Asian Journal of Pharmaceutical Education and Research
Vol -13, Issue-3, July- September 2024
ISSN:2278 7496

RESEARCH ARTICLE Impact Factor: 7.014

FORMULATION AND EVALUATION OF ANTIDIABETIC DRUG CONTAINING MICROSPHERES BY PROTEIN GELATION TECHNIQUE

Rupali P. Sable*, Sandip C. Atram, Subodh A. Urkunde, Anuja G. Gawai, Vrunda J. Rajput, Ganesh R. Padwale.

Department of pharmaceutics, Vidyabharati College of Pharmacy, Amravati – 444 602, India

*Corresponding Author's E mail: rupalisable13@gmail.com
Received 21 May. 2024; Revised 24 June. 2024; Accepted 10 June. 2024, Available online 10 July. 2024

Cite this article as: Sable RP, Atram SC, Subodh UA, Urkunde AG, Rajput VJ and Padwale GR. Formulation and Evaluation Of Antidiabetic Drug Containing Microspheres By Protein Gelation Technique. Asian Journal of Pharmaceutical Education and Research. 2024; 13(3): 296-309.

https://dx.doi.org/10.38164/AJPER/13.3.2024.296-309

ABSTRACT

This study examined and evaluated the use of protein gelation technique in the preparation of antidiabetic microspheres. The aim is to create a safe version that will increase the effectiveness of diabetes treatment and patient compliance. Microspheres were prepared by protein gelation method using biocompatible polymers and drug-voglibose. Various physicochemical properties of the formulation microspheres, such as particle size, drug loading capacity, encapsulation efficiency, in vitro drug release, and pharmacodynamic properties, were evaluated. The results of this study provide important information regarding the use of protein gelation technique-based microspheres in the delivery of anti-diabetes drugs.

Keywords: Antidiabetic drug, microspheres, protein gelation technique, sustained release, diabetes mellitus.

INTRODUCTION

Sustained release dosage forms are designed to maintain the level of the drug in the patient's blood by releasing the drug over an extended period of time[1]. It is a chemical product contained in the medicine used to diagnose, prevent, treat and treat diseases, but for men, these are just medicines extracted from the patient or health to restore health[2-3]. These drugs also have a mysterious history, so the word "drug" is a form of the word "drogues", which means the history is not clear. The word "pain" combined with the words "dis" and "easy" indicates that it is not easy or happy, or that it is a bad feeling in terms of health. As drug carriers, microspheres are one of the best ways to deliver and

control the effect of the drug at specific sites. They are characterized as free-flowing spheres composed of biodegradable or non-biodegradable proteins or synthetic polymers with ideal particle sizes of 1-1000 μm [4-7].

Microspheres form an important part of these DDS particles due to their small size and efficient carrier properties. Microspheres are widely applied in the medical field, mainly to encapsulate drugs and proteins. The drug-loaded microspheres are delivered to the target area either passively (size-based entrapment) or actively (magnetic targeting) and slowly release the encapsulated drug over a desired period of time, the duration being determined by the drug. Biological half-life and release kinetics of microsphere matrices. The biodistribution of drugs from microspheres is highly dependent on the size and fraction of drug entrapment within the microspheres [8-11]. These variables directly affect the loading efficiency of the microspheres, such as the solubility of the drug, the fraction of the dispersed phase and the fraction of the continuous phase. Polymeric microspheres and microcapsules have received much attention for the controlled delivery of therapeutically beneficial proteins [12-15].

MATERIALS AND METHODS

Materials:

Voglibose was gifted by Anthem biosciences, Bengaluru, Karnataka India. Egg Albumin and Unhydrous Ether was Supplied by Loba chemie pvt ltd. Sunflower oil purchased form Fortune Refined oil and Walnut oil purchased from Dev Ayurveda.

