https://doi.org/ 10.33472/AFJBS.6.10.2024.4895-4912

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

FABRICATION AND EVALUATION OF MUCOADHESIVE GASTRORETENTIVE MICROSPHERES OF OXCARBAZEPINE

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Article History

Volume 6,Issue 10, 2024

Received:29 Apr 2024

Accepted : 27 May 2024

doi: 10.33472/AFJBS.6.10.2024.4895-4912

ABSTRACT

This present study aimed to perform the fabrication and characterization of microsphere formulations of oxcarbazepine, converging on drug loading capacity, encapsulation efficiency, particle morphology, yield percentage, swelling index, mucoadhesive properties, and in vitro drug release kinetics. The formulations demonstrated consistent drug loading capacities and high encapsulation efficiencies, indicating robust and reproducible processes. Particle size analysis and SEM provided insights into particle uniformity and surface characteristics. The yield and swelling indices varied, identifying formulations OXCF-2 and OXCF-6 as optimal due to their high production efficiency and controlled release properties. The mucoadhesive analysis revealed that OXCF-6 and OXCF-2 maintained superior adhesion, beneficial for extended drug delivery applications. Kinetic modelling suggested that the drug release from these formulations predominantly follows zero-order kinetics, suitable for maintaining steady therapeutic levels. The study demonstrated the importance of a multi-faceted approach in developing effective microsphere drug delivery systems.

Keywords: Mucoadhesive, Gastroretentive microspheres, Oxcarbazepine, Mucoadhesive microspheres

INTRODUCTION

Mucoadhesive gastroretentive microspheres are an advanced drug delivery system designed to enhance the residence time of drugs in the stomach, improving their bioavailability and therapeutic effectiveness. These microspheres are typically composed of biocompatible and biodegradable polymers, ranging from 1 to 1000 micrometres in size, that adhere strongly to the mucosal lining of the gastrointestinal (GI) tract. This mucoadhesive property allows the microspheres to remain in the stomach for extended periods, ensuring a prolonged release of the drug and better absorption (Mishra et al., 2018). The stomach is a favourable site for drug delivery due to its predictable environment and large surface area. However, the rapid transit of stomach contents to the intestines can limit the effectiveness of many drugs, especially those absorbed primarily in the stomach or upper part of the small intestine. Gastroretentive systems, such as mucoadhesive microspheres, address this challenge by ensuring the drug remains in the stomach for a longer duration. This prolonged gastric retention improves drug absorption and enhances bioavailability, making it particularly beneficial for drugs with narrow absorption windows (Mishra et al., 2018, Beg et al., 2019, Smart, 2005).

The formulation of mucoadhesive microspheres involves selecting appropriate polymers that can adhere to the mucosal surface. Commonly used polymers include chitosan, alginate, and carbopol, which are known for their strong mucoadhesive properties. These polymers can form hydrogen bonds and electrostatic interactions with the mucus layer, facilitating prolonged adherence. Additionally, the choice of polymer affects the drug release profile, allowing for controlled and sustained release of the therapeutic agent (Beg et al., 2019, Smart, 2005, Mansuri et al., 2016). One of the significant advantages of mucoadhesive gastroretentive microspheres is their ability to provide a controlled release of the drug. This controlled release reduces the frequency of drug administration, enhancing patient compliance and minimizing side effects. For example, drugs with a short half-life can benefit from this delivery system, as the extended retention time in the stomach ensures a more consistent therapeutic effect (Smart, 2005, Khutoryanskiy, 2011, Mansuri et al., 2016).

The development and optimization of mucoadhesive microspheres involve various techniques, such as solvent evaporation, ionotropic gelation, and spray drying. Each method has its advantages and is chosen based on the desired characteristics of the final product. For instance, solvent evaporation is widely used for its simplicity and ability to produce uniform microspheres, while ionotropic gelation is favoured for its mild conditions that preserve the integrity of sensitive drugs. Characterization of mucoadhesive microspheres includes evaluating their particle size, surface morphology, drug loading efficiency, and in vitro Mucoadhesion. These parameters are crucial for predicting the in vivo behaviour of the microspheres. Additionally, in vitro release studies are conducted to assess the drug release profile, which is essential for determining the efficacy of the drug delivery system (Smart, 2005, Khutoryanskiy, 2011, Mansuri et al., 2016). In summary, mucoadhesive gastroretentive microspheres represent a promising approach for enhancing the bioavailability and therapeutic efficacy of drugs. By prolonging the gastric residence time and providing controlled drug release, these microspheres offer significant advantages over conventional drug delivery systems. Their development involves careful selection of mucoadhesive polymers and optimization of formulation techniques to achieve the desired characteristics. As research in this field continues to advance, mucoadhesive gastroretentive microspheres are expected to

play a crucial role in improving drug delivery and patient outcomes (Nadpara et al., 2012, Mishra et al., 2018).

