Indo American Journal of Pharmacy
An International Peer Review Journal

Original Article

DEVELOPMENT AND CHARACTERIZATION OF GLIBENCLAMIDE MICROSPHERES

Dr. Vijaya Kuchana[1], G. Shailaja*[1], K. Pavani[1], Bathula. Bharathi.[2]

[1]Department of Pharmaceutics, Teegala Krishna Reddy College of Pharmacy, Medbowl, Meerpet, Saroornagar, Hyderabad-500079, Telangana, India.
[2]Syncorp Clincare Technologies Pvt. Ltd, Hyderabad, India

Article Info - Received: 16-11-2017 Accepted: 29-11-2017

Abstract

The objective of the present Study was to develop and characterize of the Glibenclamide microspheres prepared by the emulsion solvent evaporation technique. Microspheres were formulated by using HPMC, liquid paraffin and acetone and characterized for their micromeritic properties, encapsulation efficiency, particle size, drug loading, FTIR, and SEM analysis. In vitro release studies were performed in phosphate buffer (pH 7.4). Stability studies were conducted as per ICH guidelines. The resulting microspheres obtained by emulsion solvent evaporation technique were free flowing in nature. The infrared spectra and differential scanning calorimetry thermographs confirmed the stable character of Glibenclamide in the drug-loaded microspheres. Scanning electron microscopy revealed that the microparticles were spherical in nature. In vitro release studies revealed that the drug release was sustained up to 12 hrs. The release kinetics of Glibenclamide from optimized formulation followed zero-order and peppas mechanism. The mechanism of drug release from the microparticles was found to be non-Fickian type.

Key Words: Controlled release, Glibenclamide, HPMC, emulsion solvent evaporation technique and drug release studies

Correspondence Address:
G. Shailaja, Department of Pharmaceutics, Teegala Krishna Reddy College of Pharmacy, Medbowl, Meerpet, Saroornagar, Hyderabad-500079, Telangana, India.

Email Id-shailaja.ip@gmail.com

Mobile Number-9059079956

1. INTRODUCTION

Microspheres defined as the flowing of the powders freely characteristics composed of proteins or synthetic polymers, which may be biodegradable. Microsphere states that as “a monolithic structure with the drug pass throughout the matrix either as a distribute of molecule or a particle dispersion, drop in the size range 1-1000 μm.[1,2] Microparticles provides constant and prolonged therapeutic action. Microspheres prepared by using emulsion solvent evaporation technique[3].

Glibenclamide agent which is widely used in the management of non-insulin dependent diabetes mellitus (type II). It is a second generation sulphonyl urea which is more potent than the first generation drugs in this class. Its biological half-life is 4- 6hrs.[4]

Due to its low biological half-life (5 hrs), it requires frequent administration to maintain plasma concentration.[5] This causes inconvenience to the patient and also leads fluctuations in plasma drug concentration that may cause inferior therapeutic effects or toxic effects. Therefore, development of controlled release dosage forms would clearly be beneficial in terms of decreased dosage requirements, thus increase patient compliance[7].

2. MATERIALS AND METHOD

MATERIALS

Glibenclamide, Hydroxy propyl methyl cellulose, Liquid paraffin, Acetone and tween 20 were purchased from S. D. Fine Chem. Labs. (Mumbai, India) All other ingredients used throughout the study were of analytical grade and were used as received.

METHOD

Emulsion solvent evaporation technique[10, 11]

The glibenclamide were formulated by emulsion solvent evaporation technique Antidiabetic such as glibenclamide microparticles were prepared by differ the drug and polymer ratios and by varying the tween 20. Required amount of glibenclamide and hydroxypropyl methylcellulose were dissolved in 10ml of acetone. The drug and polymeric solution was slowly added to 100ml of liquid paraffin containing 1% surfactant such as span 80 with constant stirring for 1hrs. The resulting microspheres were separated by filtration and washed with petroleum ether. The microspheres finally air dried over a period of 12 hrs and stored in a dessicator.

