CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

# STUDIES ON DEVELOPMENT AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS CONTAINING TIZANIDINE

**[1]Dr.Patil C C, [2]Yogitha M, [3]Vijapure VK, [4]Jorapur PN, [5]Karajagi S**
*[1]BLDEA"S SSM College of Pharmacy Vijayapura.

**Article Received:** October 2019 **Accepted:** November 2019 **Published:** December 2019

**Abstract:**
*In the present study, describes the Studies on development and evaluation of sustained release matrix tablets containing tizanidine. Were prepared by wet-granulation method using polymers like Guar gum & Ethyl cellulose in different ratios. Matrix tablet evaluated by different methods for parameters such as hardness,weight, thickness, drug content uniformity. The tablets were evaluated for in vitro release in pH 1.2 and 7.4 phosphate buffer for 12 hours in standard dissolution apparatus. In order to determine the mode of release, the data was subjected to First order, Zero order, and Pappas and Higuchi diffusion model. Uniformity in vitro drug release studies and stability studies Short term stability studies on the promising formulation indicated that, there are no significant changes in drug content. IR spectroscopic indicated that there are no drug- excipients interaction. All the granules of the formulation showed in compliance with Pharmacopoeia Standards. The developed sustain released matrix tablet of Tizanidine drug showed 12 hours of drug release and overcome the disadvantage of conventional tablets.*

**Keywords:** *Matrix tablet, Tizanidine, Guar gum, Ethyl cellulose.*

**Corresponding author:**
**Dr.CC Patil**
*Head of the Department of Pharmaceutics*
*BLDEA'S SSM College of Pharmacy Vijayapura-586103*

QR code

*Please cite this article in press CC Patil et al.,* ***Studies on Development and Evaluation of Sustained Release Matrix Tablets Containing Tizanidine.,*** *Indo Am. J. P. Sci, 2019; 06(12).*

## INTRODUCTION:

Oral route is the most preferred route for administration of drugs. Tablets are the most popular oral formulation available in the market and preferred by the patients and physician a like. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered multiple doses and therefore have several disadvantages. The primary benefit of a sustained release dosage form, compared to a conventional dosage form, is the uniform drug plasma concentration and therefore uniform therapeutic effect [1]. Matrix system are favored because of their simplicity, patient compliance etc, than traditional drug delivery which have many drawbacks like repeated administration, fluctuation in blood concentration level etc. Developing oral sustained release matrix tablets for highly water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. [2] Matrix type drug delivery systems are an interesting and promising option when developing an oral controlled release system. This review focuses on the progress made in the design of controlled release dosage forms employing various types of matrices as carriers for the active ingredients. [3] Tizanidine hydrochloride is an imidazoline derivative which act as agonist on centrally located alpha 2 receptors and this lead to myontolytice effect on skeletal muscle. It is structurally and phymacologically similar to clonidine and other alpha 2-adrenergic agonist's. The correct mechanism of tizanidine in decreasing muscle tone and Frequency of spasm is not clearly understood. About 53% to 66% of the dose administered is being absorbed through the gastrointestinal tract after oral administered is being absorbed through the gastrointestinal tract after tract after oral administered is be gaining absorbed through the gastrointestinal tract after tract oral administration and the peak plasma concentration is reached within 1 to 2 Hours . Bioavailability of tizanidine is about 34% to 40% and half-life is 2.5 hour. The drug is widely distributed throughout the body and 30% of drug bind to plasma protein. It under goes rapid and extensive first pass metabolism in the liver (approximately 95% of a dose) leading to the oxidation of the imidazoline moiety, aromatic system, and sulfur atom.[4 ] The two parameter such as low molecular weight and dose satisfy for tizanidine. Thus present study is undertaken in formulating matrix tablet by using the natural and synthetic polymer by wet granulation and direct compression method.

## MATERIAL AND METHOD:

Tizanidine Drug purchased from JPN Pharma Mumbai, Guar Gum(Loba Chemicals), Ethyl cellulose(Pallav Chemicals Limited),Micro crystalline cellulose ( Loba chemicals Pvt Ltd) other chemicals received from Store BLDEA'S SSM college of Pharmacy Vijayapur.

