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Drug Release Kinetics and In-Vitro Evaluation of Pioglitazone-Loaded Floating Microspheres for Sustained Drug Delivery

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ABSTRACT

The present study aimed to develop and evaluate pioglitazone-loaded floating microspheres for sustained drug delivery and to investigate the drug release kinetics of the prepared formulations. Floating microspheres were prepared using the emulsion solvent diffusion–evaporation technique employing ethyl cellulose and hydroxypropyl methylcellulose (HPMC) as polymeric carriers. The prepared microspheres were evaluated for percentage yield, particle size, drug entrapment efficiency, buoyancy behaviour, surface morphology, and in-vitro drug release profile. The percentage yield of the formulations ranged from 78.54% to 92.37%, while the mean particle size varied between 220 ± 6.2 µm and 395 ± 9.4 µm. Drug entrapment efficiency was found to be between 67.48% and 89.62%, indicating efficient incorporation of pioglitazone within the polymeric matrix. The microspheres exhibited excellent buoyancy in simulated gastric fluid with floating ability up to 95.48%, suggesting prolonged gastric retention. In-vitro drug release studies demonstrated sustained drug release for up to 12 hours, with the optimized formulation showing approximately 94% cumulative drug release. Drug release kinetic analysis revealed that the optimized formulation followed the Higuchi diffusion model, indicating diffusion-controlled drug release from the polymeric matrix. These findings suggest that floating microspheres are a promising gastro-retentive drug delivery system for improving the therapeutic efficacy of pioglitazone.

Keywords ; Floating microspheres; Pioglitazone; Gastro-retentive drug delivery; Drug release kinetics; Sustained drug release.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from impaired insulin secretion, insulin resistance, or a combination of both conditions. The disorder leads to disturbances in carbohydrate, lipid, and protein metabolism and is associated with long-term complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Type 2 diabetes mellitus represents the most prevalent form of the disease worldwide and is strongly associated with insulin resistance and progressive β-cell dysfunction[1,2]. The increasing global burden of diabetes highlights the need for improved therapeutic strategies capable of maintaining consistent plasma drug concentrations and enhancing treatment effectiveness.

Oral drug delivery remains the most widely preferred route of drug administration due to its convenience, patient compliance, and cost-effectiveness. However, conventional oral dosage forms often exhibit several limitations including rapid gastric emptying, short gastrointestinal residence time, and fluctuating plasma drug levels, which may reduce therapeutic efficacy. These issues are particularly significant for drugs that are primarily absorbed in the upper gastrointestinal tract or possess narrow absorption windows[3,4]. Consequently, considerable attention has been directed toward the development of modified drug delivery systems that can prolong gastric residence time and provide controlled drug release.

Gastro-retentive drug delivery systems (GRDDS) are designed to enhance gastric retention of dosage forms through various mechanisms such as flotation, swelling, mucoadhesion, or high-density systems. Among these strategies, floating drug delivery systems (FDDS) have emerged as one of the most effective approaches for prolonging gastric residence time. These systems possess a density lower than that of gastric fluids and therefore remain buoyant in the stomach for extended periods without interfering with normal gastric motility[5]. Prolonged gastric retention allows controlled drug release and enhances the bioavailability of drugs that exhibit site-specific absorption in the upper gastrointestinal tract.

Floating microspheres, also known as microballoons, represent a promising multiple-unit gastro-retentive drug delivery system. These microspheres are hollow spherical particles composed of natural or synthetic polymers that provide low density and prolonged buoyancy in gastric fluid. Their multiparticulate nature offers several advantages over single-unit dosage forms, including uniform distribution within the stomach, reduced risk of dose dumping, improved reproducibility of drug absorption, and minimized local irritation of the gastric mucosa[6,7]. Additionally, the large surface-area-to-volume ratio of microspheres facilitates efficient drug diffusion from the polymer matrix, enabling sustained drug release profiles.

The drug release behaviour of polymeric microspheres is governed by several mechanisms including diffusion through the polymer matrix, polymer erosion, and osmotic pressure-driven release. Evaluation of drug release kinetics is therefore essential for understanding the mechanism of drug liberation and predicting the in-vivo performance of the dosage form. Mathematical models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas equations are widely used to analyse dissolution data and identify the dominant drug release mechanism. Such kinetic modelling provides valuable insights into the interaction between formulation variables and drug release behaviour, facilitating optimization of controlled drug delivery systems[8].

