Advances in Bioresearch
Adv. Biores., Vol 15 (2) March 2024: 512-523
©2024 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.15.2.512523

Advances in Bioresearch

ORIGINAL ARTICLE

Design and Development of Modified Release Matrix Tablet Using Amino Acid as Carrier

Nikita Bhosale *, Atish Velhal, Prakash Jadhav, Vivek Kumar Redasani.
YSPM's, YTC Faculty of Pharmacy Wadhe Phata, Satara 415011
Email: nikhitabhosale18@gmail.com

ABSTRACT
The aim of the present study was to improve the solubility and dissolution rate of the drug Glipizide using solid dispersion sustained release matrix tablets, in management having type II diabetes mellitus. Using L-leucine as a carrier, solid dispersion was created using the solvent evaporation process. L-leucine is used as a carrier to improve solubility. The effective dispersion was then directly compacted into a matrix polymer carboxymethyl tamarind gum tablet for sustained release. The solid dispersion was characterized by Fourier transform - infrared spectroscopy (FT-IR) and confirmed that no chemical interaction during entrapment process. Differential scanning calorimetry (DSC), X-ray powder diffraction (XRD) analysis, scanning electron microscopy (SEM) and Energy dispersive X-ray analysis studies (EDX) show that leucine inhibits the crystallization of Glipizide. The matrices were prepared by dry blending of polymers and other excipients using direct compression method. The designed matrix tablets with the manufactured solid dispersions were tested for pre-compression and post-compression parameters hardness, friability, drug content, hydration studies, were carried out along with compatibility studies and In Vitro drug release studies. These tablets containing CMTG had good swelling and sustained release of glipizide over a period of 8h. In Vitro drug release data were analyzed for zero order, first order, Higuchi and korsemayer- Peppas models. The mechanism of release of drug for glipizide from diffusion controlled exhibited by higher correlation. F6 was proven as the optimized swelling matrix tablet and showed non-Fickian diffusion release mechanism. To confirm the exact mechanism of drug release from these tablets, the data were fitted to Korsemeyer -peppas equation.

KEYWORDS Solid dispersion, Glipizide, leucine, Solvent evaporation method, Sustained release**.**

Received 24.11.2023 Revised 03.01.2024 Accepted 11.02.2024

How to cite this article:
Nikita B, Atish V, Prakash J, Vivek K R. Design and Development of Modified Release Matrix Tablet Using Amino Acid as Carrier. Adv. Biores., Vol 15 (2) March 2024: 512-523.

INTRODUCTION

Most novel drug candidates now show low aqueous solubility due to the use of combinational chemistry and high-throughput screening in drug discovery in recent years. Industries typically use a suitable pharmaceutical strategy to enhance the dissolving of medications that are not very water soluble. A medicine that isn't very water soluble will take longer to dissolve in the digestive fluid than it does to be absorbed in the gastrointestinal system.[1]To successfully manufacture medications having limited solubility in water into accessible therapeutic products, a deeper comprehension of the dissolution and absorption behaviors of these pharmaceuticals is necessary.[2]Although techniques such as salt formation and particle size reduction are frequently employed to speed up drug solubility, there are practical restrictions with these approaches that mean the desired bioavailability enhancement may not always be realized. As a result, formulation strategies are being investigated to increase the bioavailability of medications that are poorly water-soluble, one of which is the solid dispersion technique. [3]and needs to be created in an appropriate dosage form. The active components in conventional dosage forms, such as capsules and tablets, are thought to enter an absorption pool right away. Sustained release formulations were created in order to achieve a prolonged therapeutic effect by continuously releasing medication over a long period of time after administration of a single dose and to eliminate the need for multiple dosage regimens, particularly for those medications that require reasonably constant blood levels over an extended period of time.[4]The use of a sustained release medication delivery system can improve patient

compliance, optimize therapy, and reduce toxicity and dose requirements. [5] Diabetes mellitus is one of the most prevalent causes of death and disability in the world. Although the fact that both type I and type II diabetes are becoming more common worldwide, type II diabetes is predicted to become more common more quickly in the coming years due to sedentary lifestyles, rising obesity rates, and decreased activity levels. After China, India is the nation that has the second-highest prevalence of diabetes, with an estimated 77 million people having received a formal diagnosis. [6]. Glipizide is a popular sulphonyl urea anti-diabetic drug used to treat type II diabetes patients. Glipizide enhances insulin production from the pancreatic islets tissue cells, raises the concentration of insulin in the pancreatic vein, and may increase the number of insulin receptors. According to the biopharmaceutical classification system (BCS), glipizide is a weak acid (pKa= 5.9) that is virtually insoluble in water and an acidic environment and a highly permeable (class II) medication. The bioavailability of the oral absorption is nearly 100%, it is uniform, quick, and complete, and its elimination half-life is 2-4 hours. A medicine that is rapidly absorbed, has a quick half-life, and has a quick elimination rate makes a good candidate for formulation for sustained delivery.[7]

Leucine (Leu) is a naturally occurring amino acid that is crucial in controlling how proteins and amino acids are metabolized. High fluidity and minimal hygroscopicity characterize the crystalline powder. It is the most promising amino acid excipient and can reduce particle agglomeration and prevent the formation of solid bridges between particles, which can prevent the attachment of powder particles. Leucine has thus been utilized in numerous earlier experiments to improve the dispersion of inhalants. [8,9,10] The SD carrier uses L-leucine in this work to create a new formulation of Glipizide that had improved flowability, dissolving rate, and bioavailability. The electrostatic attraction created by the positive charges of the amino group in Leucine and when employing Leucine as the carrier in an SD of Glipizide, the negative charges of the carboxyl group can also be used. In this work, In order to produce and keep the amorphous form of glipizide for a longer period of time, leucine was used for the first time as the carrier in an SD of glipizide, to significantly improve dissolving and flowability. By using the solvent evaporation method, an inclusion complex containing glipizide and leucine was created, and its in-vitro release was assessed. The current investigation's goal is to create glipizide matrix tablets with leucine. The effective anti-diabetic medicine glipizide was chosen to be formulated into a medication delivery device with sustained release in the form of a matrix tablet. In the design of continuous release systems, a variety of hydrophilic polymers have been studied and are now being used. rate limitation. The optimal medication concentration at the site of action must be attained while designing sustained release drugs, polymers like carboxymethylated tamarind gum (CMTG) are frequently utilized. CMTG is also used as a matrix drug release modifying agent.