Method of preparation of microspheres of antidiabetic drug:

Egg albumin was dissolved in distilled water. This solution was added drop wise into suitable oil to make emulsion. From the dropping funnel, emulsion was added drop wise in the preheated oil (125±5 C°), kept in a round bottom flask, which was continuously stirred at 1500 rpm. Add proper amount of drug into the emulsion. After heat stabilization time of 10 min the preparation was cooled to 25C°, centrifuged at 2500 rpm and supernatant was decanted. The microspheres were then suspended in anhydrous ether and stored at 4C° in an airtight container.

TableNo.1: Formulation of microsphere sunflower oil

Batch No.	Excipients	Oil	RPM	Microspheres formulation
F1	100 mg Egg Albumin	Sunflower oil	1500	Formed
F2	200 mg Egg Albumin	Sunflower oil	1500	Formed
F3	300 mg Egg Albumin	Sunflower oil	1500	Formed
F4	400 mg Egg Albumin	Sunflower oil	1500	Formed
F5	500 mg Egg Albumin	Sunflower oil	1500	Formed

Table No.2: Formulation of microsphere walnut oil

Batch No.	Excipients	Oil	RPM	Microsphere sformulation
F6	100 mg Egg Albumin	Walnut oil	1500	Formed
F7	200 mg Egg Albumin	Walnut oil	1500	Formed
F8	300 mg Egg Albumin	Walnut oil	1500	Formed
F9	400 mg Egg Albumin	Walnut oil	1500	Formed
F10	500 mg Egg Albumin	Walnut oil	1500	Formed

Percentage yield of microspheres

Every batch of prepared microspheres was carefully weighed. The total yield (%) of microspheres was obtained by dividing the mass of the prepared microspheres by the total amount of all excipients and drugs used to prepare the microspheres. This was calculated using the following equation:

$$\text{percentage yield} = \frac{\text{Actual yield of product}}{\text{Total weight of excipients and drug}} \times 100$$

Drug entrapment

Based on a dose of 100 mg, the actual content of drug in the microspheres is calculated (1 g of drug excipient). This amount was mixed to 0.1N. HCL by sonication. Transfer 1 ml from this pipette into a 10 ml volumetric flask and adjust the volume to 10 ml using buffer. The solution was filtered, appropriately diluted, and the optical density was measured spectrophotometrically at 282 nm against the corresponding blank [16]. The amount of drug captured in the microspheres was calculated using the following formula:

$$\text{Percentage drug entrapment} = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \text{ X } 100$$

Buoyancy studies

Microspheres (300 mg) were spread on the surface of a USP dissolution device (basket type) filled with 900 ml of 0.1 N HCL. The medium was stirred for 12 hours using a basket rotating at 75 rpm. The floating and settled portions of the microspheres were separated separately. The microspheres were dried and weighed. Percent buoyancy was calculated by the ratio of the mass of the remaining microspheres to the total mass of the microspheres [14].

$$\% \text{ Buoyancy} = \frac{W_f}{(W_f + W_s)} \text{ X } 100$$

Where,

W_f = weight of the floating

W_s = settled microspheres respectively.

Microscopic analysis [18]

SEM

The surface morphology of the microspheres, indicated by particle size and characteristic shape, was determined using SEM. Results show SEM images of microspheres obtained at various magnifications.

Optical microscope

Optical microscopes are one of the most widely used imaging tools due to their great flexibility, robust design, and low cost. Optical Microspherical Nanoscope (OMN) was developed as a technique that can dramatically improve the observation capabilities of existing optical microscopes.

Zeta potential

The zeta potential is determined by using a Zetasizer or by other means, and gives information on the charge of the particles and the tendency of the particles in a formulation to aggregate or to remain discrete. Particles with zeta potentials of more than +30 mV or more than -30 mV are normally considered stable.