Pioglitazone is a thiazolidinedione class antidiabetic drug widely used in the management of type 2 diabetes mellitus. It acts primarily by activating peroxisome proliferator-activated receptor-gamma (PPAR-γ), a nuclear receptor that regulates genes involved in glucose and lipid metabolism. Activation of PPAR-γ enhances insulin sensitivity in peripheral tissues such as skeletal muscle and adipose tissue while reducing hepatic glucose production, thereby improving glycaemic control in diabetic patients[9]. Despite its therapeutic efficacy, pioglitazone requires sustained plasma drug levels for optimal therapeutic effect and may exhibit variable gastrointestinal absorption when administered in conventional dosage forms.

Incorporation of pioglitazone into a floating microsphere-based gastro-retentive delivery system may significantly improve therapeutic performance by prolonging gastric residence time and enabling sustained drug release. Such systems can enhance drug bioavailability, reduce dosing frequency, and improve patient compliance during long-term antidiabetic therapy. Therefore, the present study focuses on the formulation and in-vitro evaluation of pioglitazone-loaded floating microspheres designed for sustained drug delivery. Furthermore, the drug release behaviour of the prepared microspheres was investigated using various kinetic models to elucidate the mechanism of drug release from the polymeric matrix[10].

Materials and Methods

Materials

Pioglitazone hydrochloride was obtained as a gift sample from a reputed pharmaceutical manufacturing company. Ethyl cellulose and hydroxypropyl methylcellulose (HPMC) were used as polymeric carriers for the preparation of floating microspheres. Polyvinyl alcohol (PVA) was employed as a stabilizing and emulsifying agent during microsphere preparation. Dichloromethane and ethanol were used as organic solvents for dissolving the drug and polymers. All chemicals and reagents used in this study were of analytical grade and were used without further purification.

Preparation of Pioglitazone Floating Microspheres

Pioglitazone-loaded floating microspheres were prepared using the emulsion solvent diffusion–evaporation method, a widely employed technique for the preparation of hollow microspheres intended for gastro-retentive drug delivery systems[11].

In this method, the required amount of pioglitazone and polymer (ethyl cellulose and HPMC) was dissolved in a mixture of ethanol and dichloromethane to obtain a homogeneous organic phase. The prepared drug–polymer solution was then slowly introduced into an aqueous phase containing polyvinyl alcohol (0.5–1% w/v) under continuous mechanical stirring to form an oil-in-water emulsion.

During the stirring process, diffusion of organic solvents into the aqueous phase occurred simultaneously with solvent evaporation. This process resulted in precipitation of the polymer and formation of hollow microspheres encapsulating the drug. The internal cavity formed during solvent evaporation contributed to reduced density and enabled the microspheres to float in gastric fluid.

After complete evaporation of the organic solvents, the microspheres were separated by filtration, washed with distilled water to remove residual emulsifier, and dried at room temperature for 24 hours. The dried microspheres were stored in a desiccator until further characterization and evaluation.

Evaluation of Floating Microspheres

Percentage Yield

The percentage yield of floating microspheres was determined to evaluate the efficiency of the preparation method. The yield was calculated by comparing the practical weight of the collected microspheres with the theoretical weight of the drug and polymers used during formulation[12].

Percentage Yield =Practical weight of microspheres / Total weight of drug and polymer × 100

Particle Size Analysis

Particle size of the prepared microspheres was determined using an optical microscopy technique. A small quantity of microspheres was dispersed in distilled water and placed on a glass slide. Approximately 100 microspheres were measured using a calibrated ocular micrometer, and the mean particle size was calculated[13].

Particle size distribution plays an important role in determining drug release behavior, buoyancy, and stability of microspheres.

Drug Entrapment Efficiency

Drug entrapment efficiency was determined to estimate the amount of drug incorporated into the microspheres. A known quantity of microspheres was dissolved in a suitable solvent to extract the drug. The solution was filtered and analyzed using a UV–visible spectrophotometer at the maximum absorption wavelength (λmax) of pioglitazone[14].