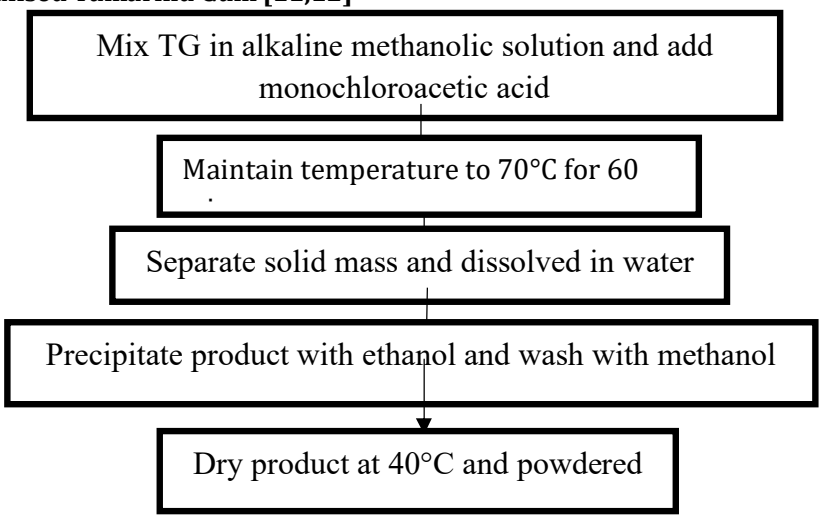
MATERIAL AND METHODS

Materials

Glipizide was supplied as a gift sample by Yarrow Chem Pvt Ltd., Mumbai. India. Tamarind Gum was gift sample from Chayya Industries, Barshi, India. Leucine was supplied as a gift sample by Loba Pharmaceuticals, Mumbai. Magnesium Stearate, Microcrystalline Cellulose, Lactose and Talc were gift samples supplied by the SD fine chemicals, Mumbai.

Methods

Synthesis of Functionalised Tamarind Gum [11,12]



Characterization of functionalized CMTG

Determination of Solubility

A blender jar was filled with a 100 ml (1% w/v) suspension of polysaccharide, which was mixed at low speed for 3 min. The suspension was put into a tube for centrifugation, which was done for 15 minutes. A 50 ml aliquot of supernatant was put into a petri plate that had already been weighed, and it was dried in a hot air oven at 105°C until the desired constant weight was reached. Then the percentage of solubility in cold water was determined and noted.

Determination of Viscosity

The needed amount of precisely weighed (1 gram) CMTG was transferred to a separate 100 ml volumetric flask. With distilled water, these were prepared to specification. The viscosity was tested after one hour. Viscosity was measured using a small sample adapter (7 ml) with Spindle No. 21 rotating at 100 RPM. The investigation was done in duplicate.[13]

Determination of Saturation Solubility of Glipizide

The solubility of Glipizide in various solvents, such as water, methanol, and phosphate buffer pH 6.8, was examined using the shake flask technique. Different solvents were used to prepare saturated Glipizide solutions, which were then agitated continuously for 24 hours using a rotary shaker. Then, Whatman filter paper was utilized to filter the solution. A UV spectrophotometer was utilized for evaluating the concentration of glipizide using the appropriate solvent as a blank at 276nm. [5]

Preparation of Solid Dispersion

Solid Dispersion Preparation Using Solvent Evaporation Method

Dispersion SDs were made using the solvent evaporation process. In Table 1, there were five different drug: carrier ratios (1:1, 1:2, 1:3, 1:4, and 1:5). These weighted ratios were utilized to establish the weights of glipizide and leucine. Method For the purpose of making solid dispersions, the drug was first dissolved in methanol, a solvent. After that, a polymer was dissolved in the solvent. (leucine) while being continuously stirred with a mechanical stirrer. On a hot plate set to 45–5°C, the solvent was allowed to evaporate while being stirred. Up till a steady weight was achieved, the evaporation process was continued. After being held in a desiccator for twenty-four hours, the solid dispersions were ground up and put through a 100 # sieve. The powders that were produced were kept in a desiccant for further investigation.

Characterization of Solid dispersion

Fourier Transform Infrared (FTIR)

With the help of a Fourier Transform Infrared Spectrophotometer, Pure glipizide and solid dispersion complex infrared spectra were recorded. A little sample was obtained and placed right on the IR platform. Then, Solid dispersion spectrum complexes and pure glipizide were captured. scanning was performed between 400 and 4000 cm.[14].

Differential Scanning Calorimetry (DSC)

Comparative Scanning Analysis of the calorimeter was done. The instrument utilized was a Perkin Elmer DSC-7 differential scanning calorimeter to record the thermograms of pure Glipizide and the solid dispersion formulation S.D.5. Samples were sealed in aluminium pans and heated from 25°C to 500°C at a rate of 10°C/min while being exposed to a nitrogen environment flowing at a speed of 10ml/min.

X-ray powder diffraction (XRD)

Powder X-ray diffraction studies were performed to check for any crystallinity in the definition after it was made and after the strength studies were performed. The powdered example was put in an aluminium test holder that had a 2.5 cm square with a profundity of 0.5 mm.

Scanning Electron Microscopy (SEM)

SEMs (Scanning Electron Microscopes; Make Jeol model 6390 LV; operating at an accelerating voltage of 3kV) were utilized to examine the samples' morphology. Before usage, samples were created by mounting powder on a brass stub with graphite adhesive and then coating them with gold**.**

Energy- dispersive X-ray analysis

An x-ray technique known as energy dispersive X-ray analysis (EDX), sometimes known as EDS or EDAX, is used to determine the elemental composition of a substance. EDX systems are attachment to Electron Microscopy instrument [SEM]. Providing essential information for understanding their chemical makeup and properties**.**

Saturation solubility determination

Saturation solubility was conducted by shake-flask method. Glipizide in excess quantity was placed in separate glass-stoppered flasks containing 10 ml of distilled water. The samples were placed on a magnetic stirrer at 37°C and at 100 rpm until equilibrium was achieved (24 hr). Whatman No. 41 filter paper was used to filter the aliquots. The filtrate was diluted appropriately with distilled water and assayed spectrophotometrically at 275 nm [15]

Determination of Drug content

By dissolving a solid dispersion containing 10 mg of medicine in 100 ml of volumetric flask and dissolving it in the least amount of methanol, the drug content was measured. The volume was adjusted using phosphate buffer (7.4), filtered through a 0.45-micron filter, and then the presence of drugs was determined using a UV double beam (Shimadzu) spectrophotometer at 275 nm. The average medication content of the resulting solid dispersion was calculated from three replicates.