Table-1: Formulation of Glibenclamide microspheres

Formula no	glibenclamide	HPMC	Liquid paraffin	Acetone	Tween80
F1	50	30	50	10	40
F2	50	60	40	-	40
F3	50	70	60	-	40
F4	50	75	30	10	40
F5	50	80	70	-	40
F6	50	90	80	20	40
F7	50	95	85	-	40
F8	50	100	90	30	40

EVALUATION PARAMETERS[12, 13, 14, 15]

After preparation of Glibenclamide microspheres were evaluated for surface morphology of microparticles, particle size, drug entrapment efficiency and drug release studies.

A. Yield of sustained microspheres

The Glibenclamide microparticles was calculated from the required amount of microspheres obtained divided by the total amount of all non-volatile components.

$$\% \text{ Yield} = \frac{\text{Actual weight of the microspheres}}{\text{Total weight of all non-volatile components}} \times 100$$

B. Particle size

Microspheres of particle was measured by optical microscopy. The eyepiece micrometer was calibrated using a stage micrometer. The microparticles were

spread over a slide and imagine under an optical microscope using an eyepiece micrometer.

C. Surface morphology of the sustained release microspheres

The surface morphology of the prepared glibenclamide microspheres was studied with the aid of a Scanning Electron Microscope (SEM).

D. Drug entrapment efficiency (DEE)

The required amount of drug entrapped was estimated by crushing 50 mg of glibenclamide microspheres by using mortar and pestle. This microspheres powder sample was poured in to a 100 ml volumetric flask and add the 7.4 phosphate buffer. After that the solution was taken in to a beaker and sonicated in a bath sonicator for 2 hours. The solution was filtered and absorbance was measured after suitable dilutions spectrophotometrically at 298 nm against blank.

Formula:

$$\text{DEE} = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \times 100$$

E. In vitro drug release study

In vitro drug release studies were carried out for all formulations in Franz diffusion cell. Microspheres equivalent to 10 mg of glibenclamide were poured into 5 ml aliquots were withdrawn at a predetermined intervals and equal volume of dissolution medium was replaced to maintain sink conditions. The necessary dilutions were made with 7.4 pH buffer and the solution was analysed for the drug content spectrophotometrically using UV-Visible spectrophotometer (Lab India, India) at 298 nm against an appropriate blank. Three trials were carried out for all formulations. From this cumulative percentage drug release was calculated and plotted against function of time to study the pattern of drug release. The results are presented in tables and figures.

Mechanism of drug release

The models used were zero order (equation 1) First order (equation 2) and Higuchi model (equation 3) and Koresmeyer Peppas model (equation 4).

i) zero order release kinetics:

$$R = K_o t \quad \text{-- (1)}$$

R=cumulative percent drug release

Ko=zero order rate constant

ii) First order release kinetics

$$\log C = \log C_o - K_1 t / 2.303 \quad \text{-- (2)}$$

Where

C = cumulative percent drug release

K_1 = first order rate constant

iii) Higuchi model

$$R = K_H t^{0.5} \quad \text{-- (3)}$$

Where

R = cumulative percent drug release

K_H = higuchi model rate constant

iv) korsermeyer peppas model

$$M t / M \alpha = K_k t^n$$

$$\log M t / M \alpha = \log K_k + n \log t \quad \text{-- (4)}$$

Where

K_k = korsermeyer peppas rate constant

'M t / M α' is the fractional drug release, n = diffusional exponent, which characterizes the mechanism of drug release.

The obtained regression co-efficient (which neared 0.999) was used to understand the release pattern of the drug from the sustained release microspheres.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The prepared glibenclamide microspheres placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2°c and refrigerator 2-8°c for a period of 30 days.