Oxcarbazepine is a widely used anticonvulsant and mood-stabilizing medication, primarily prescribed for treating epilepsy and bipolar disorder. It works by stabilizing overactive nerve membranes, preventing repetitive neuronal firing, and reducing synaptic impulse propagation. Despite its effectiveness, oxcarbazepine has some drawbacks related to its pharmacokinetics. It has a short half-life, requiring frequent doses, and its absorption in the gastrointestinal (GI) tract can be inconsistent, leading to fluctuating plasma drug levels. These factors can affect therapeutic outcomes and patient adherence. Developing mucoadhesive gastroretentive microspheres for oxcarbazepine aims to tackle these issues by enhancing the drug's bioavailability and enabling a controlled release. These systems are designed to remain in the stomach for extended periods, making them particularly suitable for drugs like oxcarbazepine that are best absorbed in the upper GI tract. By ensuring the drug stays longer in the stomach, these microspheres can improve the consistency and extent of oxcarbazepine absorption (Stancil et al., 2024, Naderi et al., 2024, Yuan et al., 2023).

One key benefit of mucoadhesive gastroretentive microspheres is their ability to prolong gastric retention. These microspheres adhere to the gastric mucosa, allowing them to stay in the stomach for longer durations. This extended stay enables a sustained release of oxcarbazepine, helping to maintain stable plasma drug levels and reducing the need for frequent dosing. Consequently, patient compliance improves since the inconvenience of taking multiple daily doses is minimized. Enhanced bioavailability is another major advantage. The longer the microspheres stay in the stomach, the more oxcarbazepine is absorbed through the gastric mucosa, leading to higher bioavailability and improved therapeutic efficacy. For epilepsy patients, this can mean better seizure control, while for those with bipolar disorder, it can result in more stable mood regulation (Yuan et al., 2023, Kharel et al., 2022, Athar et al., 2022, Rissardo and Caprara, 2020). Controlled release is another critical feature of mucoadhesive microspheres. Traditional oxcarbazepine formulations can cause spikes in plasma concentrations shortly after ingestion, followed by rapid declines. These fluctuations can lead to inconsistent therapeutic effects and more side effects. In contrast, mucoadhesive gastroretentive microspheres release oxcarbazepine at a steady rate, ensuring more consistent therapeutic levels over time. This steady release helps achieve better seizure control and mood stabilization, enhancing overall clinical outcomes.

Patient adherence is significantly improved with these microspheres. The reduced dosing frequency and consistent therapeutic effects make it easier for patients to stick to their medication regimen. Better adherence leads to improved management of epilepsy and bipolar disorder, ultimately enhancing the quality of life for patients. In inference, the formulation of mucoadhesive gastroretentive microspheres for oxcarbazepine offers a strategic solution to the drug's pharmacokinetic challenges. By prolonging gastric retention, enhancing bioavailability, and providing controlled release, these microspheres offer significant therapeutic benefits (Yeh et al., 2023, Rana et al., 2023, Wang et al., 2020, 2012, 2006, 1994). They ensure more stable plasma drug levels, reduce dosing frequency, and improve patient adherence. As research in this field progresses, mucoadhesive gastroretentive microspheres are set to play a crucial role in optimizing drug delivery and improving patient outcomes for those with epilepsy and bipolar disorder. Therefore, considering all the above facts, this present study was designed to fabricate

the development and evaluation of mucoadhesive gastroretentive microspheres of Oxcarbazepine.

MATERIAL AND METHODS

Material

The preparation of mucoadhesive gastroretentive microspheres containing Oxcarbazepine involved several key materials. Oxcarbazepine, the active pharmaceutical ingredient (API), was selected for its anticonvulsant and mood-stabilizing properties and received as a gift sample from Resenta Pharma, Baddi, Himachal Pradesh. The primary polymer, sodium alginate; Carboxymethyl Cellulose (Sodium CMC), Chitosan, and Hydroxypropyl Methylcellulose (HPMC K4M) were procured form Loba Chem, Mumbai, India. Sodium CMC and Calcium chloride ($CaCl_2$) were procured from Sigma Aldrich, Mumbai, India. Pluronic F68 and Polyvinyl Alcohol (PVA) were used as stabilizers and purchased from Himedia, India. Ethanol and water served as solvents in the preparation process and were of analytical grade arranged form Lob Chem, India. All the other chemicals, solvents and reagents were of analytical graded arranged form reputed vendors only.