In-vitro dissolution studies

In a USP dissolving apparatus II [Paddle type], accurately weighed preparations equivalent to 10 mg of Glipizide were introduced to 900 ml of dissolution media (6.8 phosphate buffer) and agitated at a speed of 50 rpm at 37 0.5°C. 5ml aliquots were removed at 5, 10, 15, 20, 25, and 30-minutes intervals and replaced with 5ml of new dissolving media (37°C). After appropriate dilution (if necessary), the obtained samples were examined using a UV-visible spectrophotometer at max 275 nm against a blank. Drug release tests were performed in triplicate. Pure Glipizide was dissolved in the same manner. The cumulative percent dissolved at different time periods was calculated using the release profile data (UV 1700.shiadzu). [16] [Table 8]

Formulation optimization of Glipizide solid dispersion sustained release tablet

The sustained release tablet was made using the direct compression approach. The matrix tablet containing solid dispersion was made by combining the corresponding weight of the solid dispersion medication and the weight of the other ingredients. The matrix tablet of glipizide was prepared employing carboxymethylated tamarind gum as a matrix former by direct compression method. The ingredients consisting of drug of solid dispersion, carboxymethylated tamarind gum, microcrystalline cellulose, lactose passed through a sieve no.60 separately and mix for 30 min to obtain uniform blend. The blend was lubricated with talc and magnesium stearate. The lubricated mixture was formed into a matrix tablet.

Evaluation of powder mixed blend of solid dispersion and excipients

Precompression parameters

Bulk Density, Tapped Density, Compressibility index, Angle of repose, and Hausner's ratio these parameters are determined. [17]

Characterization of Sustained Release tablets

After compression of powder, the tablets were tested for diameter, thickness and physical characteristics like hardness, friability, weight variation, content uniformity, hydration studies and in-vitro release with different media.[18,19,20]

Content uniformity

The consistency of the drug content in the tablets was examined. 5 tablets were weighed and crushed at random. The powder equivalent to 100 mg of medication was precisely weighed and diluted in 100ml of pH 6.8 phosphate buffer. The solution was well shaken before being subjected to sonication. Filtration using Whatman's filter paper No.41 eliminated the undissolved particles. Dilutions were then performed (if necessary). At 276 nm, the absorbance of the diluted solutions was measured. The drug concentration was estimated using the standard curve of glipizide in phosphate buffer at pH 6.8 and the drug content was calculated**.**

Hydration Studies

The formulation capacity of hydration (medium buffer uptake) was evaluated gravimetrically. For each time point each formulation of two tablets were weighted individually and expose to 900ml phosphate buffer (pH 7.5) medium under condition similar to dissolution test. Tablets were withdrawn from the media at precise time intervals, gently patted with tissue paper, weighted, dried at 60°C until constant weight was attained, and then discarded. Percent weight gain was calculated according to the following equation.

$$\% \text{ wet gain} = \frac{wet\ weight - dry\ weight}{wet\ weight} \times 100$$

In-Vitro **Dissolution Study**

The release rate of glipizide from matrix tablets was determined using United States Pharmacopoeia type II dissolution apparatus. The dissolution test was performed at 100 rpm using 900 ml of pH 1.2 for the first 2 hrs and phosphate buffer pH 6.8 after 8 hours at 37.5°C. At 30 minutes, a sample (5 ml) of the solution was removed and replaced with fresh dissolving media. The samples were filtered through a 0.45µ membrane filter and diluted suitably. Absorbance of these solutions was measured at 275 nm using Shimadzu UV Visible spectrophotometer. [21] [Table 13]

Drug Release Kinetics

In order to propose the possible release mechanism, the release pattern was evaluated to check the best fit for zero order release kinetics, Higuchi time square root equation, Korsmeyer – Peppas power law equation

and Hixson – Crowell's cube root of time equation. The adequacy of fit was evaluated by r (correlation coefficient) values.

Stability Study

For the improved formulation F6, investigations were conducted under accelerated conditions (40°C 2°C at 75% RH 5% RH). The matrix tablets were stored at 40°C± 2°C at 75% RH ± 5 % RH for accelerated temperature in closely packed with aluminium foil for 3 months. The samples were withdrawn after the first month, 2nd month and 3rd month. The samples were analyzed for its hardness, drug content and in-vitro drug release.

RESULT AND DISCUSSION

Fourier Transform Infra-Red Spectroscopy Studies

The pure Glipizide revealed cleaner and sharper peaks when compared to the spectrum of the S.D. The transform infrared spectroscopy (FTIR) spectrum of glipizide showed characteristics band at 1527 representing (C=C stretching) aromatic ring, 1687 (C=O stretching) amides. 3319 could probably be assigned to (N-H stretching). A band present at 1033 is due to (S=O stretching), 1587 (N-H bending).FTIR spectra of optimized batch of solid dispersion showed pick in 1444 representing C=C (Stretch) aromatic group. The carbonyl group C=O (Stretch) showed pick in 1687, amide group N-H (Bending) showed pick in 1582. There should be no any chemical interaction will be shown in figure 1.

Differential Scanning Calorimetry (DSC) Studies

Diffraction scanning calorimetry thermogram are shown in figure 2. It was discovered that glipizide has a characteristic endothermic peak at 219° during DSC analysis. The Glipizide -Leucine SD showed only an endothermic peak at 209°C, with no endothermic peak of glipizide. The result for the Glipizide – leucine mixture may have been due to interaction between Glipizide with higher melting point and leucine during heating process for DSC determination. The shifting forward endothermic peak of leucine and the vanishing peak of Glipizide in the Glipizide -Leucine SD suggested that Glipizide was completely soluble in the carrier and this result confirmed the miscibility of the Glipizide-Leucine SD system**.**

X-Ray Diffraction (XRD) Studies

The XRD patterns of pure drug and solid dispersions are shown in Figure 3. The diffraction patterns of the SD indicate changes in the crystalline nature of the drug. The pure medication Glipizide exhibits a highly crystalline quality in its diffraction pattern, indicated by numerous distinctive peaks at a (11°,16°, 18.5°), lower peak (10°, 21°) and numerous small peaks, indicating that it was in a crystalline form. The characteristics peak of glipizide disappeared in the diffractogram of Glipizide – leucine SD, and this was replaced by a flat diffraction peak. This result indicated that Glipizide in the Glipizide-Leucine SD may be present in an amorphous form, with grater solubility, thereby increasing its dissolution rate.