3. RESULTS & DISCUSSION

Table-2: Calibration curve of Glibenclamide

S. no	Concentration (µg/ml)	Absorbance
1	0	0
2	1	0.142
3	2	0.234
4	3	0.351
5	4	0.472
6	5	0.586

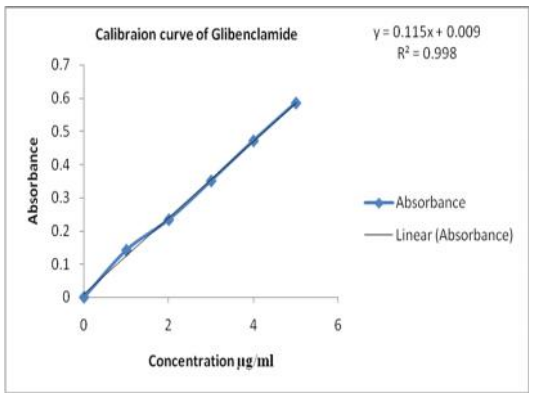


Figure-1: Calibration curve of Glibenclamide

FTIR Studies

Compatibility studies were performed using IR spectrophotometer. It is determine the pure drug and excipient comkpatability studies. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum.

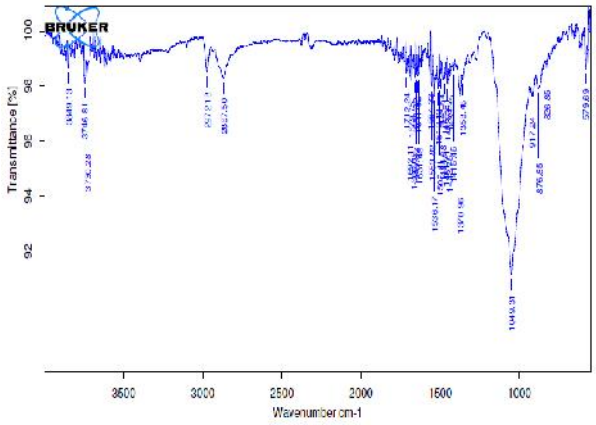


Figure-2: FTIR Spectra of Glibenclamide

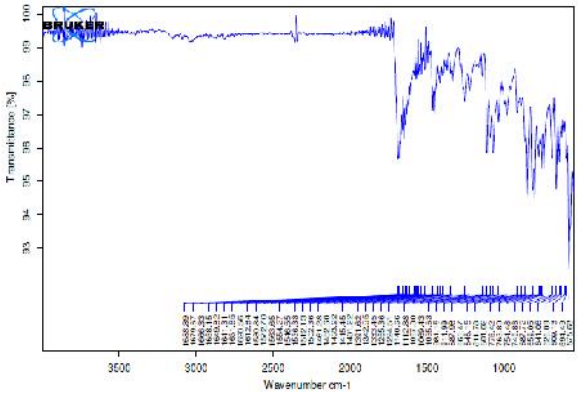


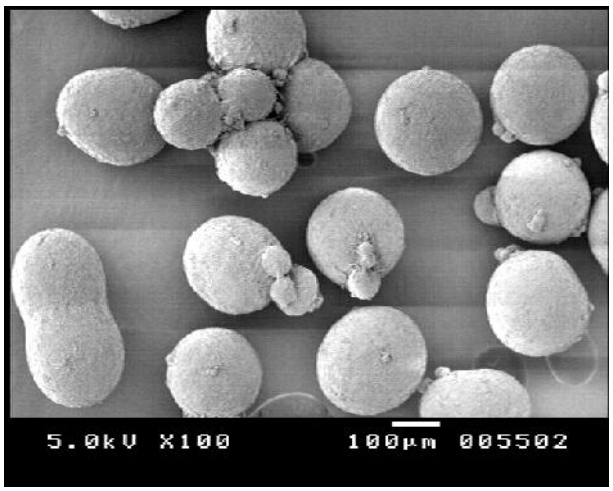
Figure-3: FTIR Spectra of Optimized formulation

Evaluation parameters

Surface topography by scanning electron microscopy (SEM)

A shows SEM photograph of optimized microspheres at 100× magnification, at 1000× magnification. SEM photographs showed discrete, spherical microspheres. SEM photographs also showed the presence of drug crystal on the surface of microspheres revealing that the microspheres were having some rough surface.