IN VITRO DRUG RELEASE:

In vitro release studies were performed in 0.1 N medium. HCl. Test conditions were as follows: microspheres containing 100 mg of drug packaged in capsules were placed in a basket in a container containing 900 ml of 0.1 N HCl medium at a temperature of 37±0.5ºC. The rotation speed of the basket was adjusted to 75 rpm. Samples of 5 ml were taken at 1hr intervals and filtered through a 0.45 µm pore size membrane filter. To maintain sink conditions, equal volumes of medium at the same temperature were added to the dissolution vessel. The optical density of the filtrate was measured at a wavelength of 282 nm and the percent drug release was calculated. Add 4ml of concentrated hydrochloric acid to a 1000ml volumetric flask, add distilled water to make 1000ml, and stir until mixed [18-19].

RESULTS AND DISCUSSION

Determination of Lambda max

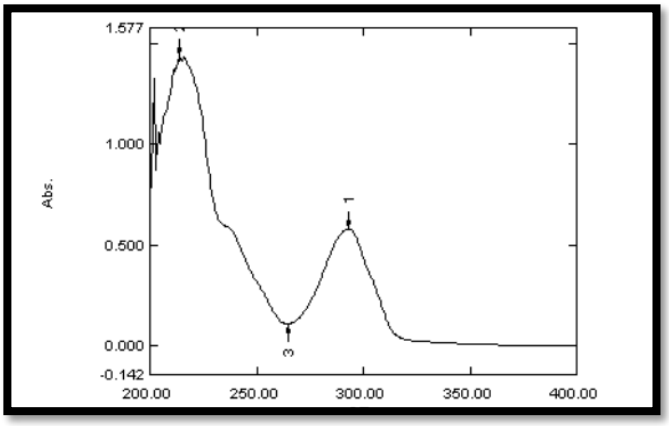

Fig No. 02: UV Spectra of voglibose

This is confirmatory analytical test for drug, showing UV spectrum as described inreference books and the absorbance curve showed characteristic absorption maxima at 282nm for voglibose.

Standard Calibration Curve of Voglibose

Table No.3: Standard calibration curve of Voglibose in Methanol at 282nm.

Concentration ug/mg	Absorbance
0	0
1	0.469
2	0.653
3	0.844
4	1.067
5	1.261

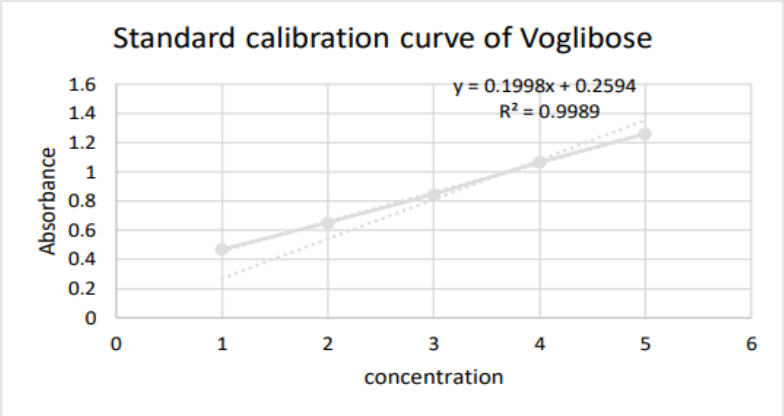

Fig No. 03: Standard calibration curve of Voglibose

Percentage yield

The highest rate was found in formulation F4, which was 90.21% of all formulations.

Microspheres were prepared with different oils and combinations to study its effect on encapsulation efficiency and used to determine its effect on flotation behavior.

Invitro Buoyancy

Choose different oils with the same formula ratios to optimize buoyancy properties. Among them, the formula containing 1 ml of sunflower oil containing 400 mg egg albumin is better.

The formulation is selected as the best based on buoyancy and encapsulation efficiency. Results from all reports confirm that changes in egg albumin concentration affect product production. The F4 formulation provides the best buoyancy performance.