SEM (Scanning Electron Microscope) Studies

Scanning electron microscope result figure 4 showed that the Glipizide- Leucine SD was seen as large slices, with smooth surface and no fine particles. This further demonstrate that the glipizide was soluble in the carrier and in an amorphous state, which was consistent with the results of DSC and X-ray powder diffraction test.

In general, greater particle size decreases and the rougher the particle surface, the lower the powder flow. Therefore, the results of the AOR measurements and SEM pictures were in agreement. The table below lists Glipizide's saturation solubility in a variety of solvents. The Glipizide – Leucine SD was superior due to improvements in particle surface morphology

Energy-dispersive X-ray analysis

The specific elements present in the Glipizide loaded L-Leucine solid dispersion using energy-dispersive X-ray spectroscopy are carbon (C) which is a fundamental element found in organic compounds, including Glipizide and the L-Leucine polymer. Hydrogen (H) is another essential element found in organic compounds, including Glipizide and the Leucine. Oxygen (O) is commonly present in organic molecules as well as in the Leucine, which may contain hydroxyl (-OH) groups. Nitrogen (N) was also present in Glipizide, which contains a pyrimidine ring & amino functional group that includes nitrogen atoms. Sulphur (S) is constituent of Glipizide, as it contains a Sulphur atom as sulphamide in its chemical structure. Various elements with intensity count and energy are presented in Figure 5

Hydration Studies

In order to more fully comprehend the mechanisms of release and the relative importance of the relevant variables, gravimetrical analysis is a helpful tool for directly assessing matrix hydration. Such behavior is caused by the strong ability of the CMTG matrix to retain water and the osmotic pressure that lactose produces, tablet with a diffusion matrix for medication release. Maximum swelling of up to three times was seen in swelling matrix pill (GF6) at eight hours. Figure 9.

Table 1: Composition of Glipizide-Leucine Solid dispersion

Formulation Number	Drug: Carrier Ratio
S.D 1	1:1
S.D 2	1:2
S.D 3	1:3
S.D 4	1:4
S.D 5	1:5

Table 2: Formula Composition of Glipizide Sustained Release Tablets of Optimized Batch of Solid Dispersion

Formula Composition of Glipizide Sustained Release Tablets of Optimized Batch of SD						
Ingredients (mg/tablet)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Solid dispersion (S.D 5) Glipizide equivalent to 10mg	60	60	60	60	60	60
Carboxymethyl tamarind gum	20	25	30	35	40	45
Microcrystalline Cellulose	160	155	150	145	140	135
Magnesium Stearate	10	10	10	10	10	10
Lactose	50	50	50	50	50	50
Talc	10	10	10	10	10	10
Total wt. of tablet (mg)	300	300	300	300	300	300

Table 3: Solubility of Gum

Sr. No	Sample	Solubility
1.	Tamarind Gum	1.59 ± 0.16 mg/ml.
2.	Carboxymethyl tamarind gum	10.53 ± 1.28 mg/ml

Table 4: Viscosity of Gum

Sr. No.	Sample	Viscosity
1.	Tamarind Gum	38.53 ± 2.21 cP
2.	Carboxymethyl tamarind gum	167.66 ± 2.5 cP

Table 5: Saturated Solubility Studies of Glipizide In Different Dissolution Media

Sr. No	Dissolution Medium	Amount of Glipizide dissolved in (mg/ml)
1.	Solubility in distilled water	0.004 mg
2.	Solubility in Methanol	0.00615 mg
3.	Solubility in phosphate buffer pH 6.8	0.00675 mg
4.	Solubility in phosphate buffer pH 7.4	0.00423 mg

Table 6: Solubility of SD in distilled water

Batch Code	Solid dispersion (using solvent evaporation method)	Ratio	Solubility (mg/ml)
1.	Glipizide: Leucine	1:1	0.09
2.	Glipizide: Leucine	1:2	0.94
3.	Glipizide: Leucine	1:3	1.09
4.	Glipizide: Leucine	1:4	1.17
5.	Glipizide: Leucine	1:5	1.21

Table 7: Determination of Drug content of Glipizide and Leucine Solid Dispersion Complex prepare using solvent evaporation method

Batch Code	Ratio	Solid dispersion (solvent evaporation method)	% Drug Content
S.D 1	1:1	Glipizide: Leucine	94.59%
S.D 2	1:2	Glipizide: Leucine	89.12%
S.D 3	1:3	Glipizide: Leucine	92.38%
S.D 4	1:4	Glipizide: Leucine	95.54%
S.D 5	1:5	Glipizide: Leucine	98.18%

Table 8: Dissolution release profile of Glipizide solid dispersion prepared by Solvent Evaporation method in PBS pH 6.8

Time	Pure Drug % CDR	(S.D1) 1:1	(S.D2) 1:2	(S.D3) 1:3	(S.D4) 1:4	(S.D5) 1:5
5	6.1 ± 1.04	18.4 ± 1.4	9.7± 1.02	14.1± 2.4	20.6± 2.1	25.4± 1.8
10	11± 1.8	28.2 ± 1.7	17.4± 1.3	21.2± 2.3	31.2± 0.8	41.5± 2.5
15	15.4± 1.5	36.3± 1.8	28.6± 1.2	32.4± 1.9	39.4±2.3	52.4± 2.6
20	22.4± 1.0	45.1 ± 2.9	36.2± 1.0	41.3± 1.2	51.2± 1.3	62.7± 1.6
25	29.5± 1.3	55.6± 0.5	43.7± 1.3	52.8± 0.5	62.4± 2.3	74.5± 1.4
30	37.1± 0.9	68.7 ± 1.2	52.8± 0.9	62.5± 0.9	72.9± 1.8	92.5± 1.5

Table 9: Evaluation of Glipizide SD and excipient blend

Batch	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Angle of Repose	Hausner's Ratio
F1	0.36	0.44	18.24	23.74	1.22
F2	0.71	0.86	17.44	25.80	1.21
F3	0.68	0.81	16.04	26.89	1.19
F4	0.70	0.89	21.34	28.24	1.27
F5	0.71	0.83	14.45	24.32	1.16
F6	0.72	0.93	22.25	24.88	1.29