The drug crystals on microspheres were may be due to the presence of un entrapped drug in dispersion medium.



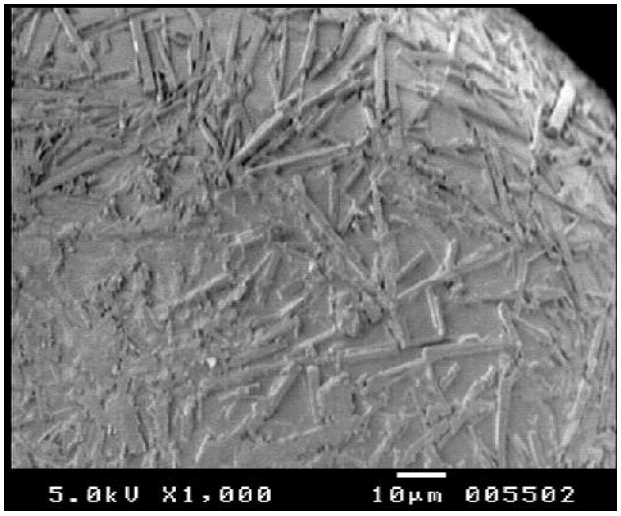


Figure-4: SEM analysis of Optimized formulation

Results of the evaluation parameters of formulated sustained release microspheres

The formulated glibenclamide microspheres were examined for different parameters such as percentage yield, drug encapsulation efficiency, particle size, and drug release studies.

Table -3: Effect of drug polymer ratio on Yield of microspheres, Particle size, Drug entrapment efficiency

Formulation code	%yield	Particle size	Drug Entrap Efficiency
F1	85.85	88.39	49.97
F2	79.55	93.64	49.01
F3	88.33	96.72	49.93
F4	84.23	85.24	48.26
F5	85.23	87.24	49.27
F6	86.23	86.15	48.22
F7	85.21	85.21	47.19
F8	85.28	87.24	49.21

Table-4: Drug release studies of all formulations

Time (hours)	F1	F 2	F3	F4	F5	F6	F7	F8
1	63.519	35.185	37.449	34.225	47.421	46.32	47.911	55.61
2	69.471	52.68	43.109	42.241	53.194	51.096	53.109	60.245
3	75.628	76.452	57.949	67.229	58.91	58.213	58.458	62.523
4	86.99	84.521	63.232	73.541	63.124	62.458	64.942	66.784
5	91.907	85.845	65.664	75.143	65.129	66.125	67.124	69.532
6	94.432	87.997	68.725	78.613	69.907	69.907	70.152	70.259
7	97.52	90.159	70.979	80.812	70.153	72.269	72.421	73.951
8	99.125	91.508	73.656	83.612	76.612	77.874	76.108	79.324
9	----------	95.743	80.256	88.312	81.908	82.742	83.615	85.965

Table-5: kinetic models

time	log T	Square root of Time	%CR	log %CR	Log% drug retained	cube root of %drug remaining
0	0	0	0	0	2	4.642689
1	0	1	5.73	0.765668	1.973813	4.549564
2	0.30102	1.413214	6.21	0.857835	1.966501	4.527242
3	0.467121	1.632051	8.4	0.929417	1.961411	4.516064
4	0.60306	2	9.52	0.987566	1.954592	4.476037
5	0.69797	2.235068	10.31	1.013837	1.953792	4.37542
6	0.768151	2.44849	62.4	1.859729	1.440809	3.12206
7	0.835098	2.64751	79	1.94839	1.061393	2.23298
8	0.91329	2.828326	98.6	1.987259	-0.39674	0.736706