Entrapment Efficiency (%) =Actual drug content / Theoretical drug content × 100

In-Vitro Buoyancy Study

The floating behavior of the prepared microspheres was evaluated using simulated gastric fluid (0.1 N HCl, pH 1.2). A known amount of microspheres was dispersed in the dissolution medium and agitated using a USP dissolution apparatus. After a predetermined time, the floating microspheres and settled particles were separated, dried, and weighed to determine buoyancy percentage[15].

Buoyancy (%) =Weight of floating microspheres / Total weight of microspheres × 100

Surface Morphology

The surface morphology of the prepared floating microspheres was examined using scanning electron microscopy (SEM). The dried microspheres were mounted on aluminium stubs using double-sided adhesive tape and coated with a thin layer of gold under vacuum before observation under the scanning electron microscope[16].

SEM analysis was used to evaluate the shape, surface characteristics, and internal structure of the microspheres.

In-Vitro Drug Release Study

In-vitro drug release studies were carried out using a USP dissolution apparatus type II (paddle method). Microspheres equivalent to a specific dose of pioglitazone were placed in 900 mL of simulated gastric fluid (0.1 N HCl, pH 1.2) maintained at 37 ± 0.5 °C with a stirring speed of 50 rpm[17].

At predetermined time intervals, samples were withdrawn and replaced with fresh dissolution medium to maintain sink conditions. The withdrawn samples were filtered and analyzed using a UV–visible spectrophotometer to determine drug concentration.

Drug Release Kinetics

To understand the mechanism of drug release from floating microspheres, the dissolution data were fitted into various mathematical models including:

- Zero-order kinetic model
- First-order kinetic model
- Higuchi diffusion model
- Korsmeyer–Peppas model

These kinetic models help to determine the drug release mechanism and characterize whether the release follows diffusion-controlled, erosion-controlled, or anomalous transport mechanisms.

Results and Discussion

Physicochemical Properties of Pioglitazone

The physicochemical properties of pioglitazone were evaluated prior to formulation development because these parameters significantly influence drug solubility, release behaviour, and formulation design. Pioglitazone belongs to Biopharmaceutics Classification System (BCS) class II, which indicates low aqueous solubility but high permeability. Drugs with poor aqueous solubility often exhibit dissolution-limited absorption, making them suitable candidates for modified drug delivery systems such as floating microspheres designed for sustained drug release[18,19].

Table 1 Physicochemical properties of pioglitazone

Parameter	Description
Drug name	Pioglitazone
Molecular formula	C19H20N2O3S
Molecular weight	356.4 g/mol
Melting point	193–194 °C
Solubility	Practically insoluble in water
BCS classification	Class II

The poor solubility of pioglitazone necessitates formulation strategies capable of improving dissolution behaviour and maintaining sustained drug levels in the gastrointestinal tract.

Percentage Yield

The percentage yield of floating microspheres was calculated to determine the efficiency of the preparation method. The prepared formulations showed satisfactory yield values ranging from 78.54% to 92.37%. The variation in yield among different formulations may be attributed to minor losses during filtration and washing processes. Higher polymer concentration resulted in improved percentage yield due to increased viscosity of the polymer solution, which reduced drug diffusion into the external aqueous phase during microsphere formation[20].

Table 2 Percentage yield of microspheres

Formulation	Percentage Yield (%)
F1	78.54
F2	82.16
F3	85.32
F4	88.45
F5	92.37
F6	89.28

Particle Size Analysis

Particle size is an important parameter influencing drug release behaviour, buoyancy, and stability of microspheres. The mean particle size of the prepared microspheres ranged from **220 ± 6.2 µm to 395 ± 9.4 µm**. An increase in polymer concentration resulted

in larger microspheres due to higher viscosity of the polymer solution. Increased viscosity leads to formation of larger droplets during emulsification, which subsequently form larger microspheres after solvent evaporation[21].

Table 3 Particle size of floating microspheres

Formulation	Particle Size (µm)
F1	220 ± 6.2
F2	248 ± 7.1
F3	280 ± 6.9
F4	315 ± 8.5
F5	350 ± 9.1
F6	395 ± 9.4

Drug Entrapment Efficiency

Drug entrapment efficiency reflects the ability of the polymer matrix to retain the drug within the microspheres. The entrapment efficiency of the prepared formulations ranged from 67.48% to 89.62%. Higher polymer concentration enhanced drug entrapment because the increased viscosity of the polymeric phase reduced drug diffusion into the surrounding aqueous phase during microsphere formation[22].

