation studies for selecting the optimized formulation.

**VALUATION OFTABLETS**

**PRE AND POST FORMULATIONSTUDIES**

**Pre-compression parameters of Glipizide**

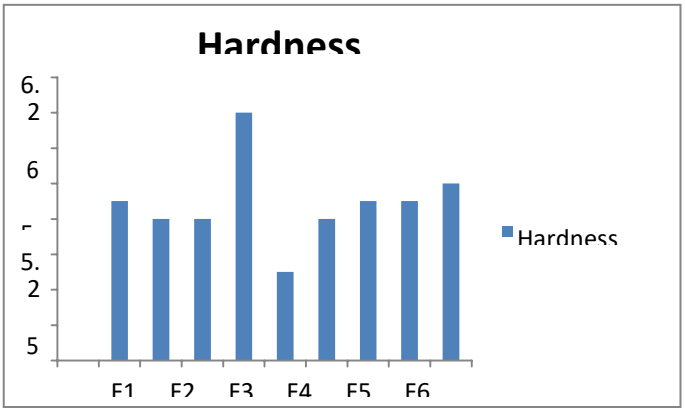
| Formulation | Bulk Density (gm\ml) | Tapped Density (gm\ml) | Carr's Index (%) | Hausne r's Ratio | Angle Of Repose |
|---|---|---|---|---|---|
| **F1** | 0.510 | 0.598 | 15.81% | 1.17 | 26.28 |
| **F2** | 0.512 | 0.597 | 15.38% | 1.18 | 26.85 |
| **F3** | 0.515 | 0.602 | 14.43% | 1.168 | 29.02 |
| **F4** | 0.505 | 0.591 | 14.64% | 1.17 | 27.75 |
| **F5** | 0.507 | 0.595 | 14.72% | 1.17 | 28.07 |
| **F6** | 0.507 | 0.597 | 14.97% | 1.176 | 28.07 |
| **F7** | 0.512 | 0.595 | 13.846% | 1.16 | 29.39 |
| **F8** | 0.515 | 0.598 | 13.91% | 1.161 | 29.74 |
| **F9** | 0.512 | 0.600 | 14.87% | 1.17 | 27.14 |

**Post compression parameters of Glipizide**

| Formulation | Avg.Wt (mg) | Diameter(mm) | Hardness (Kg\cm$^2$) | Friability | Thickness (mm) |
|---|---|---|---|---|---|
| **F1** | 121 | 6 | 5.5 | 0.11 | 4.60 |
| **F2** | 122 | 6 | 5.4 | 0.06 | 4.71 |
| **F3** | 122 | 6 | 5.4 | 0.02 | 4.90 |
| **F4** | 124 | 6 | 6.0 | 0.04 | 4.10 |
| **F5** | 120 | 6 | 5.1 | 0.14 | 4.90 |
| **F6** | 120 | 6 | 5.4 | 0.06 | 4.56 |
| **F7** | 121 | 6 | 5.5 | 0.16 | 4.44 |
| **F8** | 123 | 6 | 5.5 | 0.41 | 4.70 |
| **F9** | 119 | 6 | 5.6 | 0.14 | 4.80 |