The formulations, are selected as the best formulations depending upon their buoyancy, encapsulation efficiency. From the results of all the ten formulations, it is confirmed that the change in egg albumin concentration influences the properties of the formulations. The formulation F4 with drug is giving the best result of buoyancy property.

Entrapment efficiency

The percentage of encapsulation efficiency of various parameters of the prepared microspheres is as shown in the table. The encapsulation value varies between 78.61 and 88.69.

Formulation F4 has a high encapsulation efficiency of 88.69%, while F5 has a low encapsulation efficiency of 78.61%.

Table no. 4: Percentage yield, invitro buoyancy, drug entrapment efficiency of microspheres of voglibose

BatchNo.	Percentage yield (%)	Invitro buoyancy (h)	Entrapment efficiency (%)
F1	84.52	85.65	82.60
F2	82.98	83.75	81.73
F3	83.54	84.82	82.17
F4	90.21	91.66	88.69
F5	79.89	80.23	78.61
F6	85.15	86.24	83.04
F7	88.91	89.54	87.39
F8	86.78	87.26	83.92
F9	85.59	86.92	83.47
F10	87.66	88.22	85.21

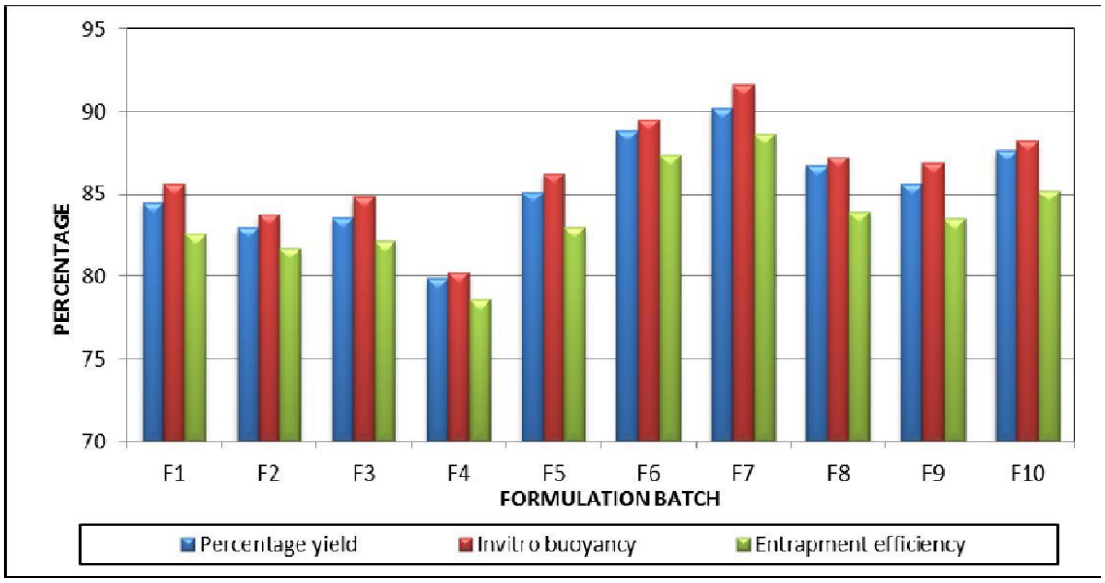

Fig.No. 4: Percentage yield, Buoyancy, Entrapment efficiency Study of Microspheres

Scanning Electron Microscopy

The surface morphology of microspheres, represented by size and shape characteristics, was determined by SEM.