**Methods:**

**Preparation of Matrix tablets: [5,6,7]**

We granulation method has been employed to prepare matrix tablets of Tizanidine using Guar Gum and EC as polymers. Different formulations were prepared by wet granulation technique. All the powders were passed through 80 mesh. Required quantities of Tizanidine, Guar Gum and Ethyl cellulose polymers were mixed thoroughly and sufficient volume of viding agent (5% w/v starch) was added slowly. After enough cohesive was obtained, the mass was sieved through 22/44 mesh. The granules were dried at 400c to 450c for 12 hrs. Once dry the granules retained on 44 mesh were mixed with 10% of fines (granules that passed through 44 mesh (Talc and magnesium stearate were finally added as glidant and lubricants. The tablets were compressed using rotary compression machine. The total weight of tablet was 100mg and each tablet contains 10 mg of Tizanidine and other pharmaceutical ingredients as listed in the table 01.

**Table No :-01 Formulation Table of Tizanidine Matrix Tablet**

| Ingredient (Formulation code) | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 |
|---|---|---|---|---|---|---|---|---|
| Tizanidine | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 20 |
| Ethyl Cellulose | 25 | 50 | 75 | | | | 37.5 | 32.5 |
| Guar Gum | | | | 25 | 50 | 75 | 37.5 | 32.5 |
| Lactose | 60 | 35 | 10 | 60 | 35 | 10 | 10 | 10 |
| Mg.Sterate | 03 | 03 | 03 | 03 | 03 | 03 | 03 | 03 |
| Talc | 02 | 02 | 02 | 02 | 02 | 02 | 02 | 02 |
| Total (Mg/Tab) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**Evaluation of post compression parameters of tablets:**
1) Hardness
2) Friability
3) Thickness
4) Weight variation
5) Drug content
6) X ray diffraction Studies.
7) Fourier transforms infrared spectroscopy analysis
8) In vitro drug release study.

**Hardness: [8,9]**
The hardness of the tablets were determined using Pfizer Hardness tester. It is expressed in kg/cm2. Six tablets were randomly picked from each formulation and standard deviation values were calculated.

**Uniformity in Thickness: [10]**
Ten Tablets were selected at random from individual formulations & thickness was measured by using Digital micrometer, which permits accurate measurement & average thickness was calculated.

**Friability:[11]**
A friability test was conducted on the tablets using an Electro lab friabilator. Twenty tablets were selected from each batch & any loose dust was removed with the help of a soft brush. The tablets were initially weighed ( Winitial) & transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again (Wfinal). The percentage friability was then calculated by.

**Weight Variation: [12,13]**
The weight variation test was conducted by weighing 20 randomly selected tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The specification of weight variation is 10 %

**Drug Content:[14]**
Ten tablets were randomly selected & allowed to equilibrate with 6.8 pH phosphate buffer solution overnight and the solution were filtered (0.45µ,milipore). After 12 hours, suitable dilution were made with 6.8 pH buffer solution to get the concentration in Beer's Range. Absorbance of the solution was noted at 228 nm using 6.8 buffer solution as blank and drug content per tablet was calculated.

**Fourier Transfer Infrared Spectroscopy:[15]**
Compatibility study was carried out to know the possible interaction between TZN and polymers used in the formulation. The samples were crushed with KBr to make pellets under hydraulic pressure of 10 tons, and then the FTIR spectra were recorded between 400 and 4000 cm-1. It was used to study the interaction between the drug and polymer. The drug and polymer must be compatible with one another to produce a stable product. Drug and polymer interaction were studied by using FTIR. IR spectral analysis of pure Tizanidine and mixture of Tizanidine with Gellen gum and EC were carried out .

**Differential Scanning Calorimentry (DSC)**
Thermal properties of the pure TZN and the physical mixture of drug and excipients were analyzed. The samples were heated in hermetically sealed aluminum pans. Heat runs for each sample were set from 30 to 3500oC at a heat ingrate of 100oC/ mm, using nitrogen as blanket gas.