Table 10: Evaluation of Sustained Release tablet

Batch	Thickness (mm)	Diameter (mm)	Hardness (kg/cm2)	Friability (%)	Weight variation
F1	2.26 ± 0.057	8.00	5.16 ± 0.288	0.42 %	197.4 ± 1.67
F2	3.33 ± 0.019	8.00	5.5 ± 0.5	0.34 %	196.3 ± 1.63
F3	2.27 ± 0.052	8.00	5.33 ± 0.288	0.33 %	196.6 ± 1.67
F4	2.34 ± 0.085	8.00	5.16 ± 0.288	0.42 %	196.2 ± 1.68
F5	2.27 ± 0.105	8.00	4.66 ± 0.288	0.37%	195.8 ± 1.39
F6	3.10 ±0.1	8.00	5 ± 0.5	0.45 %	194.8 ± 0.83

Table 11: Drug Content Determination

Formulation	F1	F2	F3	F4	F5	F6
Drug Content (%)	77.12%	89.12%	84.93%	76.49%	77.02%	97.28%

Table 12: Hydration Studies

Time (h)	1h	2h	3h	4h	6h	8h
% swelling matrix tablet	148.3±1.2	203.8± 1.4	261.7±1.1,	272.5±2.0,	305.1±1.6,	322 ± 1.9

Table 13: In-vitro dissolution drug release study

Time	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
30	2.28 ± 0.535	2.56 ± 0.48	2.27 ± 0.473	3.41 ± 0.580	2.40 ± 0.54	2.84 ± 0.90
60	3.41 ± 0.58	3.36 ± 0.34	3.45 ± 0.56	4.32 ± 0.47	3.12 ± 0.57	3.65 ± 0.90
90	5.17 ±0.67	5.29 ± 0.65	4.95 ± 0.27	5.25 ± 0.55	4.96 ± 0.33	5.76 ± 0.594
120	8.39 ±0.45	8.38 ± 0.6	7. 25 ± 0.60	8.39 ± 0.50	7.36 ± 0.47	8.35 ± 0.65
180	20.95±0.96	21.05 ± 0.51	18.67 ± 0.55	20.96 ± 0.86	18.67 ±0.55	21.05 ± 0.46
240	35.27 ±0.39	35.79 ± 0.66	32 ± 0.29	34.62 ± 0.60	32.33 ± 0.60	35.56 ± 0.68
300	53.48 ±0.68	53.95 ± 0.26	48.73 ± 0.65	51.35± 0.65	50.03± 0.63	53.89 ± 0.40
360	73.83 ±0.41	74.69 ± 0.54	67.46 ± 0.31	69.51± 0.26	68.84 ± 0.51	74.76 ± 0.53
420	76.4 ±0.42	78.54± 0.83	71.45 ± 0.23	72.47± 0.78	71.31 ± 0.40	85.92 ± 0.61
480	81.26 ± 0.75	83.4 ± 0.75	76.12 ± 0.57	79.65 ± 0.34	78.08 ± 0.49	94.5 ± 0.22

Table 14: Drug release kinetics study for optimized formulation

Model	Line Equation	Regression Equation (R^2)
Zero order	y = 0.2266x - 12.911	0.9521
First order	y = 0.0036x + 0.4906	0.9315
Higuchi model	y = 4.3792x - 19.522	0.8179
Korsmayar Peppas model	y = 0.0023x - 0.1291	0.9767

Table 15: After exposure to accelerated stability condition the formulation was analysed for various evaluation parameters result were shown in table

Time	Appearance	Hardness (Kg/cm²)	Friability (%)	Drug Content (%)	%drug release
Initial	White	5 ± 0.5	0.45%	97.28%	94.5 ± 0.22
1st month	No change	5 ± 0.5	0.44%	97.15%	94.5 ± 0.22
2nd month	No change	5	0.41%	97.03%	94.3 ± 0.02
3rd month	No change	4.99 ± 0.288	0.40%	96.94%	93