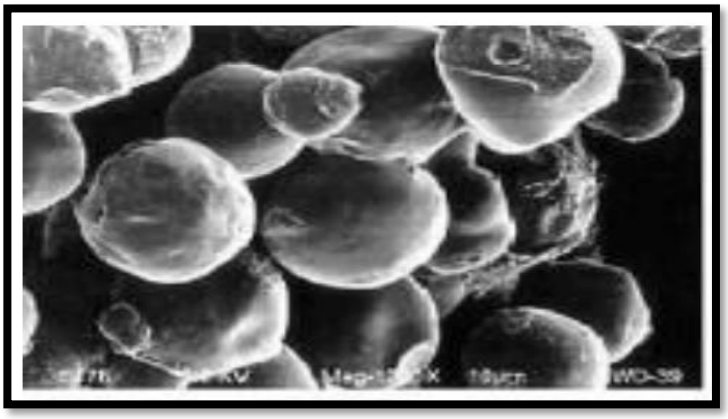

Fig No. 05: Microspheres image (SEM)

Optical Microscopy

Morphological studies were performed by optical microscopy (OM). Examine microspheres under illumination with a 10x lens.

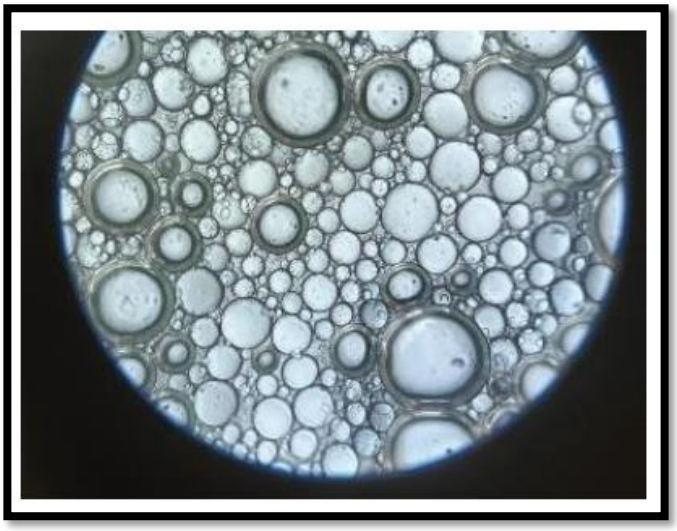

Fig No. 06: Microspheres images (compound)