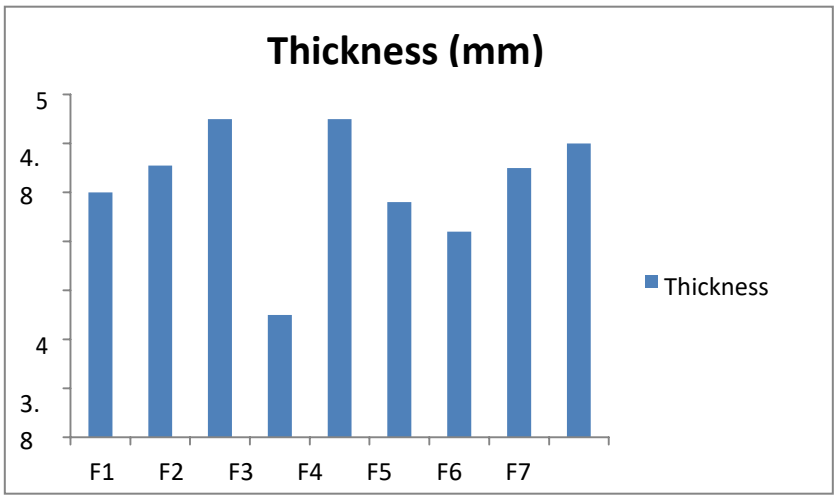
**AVERAGE HARDNESS OF THE FORMULATION**

**Bar diagram of Average hardness of formulations**




**AVERAGE THICKNESS OF THE FORMULATIONS**

**Bar diagram of Average thickness of the formulations**




**DISSOLUTIONSTUDIES**

| Time(hrs) | 0hr | 1hr | 2hr | 4hr | 6hr | 8hr | 10hr | 12hr | 14hr |
|---|---|---|---|---|---|---|---|---|---|
| **F1** | 0 | 22.36 | 34.23 | 55.63 | 69.77 | 76.54 | 81.43 | 93.52 | 96.07 |
| **F2** | 0 | 23.46 | 33.12 | 53.73 | 60.26 | 77.02 | 82.45 | 96.9 | 96.9 |

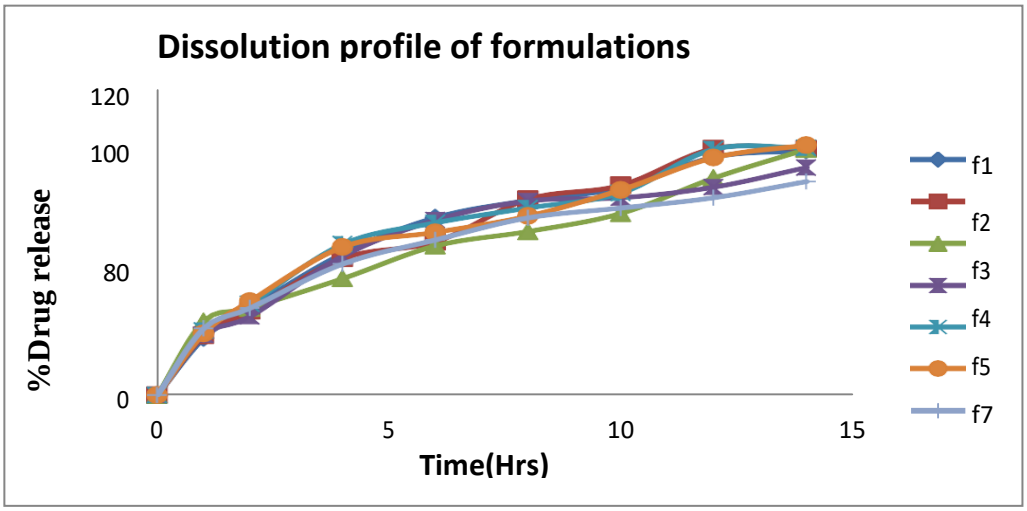
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **F3** | 0 | 17.94 | 34.23 | 45.82 | 58.66 | 64.32 | 71.42 | 85.30 | 96.62 |
| **F4** | 0 | 23.74 | 30.92 | 54.66 | 68.74 | 76.28 | 77.54 | 81.71 | 89.44 |
| **F5** | 0 | 25.39 | 35.88 | 59.35 | 67.71 | 73.56 | 79.43 | 96.62 | 97.17 |
| **F6** | 0 | 24.29 | 36.99 | 58.25 | 63.98 | 70.39 | 80.64 | 93.31 | 98.28 |
| **F7** | 0 | 26.22 | 34.23 | 51.57 | 61.01 | 69.67 | 73.53 | 77.57 | 83.92 |
| **F8** | 0 | 20.70 | 39.75 | 54.93 | 70.64 | 78.09 | 84.12 | 91.38 | 99.11 |
| **F9** | 0 | 21.53 | 36.44 | 67.63 | 79.91 | 85.51 | 89.65 | 94.41 | 99.38 |

Dissolution studies are done by using Paddle type dissolution apparatus. Here total nine formulations are sent for dissolution study in order to list out the optimized formulation.