**In Vitro drug release study:[16]**
The in vitro dissolution studies were carried out using USP dissolution apparatus type (basket method) at 100 rpm. Dissolution test was carried out for a total period of 12 h using 0.1 N HC1 (pH 1.2) solution (900 ml) for the rest of the period. 5ml of the samplet was withdrawn at regular interval and replaced with the same volume pre-warmed (37 +_ 0.50C) fresh dissolution medium. The samples withdrawn were filtered and the drug content in each sample was analyzed after suitable dilution by UV spectrometric method.

**Stability Studies:**
In the present work stability studies were out at 400 C for period of 90 days. The formulations were evaluated for drug content after 90 days.

**RESULT:**

Table No:- 02 Pre-compression Analysis

| Formulation code | Bulk density | Tapped density | Carr's Index | Hausner density | Angle of repose |
|---|---|---|---|---|---|
| T1 | 0.409 | 0.434 | 5.76 | 1.058 | 22.82 |
| T2 | 0.394 | 0.417 | 5.51 | 1.058 | 19.74 |
| T3 | 0.409 | 0.434 | 5.76 | 1.061 | 25.94 |
| T4 | 0.409 | 0.434 | 5.76 | 1.061 | 28.22 |
| T5 | 0.387 | 0.407 | 5.37 | 1.056 | 23.70 |
| T6 | 0.387 | 0.409 | 5.37 | 1.058 | 28.21 |
| T7 | 0.394 | 0.417 | 5.51 | 1.056 | 25.46 |
| T8 | 0.394 | 0.417 | 5.51 | 1.058 | 21.31 |

Table No 03:-Post Compression Evaluation:-

| Formulation code | Bulk density | Tapped density | Carr's Index | Hausner density | Angle of repose |
|---|---|---|---|---|---|
| T1 | 100.5 | 2.62 | 5.97 | 0.64 | 96.66 |
| T2 | 100.7 | 2.89 | 6.79 | 0.79 | 96.26 |
| T3 | 100.4 | 2.60 | 6.20 | 0.89 | 97.26 |
| T4 | 100.7 | 3.02 | 5.97 | 0.69 | 97.14 |
| T5 | 100.4 | 3.12 | 6.66 | 0.74 | 97.26 |
| T6 | 100.9 | 3.14 | 7.15 | 0.88 | 97.85 |
| T7 | 101.5 | 2.90 | 5.99 | 0.39 | 96.42 |
| T8 | 101.2 | 3.30 | 6.70 | 97.26 | 97.26 |

Table No04:-In-Vitro Drug Release Study of Matrix Tablet

| SL.NO | TIME | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 |
|---|---|---|---|---|---|---|---|---|---|
| | 0.5 | 5 | 20.21 | 19.8 | 18.59 | 16.7 | 15.89 | 15.76 | 14.82 |
| | 1 | 34.49 | 29.64 | 35.02 | 29.64 | 32.2 | 29.64 | 32.33 | 30.98 |
| | 1.5 | 48.09 | 43.24 | 43.11 | 46.07 | 45.53 | 43.51 | 44.05 | 43.51 |
| | 2 | 53.08 | 50.25 | 47.55 | 51.19 | 49.54 | 49.04 | 53.05 | 53.58 |
| | 3 | 53.57 | 50.83 | 48.57 | 52.02 | 50.83 | 49.88 | 52.14 | 53.92 |
| | 4 | 54.41 | 52.97 | 50.83 | 57.14 | 53.21 | 52.61 | 56.54 | 55 |
| | 5 | 56.78 | 55 | 55 | 58.75 | 55.35 | 56.19 | 62.73 | 58.57 |
| | 6 | 59.16 | 59.28 | 56.78 | 59.64 | 57.38 | 58.57 | 66.3 | 60.59 |
| | 7 | 63.81 | 62.5 | 59.16 | 66.3 | 62.02 | 61.42 | 69.76 | 62.26 |
| | 8 | 68.21 | 65.11 | 62.26 | 70.95 | 65.83 | 63.33 | 75.23 | 66.42 |
| | 9 | 72.85 | 71.07 | 64.52 | 72.26 | 68.57 | 66.3 | 82.03 | 75.95 |
| | 10 | 79.41 | 73.8 | 68.57 | 76.66 | 75.84 | 68.92 | 88.92 | 82.97 |
| | 11 | 82.51 | 78.21 | 72.5 | 82.97 | 80.83 | 74.88 | 93.72 | 83.57 |
| | 12 | 87.14 | 82.38 | 78.21 | 86.07 | 86.54 | 82.97 | 97.26 | 88.83 |