Zeta potential

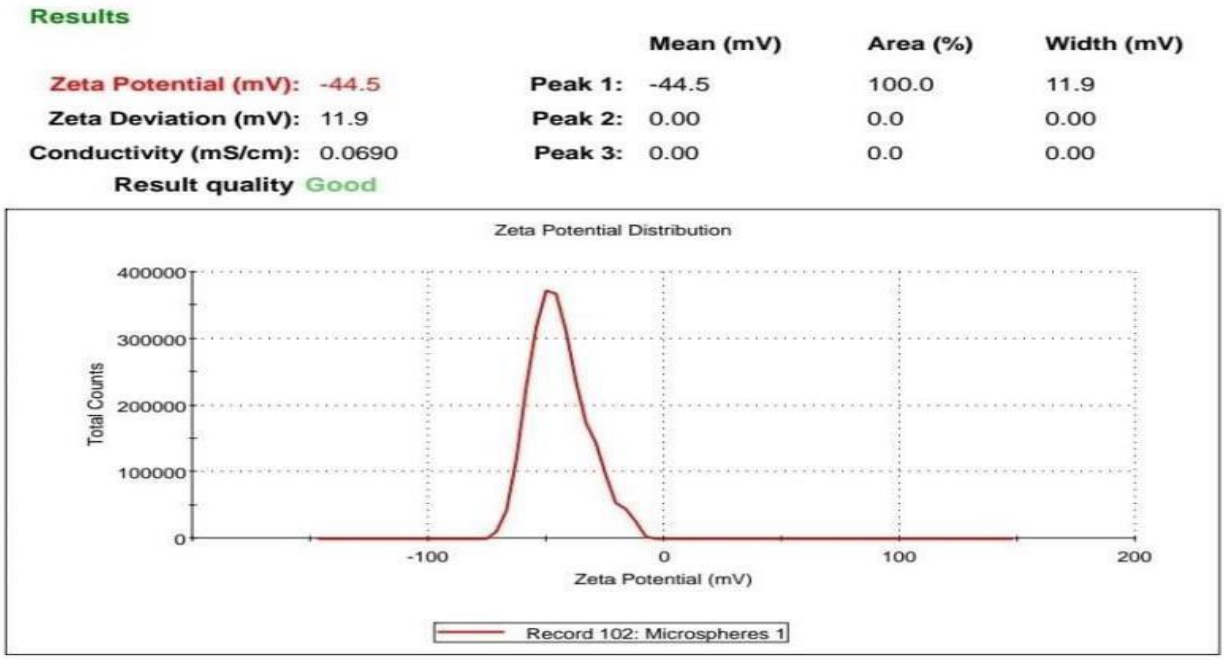

Fig No. 7: Zeta Potential of Microsphere

INVITRO RELEASE PROFILE

Table no. 05 . Invitro release profile

Time (hours)	% Cumulative Drug Release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	20.03	12.05	14.18	10.01	12.91	10.56	8.25	15.23	12.11	9.54
2	35.56	32.56	31.56	28.19	22.12	15.99	13.11	25.76	22.77	13.84
4	54.14	53.29	45.25	62.43	35.12	28.21	24.72	37.45	30.99	24.15
6	69.65	77.38	63.14	76.37	52.64	44.14	40.99	53.28	48.12	43.09
8	89.14	96.38	92.02	98.24	78.11	58.98	56.25	79.54	69.82	54.69

10	91.23	97.26	94.05	98.98	94.42	78.68	72.84	90.47	93.51	72.74
12	93.05	98.86	96.13	99.02	96.05	87.04	90.12	91.05	94.13	85.25