Table 4 Drug entrapment efficiency

Formulation	Entrapment Efficiency (%)
F1	67.48
F2	72.16
F3	78.35
F4	82.41
F5	89.62
F6	85.74

In-Vitro Buoyancy Study

The floating ability of microspheres is a critical parameter in gastro-retentive drug delivery systems. The prepared microspheres exhibited excellent buoyancy in simulated gastric fluid. The buoyancy percentage ranged from 72.16% to 95.48%, indicating effective floating behaviour and prolonged gastric retention. The hollow structure formed during solvent evaporation contributes to reduced density, allowing the microspheres to remain buoyant for extended periods[23].

Table 5 Buoyancy of floating microspheres

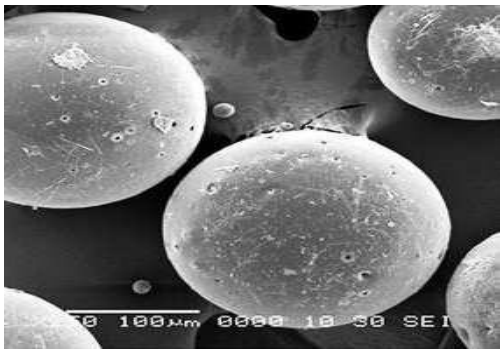
Formulation	Buoyancy (%)
F1	72.16
F2	78.45
F3	84.32
F4	88.57
F5	95.48
F6	91.36

Surface Morphology

The morphology of floating microspheres was examined using scanning electron microscopy.

Figure 1 SEM image of floating microspheres

The SEM images revealed that the microspheres were spherical in shape with smooth surfaces and hollow internal structures. The presence of an internal cavity confirms successful formation of floating microspheres and explains their buoyant behaviour in gastric fluid[24,25].



In-Vitro Drug Release Study

The drug release profile of pioglitazone from floating microspheres was evaluated using simulated gastric fluid.

The formulations demonstrated sustained drug release for up to 12 hours, indicating the suitability of microspheres for prolonged drug delivery.

Table 6 In-vitro drug release profile

Time (hr)	F1	F2	F3	F4	F5	F6
1	18	16	15	14	12	13
2	28	26	24	22	20	21
4	42	39	37	35	32	34
6	55	52	49	46	44	45
8	68	64	60	57	55	58
10	80	77	74	71	69	70
12	90	88	85	82	94	87

Among the prepared formulations, F5 exhibited the highest cumulative drug release (94.12%) at 12 hours, indicating optimal polymer concentration for sustained drug delivery.

Drug Release Kinetics

To understand the mechanism of drug release, the dissolution data were fitted to different kinetic models.

Table 7 Drug release kinetic models

Model	R^2 value
Zero order	0.945
First order	0.962
Higuchi	0.987
Korsmeyer-Peppas	0.971

The optimized formulation followed the Higuchi model, indicating diffusion-controlled drug release from the polymeric matrix. The Korsmeyer–Peppas model suggested non-Fickian diffusion, which indicates that both diffusion and polymer relaxation contribute to drug release from floating microspheres[26-29].

Conclusion

The present study successfully developed pioglitazone-loaded floating microspheres using the emulsion solvent diffusion–evaporation technique for sustained drug delivery. The prepared microspheres exhibited satisfactory physicochemical characteristics, including good percentage yield, appropriate particle size distribution, and high drug entrapment efficiency. The floating microspheres demonstrated excellent buoyancy in simulated gastric fluid, confirming their ability to remain buoyant for extended periods and thereby enhance gastric residence time.

Surface morphology analysis using scanning electron microscopy revealed that the microspheres were spherical in shape with smooth surfaces and hollow internal structures, which are essential features for floating drug delivery systems. The in-vitro drug release study showed sustained release of pioglitazone for up to 12 hours, indicating that the developed microspheres are capable of maintaining prolonged drug release.

Drug release kinetic analysis revealed that the optimized formulation followed the Higuchi diffusion model, suggesting that drug release was primarily controlled by diffusion through the polymeric matrix. The Korsmeyer–Peppas model indicated non-Fickian diffusion, implying that both diffusion and polymer relaxation mechanisms contributed to drug release.