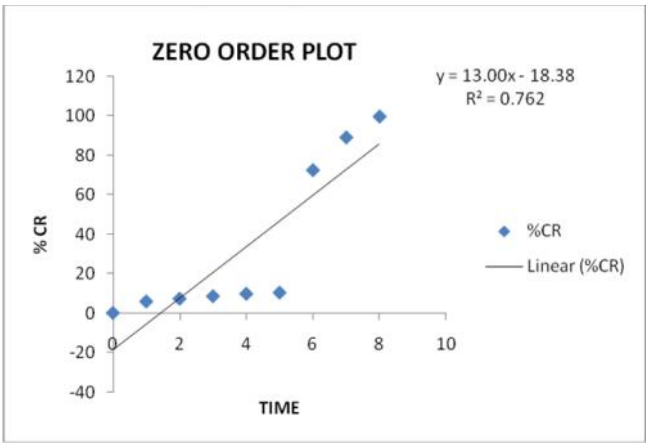


Figure -5: Zero order kinetics

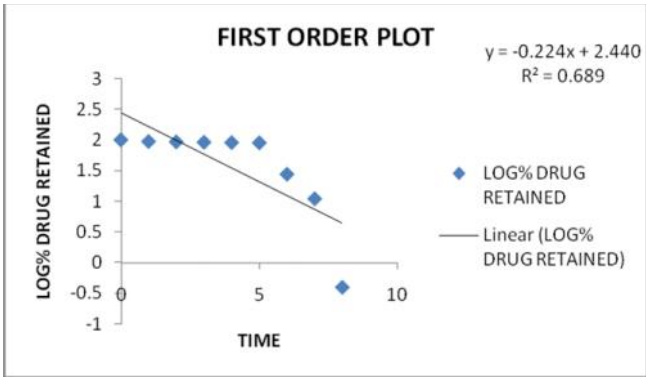


Figure -6: First order kinetics

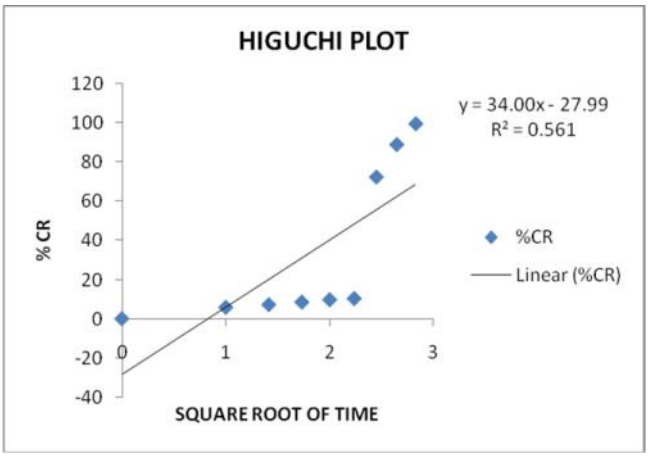


Figure -7: Higuchi model

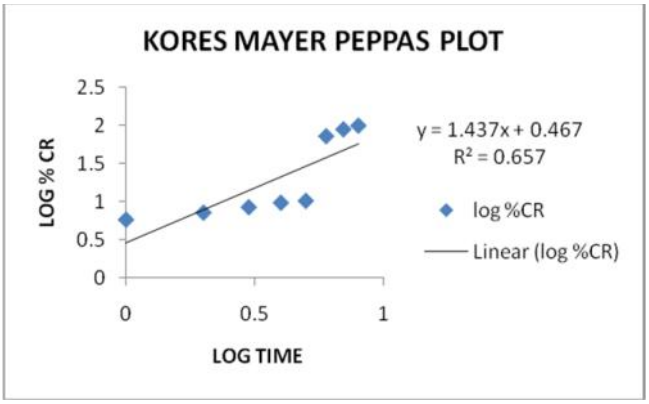


Figure -8: Kores mayer peppas model

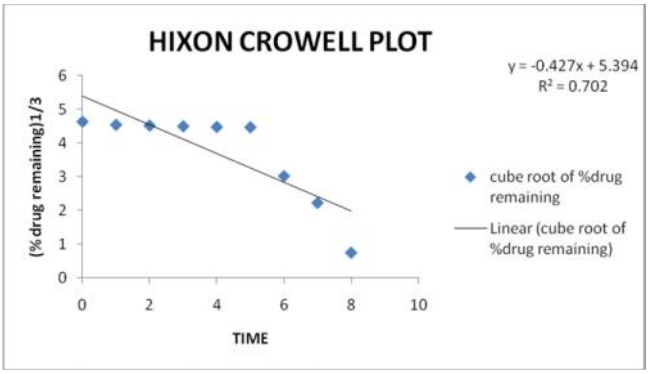


Figure -9: Hixon crowell plot

Table-6: Correlation coefficient values for Microspheres

Drug Kinetics	Optimised Formula
First-Order	0.8587
Zero-Order	0.8587
Higuchi	0.9415
korsermeyer peppas	0.9756

4. CONCLUSION

The present study was to prevent extensive metabolism of the drug and consequently to enhance the bioavailability of the drug. It is from the glibenclamide microparticles.

These microspheres are used to treatment of type 2 diabetis. The glibenclamide microparticles were formulated by emulsion solvent evaporation technique method using synthetic polymer such as hydroxyl propyl methyl cellulose. These polymer as retarding polymers and evaluated for parameters like particle size, drug loading. Microspheres morphology was evaluated by SEM.

The yield and entrapment efficiency was high for Sodium alginate microspheres were Particle size, entrapment efficiency and production yield were influenced by the type of polymer, polymer concentration, stirring speed and combination of polymers. *In vitro* dissolution of optimized formulations of various Polymer in pH 7.4 formulations are releasing the drug up to 8 hrs.

5. REFERENCES

1.Jayakrishnan A, research article on formulate and characterization of polymeric microspheres by using biodegradable polymeric microspheres as drug carriers.

2. Vyas SP, formualation of polymeric microspheres as drug delivery system as sustained concepts and advances.