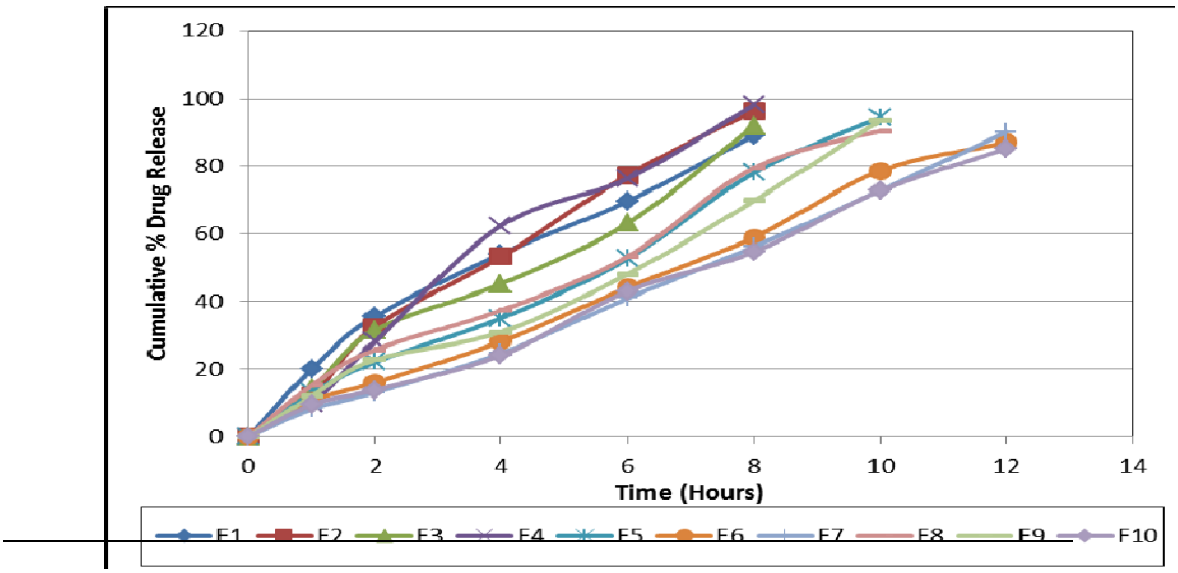

Fig. No. 08: Invitro Dissolution Release Profile for F1 – F10

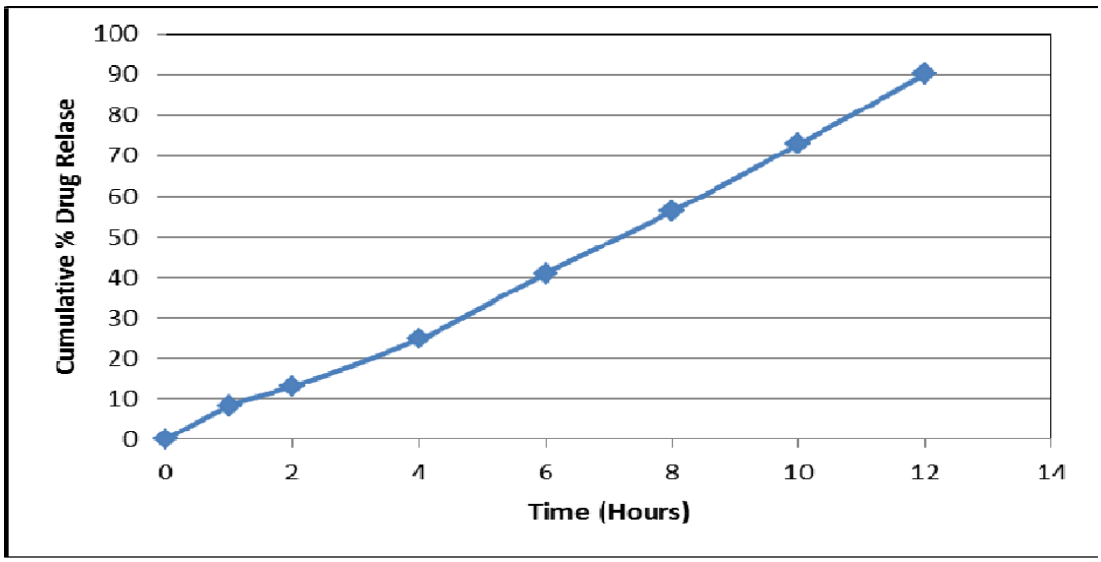

Fig. No. 09: Invitro Dissolution Release Profile for Best Formulation F4

According to the in vitro dissolution study of all formulations (F1-F10), F4 formulation released approximately 90.12% of the drug after 12 hours, complete release. Therefore, F4 formulation was selected as the best formulation among all groups.

CONCLUSION

The production and evaluation of anti-diabetic drugs containing microspheres via protein gelation technique represents a useful method for drug delivery in diabetes management. A comprehensive evaluation of physicochemical properties, including particle size, loading capacity and encapsulation performance, as well as in vitro drug release and pharmacodynamic studies, provides good results for the study of microspheres.

The production and evaluation of anti-diabetic drugs containing microspheres via protein gelation technique represents a useful method for drug delivery in diabetes management. A comprehensive evaluation of physicochemical properties, including particle size, loading capacity and encapsulation performance, as well as in vitro drug release and pharmacodynamic studies, provides good results for the study of microspheres.

Determination of Lambda max of the antidiabetic drug voglibose and establishment of a standard calibration curve to ensure the accuracy and sensitivity of the analytical method used in this study. Scanning electron microscopy (SEM) and optical microscopy further elucidated the morphology of microspheres and contributed to the understanding of their structure.

Overall, the results demonstrate the possibility of using protein gelation-based microspheres as a viable strategy to achieve drug delivery, thereby improving patients' compliance and compliance with diabetes treatment. Further research can focus on improving the quality of the process and conducting clinical and clinical studies to confirm the effectiveness and safety of this microsphere construct in the real environment.