**DISSOLUTION STUDIES**

Dissolution table of formulations in 6.8 Phosphate bufferGRAPHS OF

Dissolution profile of different formulations



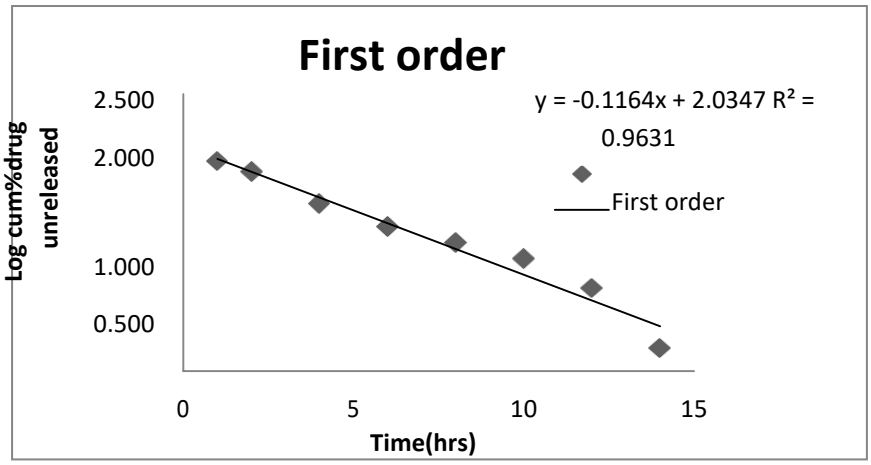

**DRUG RELEASEKINETICS**

In order to describe the kinetics of the release process of drug from sustained release preparations, the data were fitted with different kinetic models. The first order equation describes the release from systems when dissolution rate is dependent on the concentration of the dissolving species. The Higuchi square root equation describes the release from systems from where the solid drug is dispersed in an insoluble matrix and the rate of drug release is relate to the rate of drug diffusion. The release from the sustained release tablets is found to be diffusion type. Thegoodness of fit is shown through determination of correlation coefficient. Very high correlation coefficient (Close to 1) for a particular kinetic model indicates that the release can be characterized by that model.

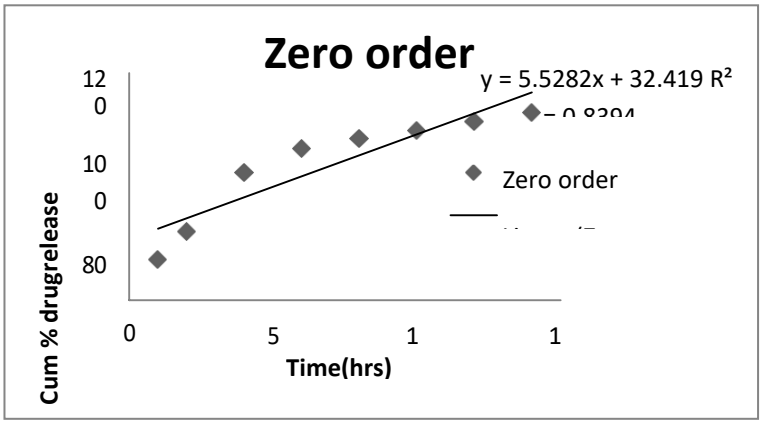
**Percentage drug release in different time**

| Time in(Hr) | %Drug released | %Drug unreleased | Log% drug released | Log% drug unreleased | Log T | Sqt T |
|---|---|---|---|---|---|---|
| 0 | 0.0 | 100 | 0.0 | 2.0 | 0.000 | 0.000 |
| 1 | 21.53 | 78.47 | 1.333 | 1.895 | 0.000 | 1.000 |
| 2 | 36.44 | 63.56 | 1.5616 | 1.803 | 0.301 | 1.414 |
| 4 | 67.63 | 32.37 | 1.8301 | 1.510 | 0.602 | 2.000 |
| 6 | 79.91 | 20.09 | 1.9026 | 1.303 | 0.778 | 2.449 |
| 8 | 85.51 | 14.49 | 1.9320 | 1.161 | 0.903 | 2.828 |
| 10 | 89.65 | 10.35 | 1.9526 | 1.015 | 1.000 | 3.162 |
| 12 | 94.41 | 5.59 | 1.9750 | 0.747 | 1.079 | 3.464 |
| 14 | 99.38 | 0.62 | 1.9973 | 0.207 | 1.146 | 3.742 |