3. DF Bain , development and characterization of micropaticles by using spray drying J Microencap 1999; 16: 453-474.

4. Jalil R, Nixon JR. Microencapsulation using poly(l-lactic acid) I: microcapsul properties

affected by the preparative technique. J Microencap 1989; 6: 473 -484.

5. Huang YY, Chung TW, Tzeng TW. Drug release from PLA/PEG microparticulates.Int J

Pharm 1997; 156: 9 -15.

6. Edlund U, Albertsson AC. Development and characterization of microspheres from biodegradable polymer. J Poly sci: Part A: Poly che, 2001; 36: 1976–1998.

7. Abdul ArifMallick., Barik B.B., PrakashChSenapati. (2005) design, preparation and in vitro evaluation of biodegradable polymers. 4 (1), 369-375.

8. Cheu S.J., Chen R.I., Chen P.F., Lin W.J. (2001) Journal of Microencapsulation, 18(5), 559-565.

9.Chandy A., Sudish Rail., Manigauha A., Suresh Sahu. (2009) J.PharmaDosage Forms and Tech, 1(1), 29-32.

10. MeralYuce., KandemirCanefe. (2008) Turk J. Pharm. Sci, 5 (3), 129-142. PerumalD., Dangor C.M., Alcock R. S., Hurbans N., Moopanar K.R. (1999) Journal of Microencapsulation, 16(4), 475-487.

11 . Deore B.V., Mahajan H.S., Deore U.V. (2004) Int J ChemTech Research, 1(3), 634-642.

12. Tamer Guneri.,MesutArici., GokhanErtan. (2004) Fabad j. pharm. Sci, 29, 177-184.

13. Kotadiya R., Patel V., Patel H., Koradiya H. (2009) Int J Green Pharmacy, 14, 58-62.

14. BhaskarMazumder., Sanjib Bhattacharya., AnindyaMaity.The review on hallow microspheres and development methods and used polymers. (2009), 1(3), 905-913.

15. Sunit Kumar Sahoo., Barik B.B., (2005) The review on controlled release microspheres and its applications , 4 (1), 369-375.

16. Cheu S.J., Chen R.I., Chen P.F., Lin W.J. (2001) Journal of Microencapsulation,The controlled release polymers and its applications in pharameceutical industry 18(5), 559-565.

Conflict of Interest: None
Source of Funding: Nil