Overall, the developed floating microspheres represent a promising gastro-retentive drug delivery system for pioglitazone, which may enhance drug bioavailability, reduce dosing frequency, and improve therapeutic efficacy in the management of type 2 diabetes mellitus.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, et al. IDF diabetes atlas: Global and regional diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.
2. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2023;401:1807-1820.
3. Kumar A, Sharma S, Kamble R. Advances in oral controlled drug delivery systems. Drug Deliv Transl Res. 2021;11:1057-1073.
4. Patra JK, Das G, Fraceto LF, et al. Nano-based drug delivery systems: recent developments and future prospects. J Nanobiotechnology. 2020;18:71.
5. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems. Pharmaceutics. 2021;13:1021.
6. Bera H, Boddupalli S. Floating drug delivery systems: a review of approaches and technologies. Int J Pharm. 2020;590:119980.
7. Chavda H, Patel C. Floating microspheres as a gastroretentive drug delivery system: recent developments. AAPS PharmSciTech. 2021;22:235.
8. Siepmann J, Peppas NA. Higuchi equation: derivation, applications and use in drug delivery modelling. Int J Pharm. 2021;593:120146.
9. DeFronzo RA, Norton L, Abdul-Ghani M. Renal, metabolic and cardiovascular considerations of pioglitazone therapy. Diabetes Care. 2020;43:279-289.
10. Patel V, Patel H, Panchal S. Formulation and evaluation of gastroretentive floating microspheres for sustained drug delivery. Pharmaceutics. 2022;14:1507.
11. Chavda H, Patel C. Floating drug delivery systems: recent advances and future perspectives. AAPS PharmSciTech. 2020;21:120.
12. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 2019;76:331-341.
13. Raval JA, Patel MM. Formulation and characterization of floating microspheres for gastroretentive drug delivery. Drug Dev Ind Pharm. 2020;46:1118-1127.
14. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2019;123:243-251.
15. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems. Pharmaceutics. 2021;13:1021.
16. Goldstein JI, Newbury DE, Joy DC. Scanning Electron Microscopy and X-ray Microanalysis. 4th ed. New York: Springer; 2018.
17. Siepmann J, Peppas NA. Higuchi equation: derivation, applications and use in drug delivery modelling. Int J Pharm. 2021;593:120146.
18. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;12:413-420.
19. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: importance and enhancement techniques. ISRN Pharm. 2012;2012:195727.
20. Bansal S, Aggarwal G, Rana V, Kaur IP. Development and evaluation of floating microspheres for controlled drug delivery. Drug Deliv. 2018;25(1):106-115.
21. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory agents indomethacin, ibuprofen and ketoprofen. J Control Release. 1989;10:167-175.
22. Soppimath KS, Kulkarni AR, Rudzinski WE, Aminabhavi TM. Microspheres as floating drug delivery systems to increase gastric retention of drugs. Drug Metab Rev. 2001;33(2):149–160.
23. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. J Pharm Sci. 1992;81(2):135–140.
24. Freitas S, Merkle HP, Gander B. Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. J Control Release. 2005;102(2):313–332.
25. Golandaz G, Pal A, Vaibhav Uplanchiwar, Rupesh Gautam. A *Butea Monosperma* flower partially reduces high fat diet induced obesity in experimental rats. Obesity Medicine, 17(2020) 100179. doi: https://doi.org/10.1016/j.obmed.2019.100179.

26. Parashar S, Uplanchiwar V, Gautam R.K., Goyal S. *In-Vitro* antioxidant and *in-vivo* hepatoprotective activity of ethanolic extracts of *Ziziphus rugosa* L leaves. Indian drugs, 2019, 56(7):69-75.
27. Vaibhav Uplanchiwar, M.K. Gupta, Rupesh K. Gautam. Bioactivity guided isolation of memory enhancing compound from chloroform extract of roots of *Plumbago Zeylenica* Linn. Asian Journal of Clinical Research, Volume 11 (7), 2018: 497-500.
28. Vaibhav Uplanchiwar, M.K. Gupta, Rupesh K. Gautam. Memory enhancing effect of various polar and non polar extracts of *Plumbago Zeylanica* Linn. Roots. International Journal of Green Pharmacy, Jan-June 2018 (Suppl).12 (1).
29. Peppas NA, Sahlin JJ. A simple equation for the description of solute release. III. Coupling of diffusion and relaxation. Int J Pharm. 1989;57:169–172.

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