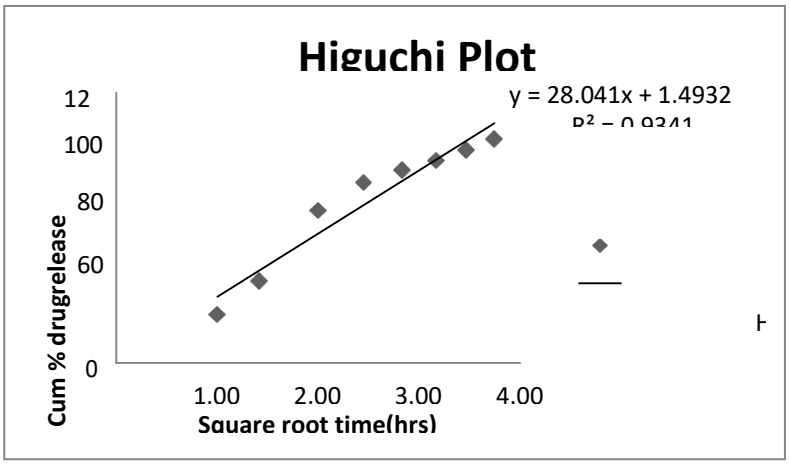
**First order plot**



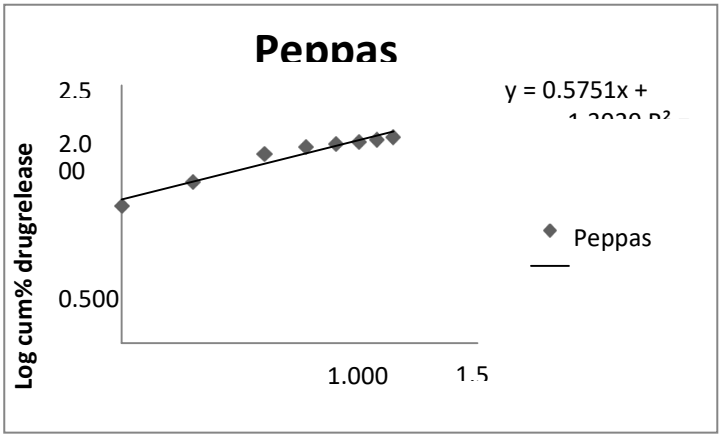

zero order plot




Higuchi plot




Peppas plot




The diffusion exponent "n" was found to be 0.6937,and the drug follows Non-Fictions which indicates that the release of drug from the tablets was **anomalous transport(Diffusion and erosion)** (0.5< n)

In order to understand the mechanism and kinetics of drug release data of the In-Vitro dissolution study were analyzed with various kinetic equations like Zero order model (% cumulative drug release Vs time ), first order model (log % amount remaining Vs time),Higuchi model (% cumulative drug release Vs Square root of time ). Korsmeyer-Peppas model (log % cumulative drug release Vs logtime).

Coefficient of correlation ($r^2$) values were calculated for the linear curves obtained by regression analysis of the above results. The formulation F9 which have n value greater than 0.5 shows the anomalous transport & best fitted with Korsemeyer-Peppas i.e ( $R^2$=0.9473).

**DISSOLUTION STUDIES**

Various solid matrix formulations were prepared with swellable and non-swellable polymers (HPMC K100CR, Eudragit L-100) in solid matrix using direct compression method.In the dissolution studies of all formulations, the formulation containing HPMC alone that is F1, F2, F3, F4 show 95% dissolution but shows fluctuations.The formulation containing Eudragit that is F5, F6, F7, F8 doesn't showbetterdissolution profile.The formulation 9 (F9), drug release profile is 99.38%, rest of all formulations. In the formulation 9 (F9) having swellable polymer HPMC K100CR and non-swellable polymer (Eudragit L-100) showing better drug release profile. Hence the combination of both polymers are better suitable for sustained releasedelivery.Thus , formulation 9 having both HPMC and Eudragit polymers in the ratio of 1:1 show 99.38% drug release for prolong time. So, all the *In-vitro* evaluation studie, preformulation studies, powder characteristics, tablet evaluation studies proved to be satisfactory for the drugdelivery.

**SUMMARY & CONCLUSION**

In the conclusion Glipizide Sustained release tablets were prepared by Direct Compression method using different polymers i.e HPMC & Eudragit and combination of both show drug release in a sustain manner. Although there are number of difficulties to be worked out to achieve prolong time of drug release a large number of companies are focusing towards commercializing this technique ie in a inexpensive, less dose, high drug release effect for a prolong time. So Glipizide, an antidiabetic drug which is sulphonyl urea derivative used to treat Type II diabetes can be delivered by using Matrix tablet by sustain drug delivery to increase pharmacological activity with a reduced dose and frequency.