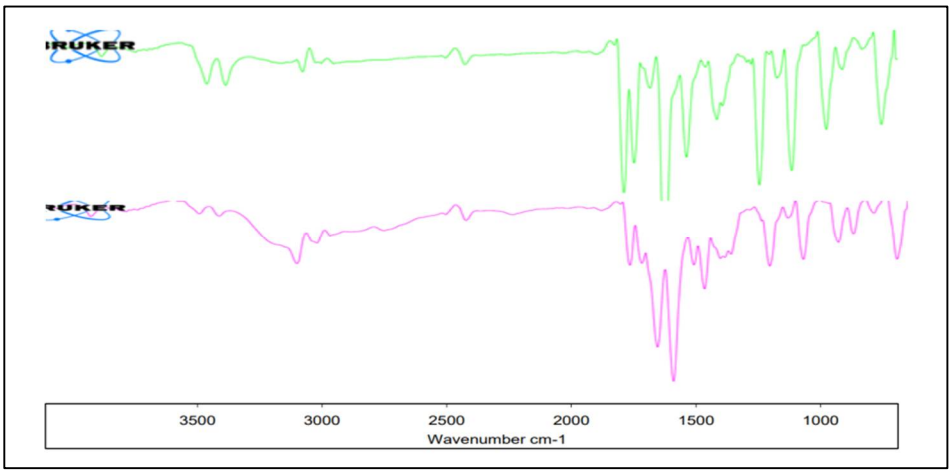


Figure 1: FTIR of Pure drug and Solid dispersion

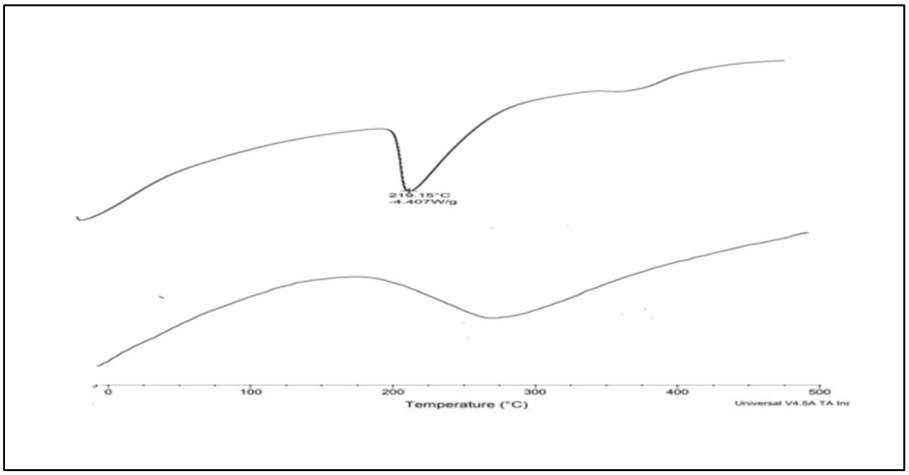


Figure 2: DSC of Pure drug and Solid dispersion

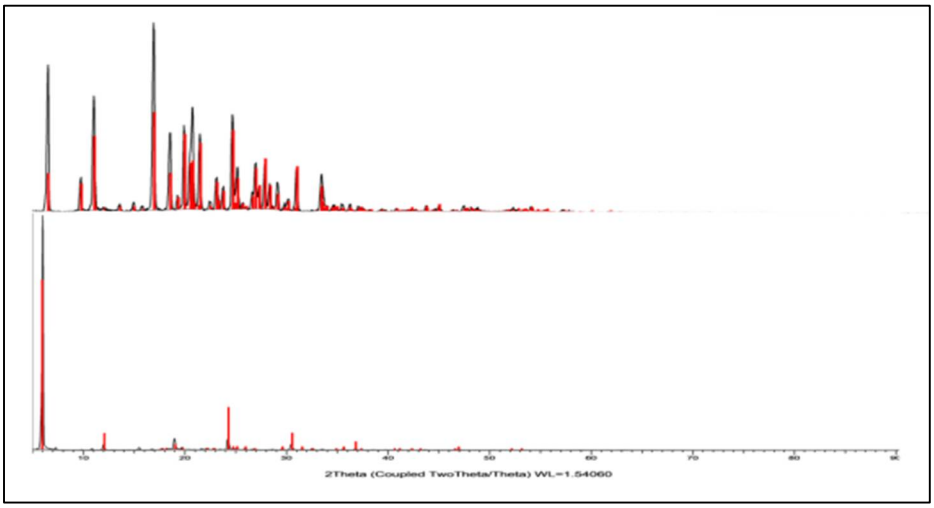


Figure 3: XRD peak of pure drug and solid dispersion

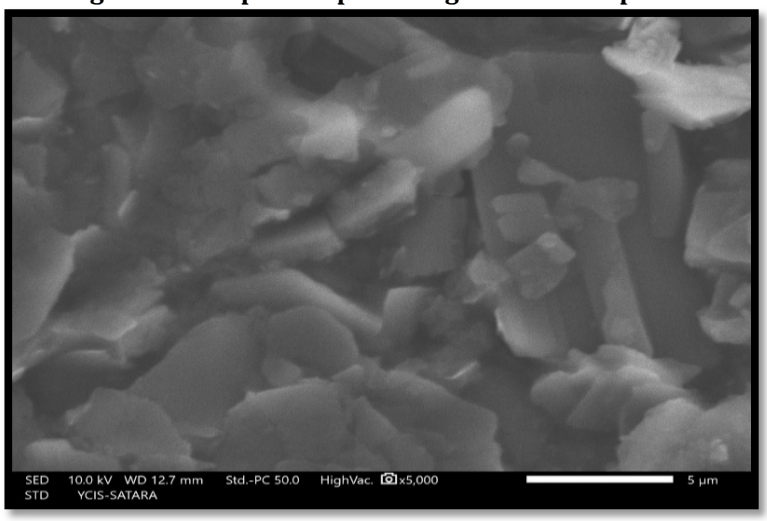


Figure 4: Scanning electron microscope

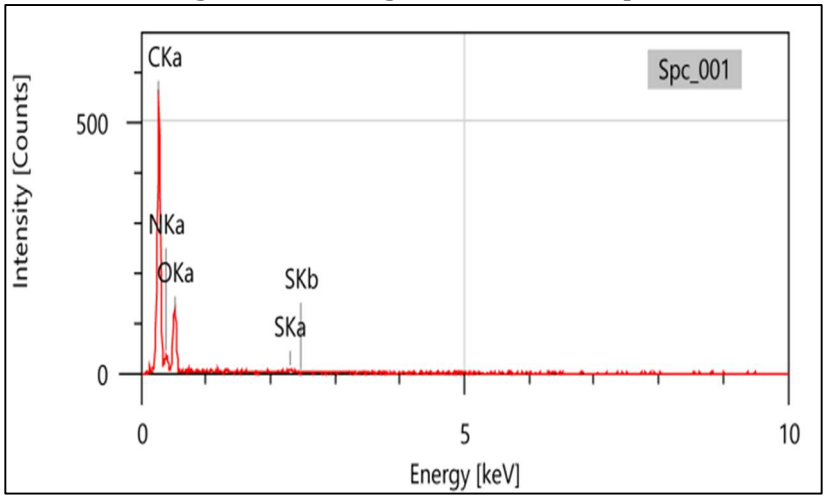


Figure 5: Energy -dispersive X-ray analysis

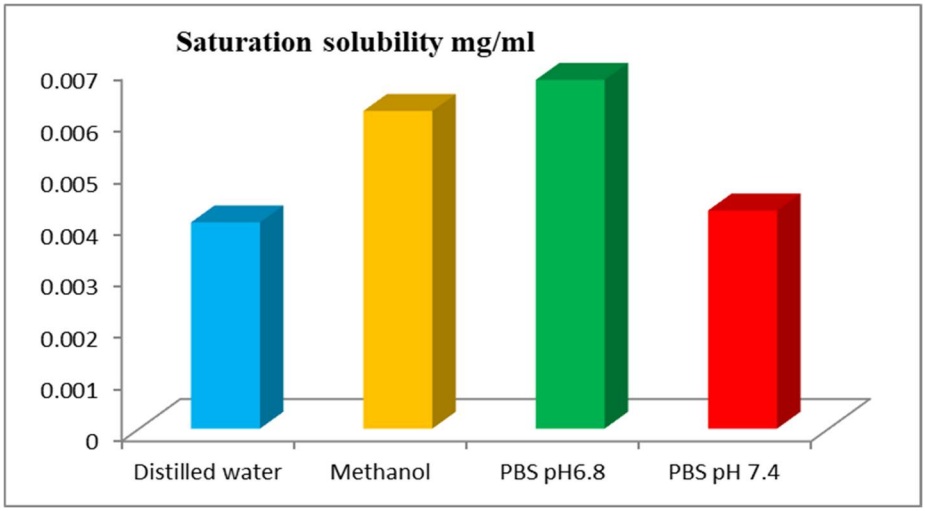


Figure 6: Saturated Solubility Studies of Glipizide In Different Dissolution Media