Figure No:-01In-Vitro drug release study of Tizanidine Matrix Tablets

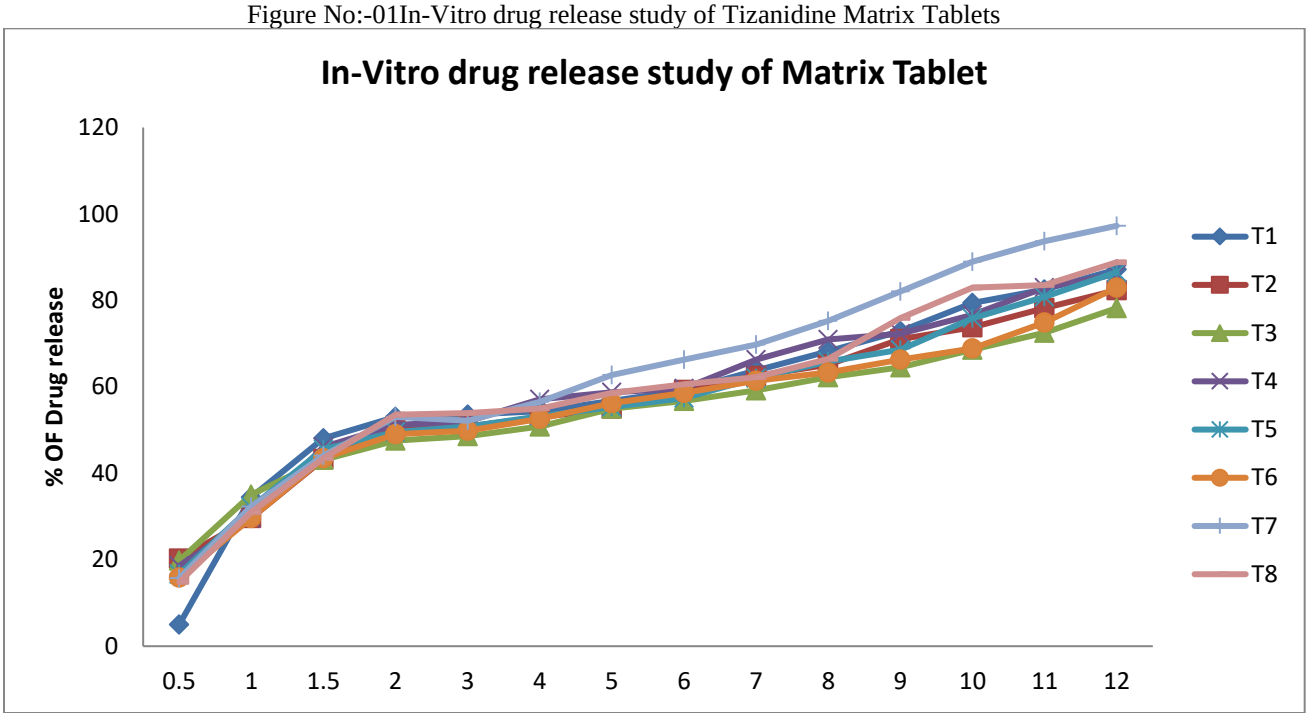
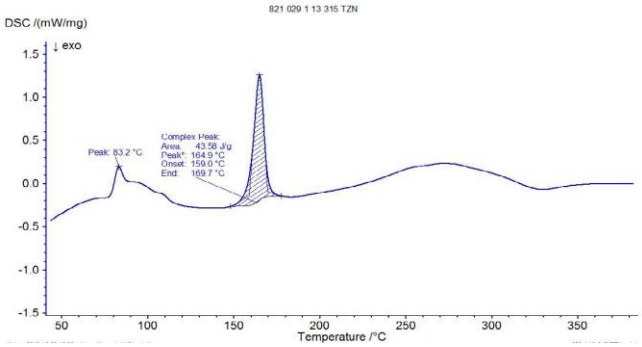