**REFERENCES**


1. Altaf AS, Friend DR, MASRx and COSRx Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York,2003.
2. Vidyadhara S, Rao PR., Prasad JA., Indian J. Pharm Sci, 66, 188-192 (2004).
3. Reddy KR., Mutalik S, Reddy S, AAPS Pharm. Sci. Tech., 4, 1-9,(2003)
4. Mohammed AD., James LF., Michael HR., John EH., Rajabi-Siahboomi AR., Phar. Dev. Tech., 4, 313-324(1999).
5. Lee BJ, Ryu SG, Cui JH, Drug Dev. Ind. Pharm., 25, 493-501(1999).
6. Gwen MJ and Joseph RR, In Banker GS and Rhodes CT, Eds., Modern Pharmaceutics,3rdEdn,Vol.72,MarcelDekkerInc.NewYork,1996,575.
7. Salsa T, Veiga F And Pina M.E, Drug Develop. Ind. Pharm., 1997, 23,931.
8. Jantzen GM, Robinson JR, Sustained and controlled-release drug delivery systems, in Banker GS, Rhodes CT (Eds.) Modern Pharmaceutics, Third Edition, Revised and Expanded, Drugs and The Pharmaceutical Sciences, vol 72., Marcell Dekker, Inc., New York, 1995,575-609.
9. Altaf AS, Friend DR., MASRx and COSRx Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology Marcell Dekker Inc., New York,2003.
10. Wani MS, Controlled Release System-A Review, 2008, 6 (1), www.pharmainfo.net/review.
11. Jantzen GM, Robinson JR, Sustained and controlled-release drug delivery systems, in Banker GS, Rhodes CT (Eds.) Modern Pharmaceutics, Third Edition, Revised and Expanded, Drugs and The Pharmaceutical Sciences, vol 72., Marcell Dekker, Inc., New York, 1995,575-609.
12. Brahmankar HA, Jaiswal SB, Biopharmaceutics and Pharmacokinetics A Treatise, Vallabh Prakashan, 2000, 348-357 and337.
13. Venkatraman S, Davar A, Chester A, Kleiner

L, Wise DL, An overview of controlled release systems, Handbook of Pharmaceutical Controlled Release Technology, New York, Marcel Dekker, Inc.,2000,431-465.

14. Qiu Y, Zhang G and Wise DL, Research and Development Aspects of Oral Controlled-Release Dosage Forms, Handbook of Pharmaceutical Controlled Release Technology, New York, Marcel Dekker, Inc., 2000,465-503.
15. Kamboj S, GuptaGD, Matrix Tablets: An Important Tool for Oral Controlled-Release Dosage Forms, 2009, 7(6),www.pharmainfo.net/review.
16. Lieberman HA, Lachman L and Schwartz JB., Pharmaceutical Dosage Forms: Tablets, Volume 3, 2nd edition,199-287.
17. Sayed I. Abdel-Rahman, Gamal MM, El-Badry M, Preparation and comparative evaluation of sustained release metoclopramide hydrochloride matrix tablets, Saudi Pharmaceutical Journal (2009) 17, 283-288.
18. Chandran S, Laila FA and Mantha N, Design and evaluation of Ethyl Cellulose Based Matrix Tablets of Ibuprofen with pH Modulated Release Kinetics,IndianJournalofPharmaceyticalSciences,September-October2008.
19. Gothi GD, Parinh BN, Patel TD, Prajapati ST, Patel DM, Patel CN, Journal of Global Pharma Technology, 2010; 2(2):69-74.
20. Basak SC, Reddy JBM, and Lucas Mani KP. Indian
21. Varshosaz J, Tavakoli N and Kheirolahi. AAPS PharmSciTech 2006; 7(1) ArticleRaghvengra Rao NG, Gandhi S, and Patel T. International Journal of Pharmacy and Pharmaceutical Sciences, Vol.1, Suppl 1, Nov.-Dec. 2009. 23)Shivhare UD, Adhao ND, Dr. Bhusari KP, Dr. Mathur VB and Ambulkar UD. International Journal of Pharmacy and Pharmaeutical Sciences, Vol. 1, Issue 2, Oct-Dec.2009.
22. Kamboj, S., Gupta, G. D., Matrix Tablets: An Important Tool for Oral Controlled- Release Dosage Forms, 2009, 7(6),www.pharmainfo.net/review.
23. Brahmankar, H. A., Jaiswal, S. B., Bio pharmaceutics and Pharmaco kinetics A Treatise, Vallabh Pr