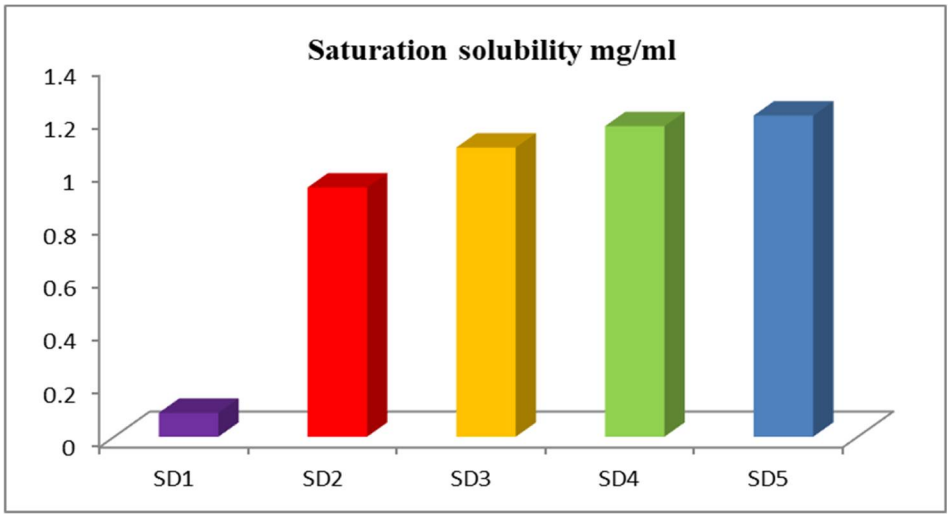


Figure 7: Solubility of SD in distilled water

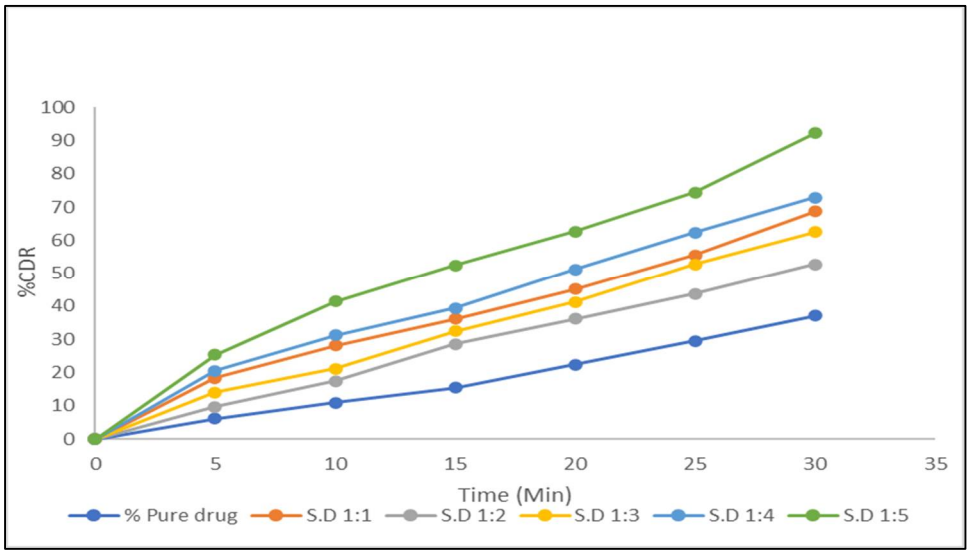


Figure 8: Dissolution release profile of Glipizide solid dispersion prepared by Solvent Evaporation method in PBS pH 6.8

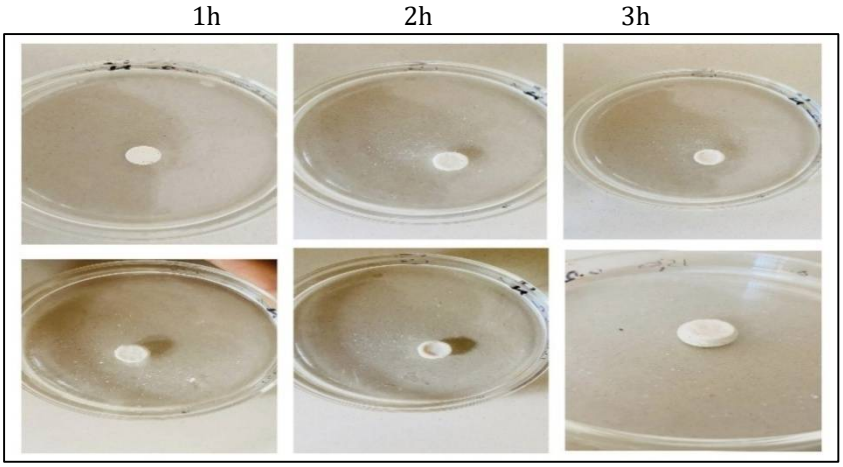


Figure 9: Swelling behavior of optimized matrix tablet at different time intervals