Figure:-02 DSC Thermographs of Pure Drug(A), Dummy (B), Matrix tablet(C)



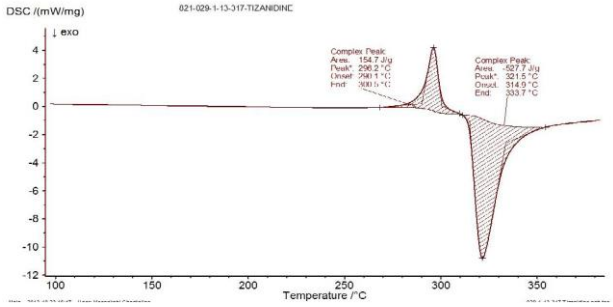



Figure No:-03FTIR Spectroscopy Of Drug (A), Matrix Tablet(B).

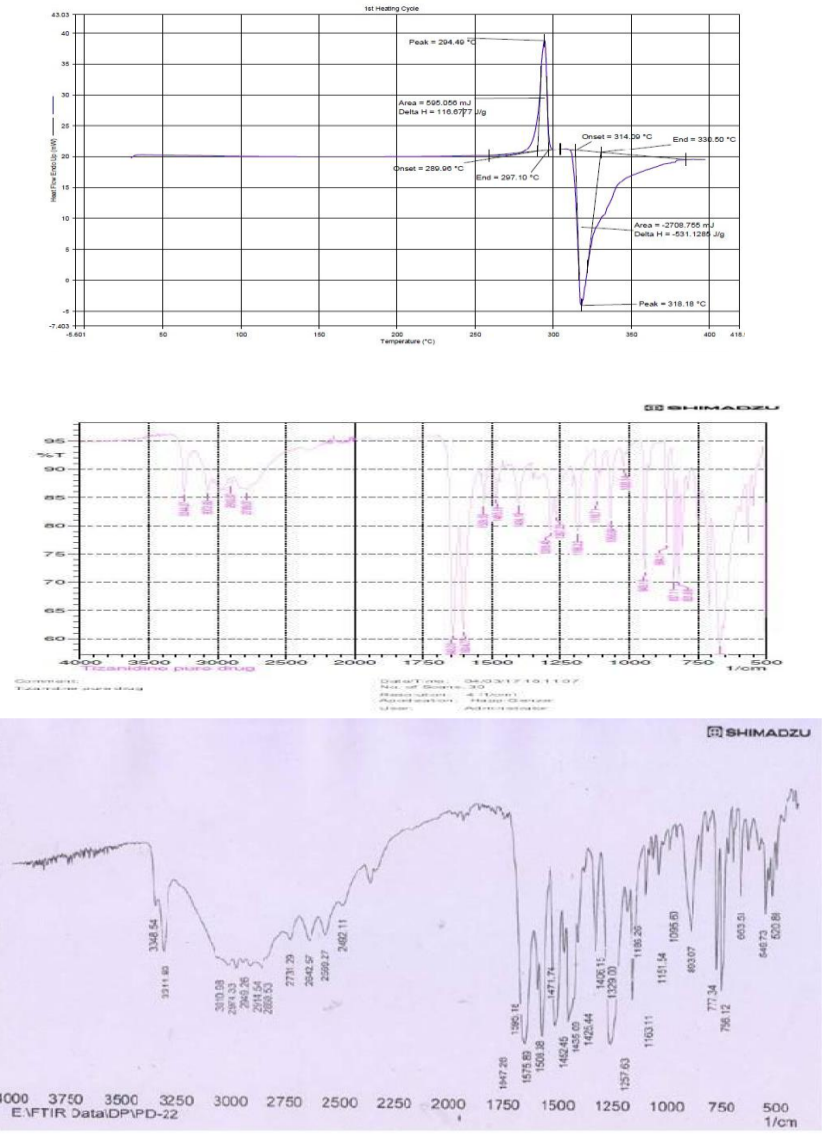



Table No:-05 Kinetic Of Drug release Of Tizanidine Matrix tablets

| Formulation code | Zero Order | First Order | Higuchi Model | Peppas Model |
|---|---|---|---|---|
| T1 | 0.8149 | 0.9230 | 0.9342 | 0.9055 |
| T2 | 0.8241 | 0.9399 | 0.9497 | 0.9350 |
| T3 | 0.7878 | 0.9121 | 0.9303 | 0.9047 |
| T4 | 0.8231 | 0.9410 | 0.9476 | 0.9084 |
| T5 | 0.8261 | 0.9139 | 0.9379 | 0.8869 |
| T6 | 0.7980 | 0.9017 | 0.9314 | 0.8906 |
| T7 | 0.8964 | 0.8892 | 0.9793 | 0.9483 |
| T8 | 0.8312 | 0.9254 | 0.9406 | 0.8874 |

Stability Study of Tizanidine Matrix Tablets:- The short term stability study of tizanidine matrix tablet was carried out. The percentage degradation of drug not more than 1%.

## DISCUSSION:

Tizanidine, a central skeletal muscle relaxant reduces muscle spasm by acting centrally as an agonist of a2-arenergle receptor, comes under class-2 category of BCS classification of drugs which have low solubility and more germ ability, the poor aqueous solubility and dissolution rate of hydrophobic drugs is a major problem for the formulation of solid dosage form to the formulation. In case of hydrophobic drug dissolution rate is the rate limiting step and absorption of drugs, poor aqueous solubility and the poor dissolution rate resulting into a decreased Bioavailability In the present work, an attempt was made to prepare matrix tablets of Tizanidine by using Guar Gum and Ethyl cellulose by wet granulation method of controlled release. The result of granule evaluation suggested that all the prepared granules exhibited good and excellent flow properties, as the angle of repose values were less that 30 A good packing ability of the granules was indicated by Carr's compressibility index and Hauser's ratio. The weight, thickness and drug contents of all tablets were found to be form with their low standard deviation values. The hardness was in the range of 5.9 to 7.2 kg cm and friability was in the rag of 0.3 to 0.8% and drug content was in the range of 96.42% to 97.85%. IR spectrum of Tizanidine exhibited peaks at 3364.93 cm due to N-H stretching. Peaks at 1616.4. 