REFERENCES:

1) Rastogi V, Shukla SS, Singh R, Lal N and Yadav P. Microspheres: a promising drug carrier. Journal of Drug Delivery and Therapeutics. 2016 ;6(3):18-26.

2) Li Q, Chang B, Dong H and Liu X. Functional microspheres for tissue regeneration. Bioactive Materials. 2023; 25:485-99.

3) Singh C, Purohit S, Singh M and Pandey BL. Design and evaluation of microspheres: A Review. Journal of drug delivery research. 2013;2(2):18-27.

4) Gurung BD and Kakar S. An overview on microspheres. Int J Health Clin Res. 2020;3(1):11-24.

5) Fu Z, Cui J, Zhao B, Shen SG and Lin K. An overview of polyester/hydroxyapatite composites for bone tissue repairing. Journal of Orthopaedic Translation. 2021; 28:118-30.

6) Kumari N, Aggarwal G and Harikumar SL. Mucoadhesive microspheres: A review. Journal of Drug Delivery and Therapeutics. 2014;4(5):48-54.

7) Patel S, Kumhal RP, Dinesh PA and Gorantli CC. A Review on Microspheres: Types, Methods of Preparation, Effects of Process Variables and Applications. American Journal of Pharm Tech Research. 2020;10(4):123-40.

8) Rafiee MH and Rasool BK. An overview of microparticulate drug delivery system and its extensive therapeutic applications in diabetes. Advanced Pharmaceutical Bulletin. 2022;12(4):730.

9) Khan M, Ansari VA, Kushwaha P, Kumar A and Akhtar J. Mucoadhesive microspheres for controlled delivery of drugs. Asian J Pharm Clin Res. 2015;8(4):17-20.

10) Garg A and Upadhyay P. Mucoadhesive microspheres: a short review. Asian journal of pharmaceutical and clinical Research. 2012;5(3):24-7.

11) Samanta MS, Gautam DE, Chandel MW, Sawant GA and Sharma KI. A review on microspheres as a novel controlled drug delivery system. Asian J Pharm Clin Res. 2021;14(4):3-11.

12) Kapil Kumar KK and Rai AK. Development and evaluation of floating microspheres of curcumin. 2003;20(3):305-13.

13) Sharma M. Formulation and evaluation of sodium alginate beads by emulsion gelationation method. Asian Journal of Pharmaceutics (AJP). 2017;11(01): S101-S106.

14) Dhakar RC, Maurya SD, Aggarwal S, Kumar G and Tilak VK. Design and evaluation of SRM microspheres of metformin hydrochloride Pharmacie Globale (IJCP). 2010;1(07): 1-5.

15) Jain AK, Sahu P, Mishra K and Jain SK. Repaglinide and Metformin-Loaded Amberlite Resin-Based Floating Microspheres for the Effective Management of Type 2 Diabetes. Current Drug Delivery. 2021;18(5):654-68.

16) Franklin CK, Daniel ON, Judith CD, Bright UN, Mumuni A, Paul AA and Anthony AA. Potential enhancement of metformin hydrochloride in solidified reverse micellar

solution-based PEGylated lipid nanoparticles targeting therapeutic efficacy in diabetes treatment, Heliyon, 2022; 8(4): 22-28.

17) Mastiholimath VS, Dandagi PM, Gadad AP, Mathews R and Kulkarni AR. In vitro and in vivo evaluation of ranitidine hydrochloride ethyl cellulose floating microparticles. Journal of Microencapsulation. 2008;25(5):307-14.

18) Lengyel M, Kállai-Szabó N, Antal V, Laki AJ and Antal I. Microparticles, microspheres, and microcapsules for advanced drug delivery. Scientia Pharmaceutica, 2019; 87(3):20.

19) El-Kamel AH, Sokar MS, Al Gamal SS and Naggar VF. Preparation and evaluation of ketoprofen floating oral delivery system. International journal of pharmaceutics. 2001 Jun 4;220(1-2):13-21.