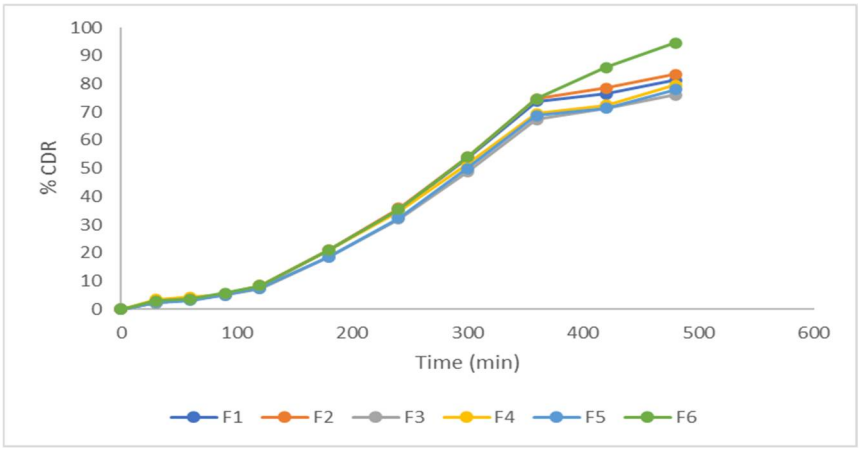


Figure 10: *In Vitro* dissolution profile of formulation F1- F6

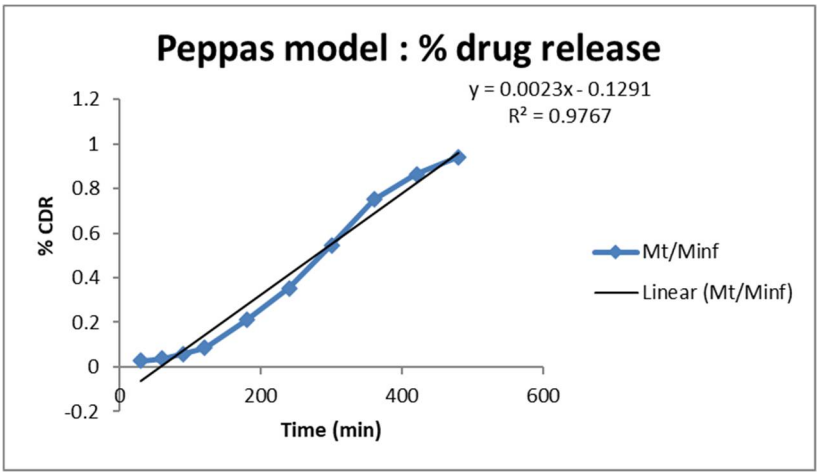


Figure 11: Korsmeyer Peppa's model kinetics study for optimized formulation F6

CONCLUSION

The goal of the current study is to improve glipizide's solubility and dissolution so that it will work better with sustained release drug delivery systems. Leucine was successfully synthesized in this study as the carrier for a unique SD loading Glipizide using the solvent evaporation method. From results it was revealed that Glipizide to Leucine ratio 1:5 (S.D-5) method has shown highest increment in saturated solubility (1.21 mg/ml) and dissolution rate (92.5%) of Glipizide. Six formulations were fabricated using with suitable rate

controlling polymers like Carboxymethyl tamarind gum. CMTG is used as matrix drug release modifying agent.

The In-vitro dissolution study was performed for various formulations. Based on the results F6 was shown highest drug release 94.5% within 8 hrs. The release of drug from all formulation followed diffusion-controlled release followed by korsmeyer- peppas which was confirmed by higher correlation coefficient values. In the present study, revealed that L-leucine use carrier in solubility enhancement and also CMTG has a better matrix agent in formulation development of modified release drug delivery system.

REFERENCES

1. Horter D, Dressman JB, (1997). Influence of physicochemical properties on dissolution of drug in the gastrointestinal tract, Adv Drug Del, 53, 1997, 3-14.
2. Rawat A, Verma S, Kaul M, Saini S. (2011). Solid Dispersion: A Strategy For Solubility Enhancement. Int J Pharm Tech;3(2):1062-1099
3. James Swarbrick, James C Boylan. (1992). Encyclopedia of Pharmaceutical Technology, Marcel Dekker: New York, 3, 337 – 345.
4. H. D. Zalte et. al. (2013). Review on Sustained Release matrix tablet; Vol 3,17-29
5. Loen shargel, Andrew BC Yu. (1985). Applied Biopharmaceutics and Pharmacokinetics 2nd ed. ACC.
6. https://www.who.int/news-room/fact-sheets/detail/diabetes
7. Shallu Sandhan et al., (2013). Formulation and evaluation of sustained release matrix tablets of glipizide ;1 (4): 89-94.
8. Rotth€auser B et al. (1998). Optimization of an effervescent tablet formulation containing spray dried L-leucine and polyethylene glycol 6000 as lubri- cants using a central composite design. Eur J Pharm Biopharm; 46: 85–94.
9. Sou T et al. The effect of amino acid excipients on morphology and solid- state properties of multi-component spray-dried formulations for pulmonary delivery of biomacromolecules. Eur J Pharm Biopharm 2013; 83: 234–243.
10. Vartiainen V et al. (2016). Drug permeation and cellular interaction of amino acid-coated drug combination powders for pulmonary delivery. Int JPharm; 504: 89–97.
11. Kaur G, Mahajan M, Bassi P. (2013). Derivatized Polysaccharides: Preparation, Characterization, and Application as Bioadhesive Polymer for Drug Delivery. Int J Polym Mater. 62(9):475–81
12. Ponnikornkit B, Ngamsalak C, Huanbutta K, Sittikijyothin W. (2015). Swelling Behaviour of Carboxymethylated Tamarind Gum. Adv Mater Res.1060:137–40.
13. Bansal J, Kumar N. (2014). Extraction and Evaluation of Tamarind Seed Polysaccharide as Pharmaceutical In situ Gel Forming System. Am J Sci Res. 9(1):1–5.
14. D. Choudhary et al., (2009). Enhancement of solubility and dissolution of glipizide by solid dispersion (kneading) technique. doi : 10.4103/0937-8398.
15. K.P. Sampath Kumar, et al (2012). Sustained Release Drug Delivery System Potential. Vol 1, No. 2 ISSN 2277- 7695.
16. Mayur D. (2019). Solubility and dissolution enhancement of poorly water-soluble Glimepiride by using solid dispersion technique. Vol 4, 97-104
17. Lachman L, Liberman HA, Kanig JL. (1990). The Theory and Practice of Industrial Pharmacy. 3rd Ed., Mumbai: Varghese publishing house. 296-302.
18. Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare. Delhi: Controller of Publications. 1996; 2:182.
19. Sreekanth SK, Palanichamy S, Rajasekharan T, Thanga AT. (2010). Formulation and evaluation studies of floating matrix tablets of nifedipine. Int J Pharm Bio Sci. 1(2).10-18
20. Kameswara rao S, Dasari Nageswara R (2014). Formulation. Evaluation of gastro retentive floating drug delivery system of Atenolol. The pharma innovation journal. 3(5):11-18.
21. Arthur O, Marie D, Raimar L. (2008). Pharm Res; 25(12):2778-85.