1650.16 And 1655.94 cm due to C=C, C=N stretching. There bands confirm the structure of Tizanidine the similar peaks with the little alteration were observed in the septum mixture of the drug and other polymers like GG & CC indicated that there is no drug into polymer interaction and chemical The thermal behavior of the matrix tablet was studied using DSC in order confirm the formulation solid inclusion. The DSC thermo gram of Tizanidine show an endothermic peak at 2970 c and corresponding to melting point. The characteristics endothermic peak at 2970 c disappears in the thermo gram of T7 matrix formulation and shows 330.50 indicate the uniform dispersion the drug in the amorphous form in tablet figure. The In-vitro drug release study was perfixened by using distributor rate set approaxtum in 0/1 N Hcl for 2 hours and 7.4 Phosphate buffer till the end of the study. The dissolution results indicates that the tablets were capable of recessing up to 12 bones depending upon the formulation variables among the all formulations T7 & T8 were optimized on the basis of release profile. The tablets (T7) prepared with the GG a& ECC shown a maximum release 97.26% and T3 shows drug release 78.21% at the end of 12 hours. The release data were fitted according to Zero order, higuchi's order, Peppas's orde First order Base on the result of evaluation the data of all formulation were optimized because of their sustained release property. The matrix tablet of Tizanidine were subjected to the stability study oat 40c .The samples were analyzed after 90. days for their physical appearances drug content vales No appropriate change observed. The stability results suggest that the drug is there in the intact form in the formulation during the storage.

## REFERENCES:


1. Basavaraj, BS Rao, Kulkarni SV, Patil P and Surpur C. Design and Characterization of Sustained Release Aceclofenac Matrix Tablets Containing Tamarind Seed Polysaccharide. J.Pharm. tech. 2011:1(1)17-21
2. Patel M, Gevariya HB. Formulation and statistical optimization of proponolol matrix tablet. World journal of pharmaceutical research. 2012;1(1):120-7.
3. Hemnani M, Patel U, Patel G, Daslaniya D, Shah A, Bhimani B. Matrix tablets: A tool of controlled drug delivery. American journal of pharmatech research. 2011;1(4):127-43.
4. Adimoolamsenthil,ChavaGajendrasnhAmbuji,patelJyotindraNatvarlal, Jimson Jose,NarayananaSwamyV.B,Internationalreasarch journal of pharmacy www.irjponline.com.
5. Izhar Ahmed Syed., Yamsani Madhusudan Rao., "A Modified release Drug Delivery Device: Multilayered Matrix Tablets" Am. J. Pharm Tech Res.2012;2(3)ISSN:2249-3387.,http://www.ajptr.com
6. D. Krishnarajan., C. Mahesh Reddy., SasikanthKanikanti., N Senthil Kumar.,and M. Purushothanman., 2013 "Formulation and evaluation of sustained release matrix tablets of levofloxacin using natural polymer" Pharmacophore 2013, Vol. 4(5) 146-157USACODEN:PHARM 7 ISSN 2229-5402.thttp:www.pharmacophorejournal.com.
7. Thombre NA, aher AS, Wadkar AV, Kshirsagar SJ " A Review on Sustained Release Oral Drug Delivery System" International Journal for Pharmaceutical Research Scholars (IJPRS)., V-4, I-2, 2015., ISSN No: 2277-7873.
8. PrajapatiB.G,Patel.K.R.Design and in vitro evaluation if Nicrorandil sustained release matrix system . Int. J. Pharm. Sci. Rev. and Res 2010: 1 (1) : 33-38.
9. Tabandeh H, mortazavi SA., Guilani TB., Preparation of sustained release Matrix tablets of Asprin with Ethylcellulose, Eudraigit RS100 and

Eudraigit RL 100 and studying the release profile and their sensitivity to Tablet hardness., Iranian Jouranl of pharmaceutical research 2003, 201-206.

10. . Shaikh RG, Sharma AR, Patel KN, Patel BA, Patel PA., Design and optimization and evaluation of Orally Disintegrating Tablet of Antiemetic Dug Int. J. Pharm, Res. Scholars. 2012;1(2); 281-295.
11. Harish NM, Chrayulu NR, Shenoy KRP. Formulation, Design and Optimization of Sustained release tablets of Terbutalinesulphate,. Ind. J. Pharm. Edu. Res. 2011; 45(3).
12. Chaithaluru k, Tadikonda R, Gollapudi R, Kandula KK, Formulation and invtro Evaluation of sustained release matrix tablets of losartan potassium Asian J. Pharm. Clin, Res. 2011; 4 (3).
13. Azharuddin M, Kamath K, Pillai SS, Panneerselvam T, Sharbarya AR. Formulation and evaluation of controlled release matrix tablets of antihypertensive drug using natural and synthetic polymers. Researc in Biotechnology. 2011; 2(4): 26-32.
14. Basawaraj S. Patil ,Sandeep S. Tate, Upendra Kulkarni, Hariprasanna R.C., Guruj V. Wadgeri. Development and evaluation of MucoadhesiveBuccal Tablets Of Tizanidine Hydrochloride using Natural Polymer Xanthan gum., Vol-8. Issue-2. ISSN 0976-44X.
15. GhulamMurtaza, HanifUllah, Shujaat Ali Khan , Sadullah Mir, AbidaKalsoom Khan, Bushra Nasir, SairaAzhar and Mubashir Ali Abid., Formulation and invitro dissolution characteristic of sustained release Matrix tablets of Tizanidine Hydrochloride.
16. Nayana S M., KirankumarNavade., Nethravathi A., K. Sumana., Suresh V Kulkarni., Influence of natural gums and synthetic polymers on the sustained releas Matrix tablets of Tizanidine Hydrochloride., World journal of pharmacy and pharmaceutical science ., vol-4, issue-05., 1639-1652. Issn:2278-4357.