Methods

Preparation of microsphere formulations

To prepare Oxcarbazepine mucoadhesive gastroretentive microspheres, sodium alginate was first dissolved in water to form a uniform polymer solution. Oxcarbazepine was then carefully added to this solution, ensuring thorough mixing for even distribution of the drug. Depending on the specific formulation, additional polymers such as Sodium CMC or Chitosan, were incorporated into the mixture to enhance mucoadhesive properties and control the drug release rate. Once the polymer-drug solution was ready, a calcium chloride solution was prepared as the coagulation medium. The polymer-drug mixture was slowly added dropwise into the calcium chloride solution using a syringe or similar device while stirring continuously. This process, known as ionotropic gelation, facilitated the formation of microspheres as the sodium alginate reacted with the calcium ions. To stabilize the microspheres, Pluronic F68 and Polyvinyl Alcohol (PVA) were added to the mixture. These stabilizers helped prevent the microspheres from aggregating and ensured a uniform size distribution. Stirring was continued for a sufficient time to allow complete cross-linking and formation of the microspheres. After the formation of the microspheres, the mixture was filtered or centrifuged to collect the microspheres. They were then washed thoroughly with water to remove any residual calcium chloride and other impurities. Finally, the microspheres were dried at room temperature or in a vacuum oven to achieve the desired consistency and stability. By following these steps, Oxcarbazepine mucoadhesive gastroretentive microspheres with enhanced bioavailability and controlled release properties were obtained. This method not only improved the therapeutic efficacy of Oxcarbazepine but also enhanced patient compliance by reducing the frequency of dosing.

Table 1. The composition of the microsphere formulations

Formulation	Amount of Na-alginate (g)	Amount of Oxcarbazepine (g)	Polymer	Amount of Additive Polymer (g)	Drug/Na-Alginate Ratio	Coagulation Medium ($CaCl_2$ Solution)
OXCF-1	2	0.1	Sodium CMC	1	0.05:1	1.5%
OXCF-2	2	0.1	Sodium CMC	2	0.05:1	1.5%
OXCF-3	2	0.1	Sodium CMC	3	0.05:1	1.5%
OXCF-4	2	0.1	Chitosan	1	0.05:1	1.5%
OXCF-5	2	0.1	Chitosan	2	0.05:1	1.5%
OXCF-6	2	0.1	Chitosan	3	0.05:1	1.5%

Characterization of the Oxcarbazepine Mucoadhesive Gastroretentive Microspheres

Particle Size and Morphology:

To analyze the particle size and surface morphology of the microspheres, scanning electron microscopy (SEM) was used. First, the microspheres were thoroughly dried to remove any moisture that could interfere with the imaging process (Hardenia et al., 2011). Then, they were carefully mounted on aluminum stubs using a conductive adhesive tape to keep them securely in place during the analysis. To prevent any issues with electrical charging under the electron beam, a thin layer of gold was applied to the samples using a sputter coater. This step ensured that the images would be clear and detailed. Once the samples were ready, they were placed in the SEM chamber. The SEM provided high-resolution images at various magnifications, allowing us to closely examine the microspheres. These images revealed important details about the size distribution, shape, and surface texture of the microspheres. By studying these images, we could assess the uniformity and structural integrity of the microspheres, ensuring they met the desired quality for effective drug delivery (Das and Ng, 2010).

Drug Loading Efficiency and Encapsulation Efficiency:

To determine the amount of Oxcarbazepine loaded into the microspheres and the encapsulation efficiency, UV-Visible spectrophotometry was used. First, a known quantity of the microspheres was carefully weighed and then dissolved in a suitable solvent to release the encapsulated drug. The solution was then filtered to remove any particulate matter, ensuring a clear sample for analysis. Next, the filtered solution was subjected to UV-Visible spectrophotometry. The absorbance of the solution was measured at 254 nm wavelength corresponding to Oxcarbazepine. By comparing the absorbance values to a standard calibration curve prepared with known concentrations of Oxcarbazepine, the amount of drug present in

the solution was quantified. This measurement allowed us to calculate both the drug loading efficiency, which is the amount of drug actually encapsulated within the microspheres relative to the initial amount used, and the encapsulation efficiency, which indicates the effectiveness of the encapsulation process. These values ensured that the microspheres contained the correct dosage of Oxcarbazepine for effective therapeutic use (Yadav and Jain, 2011).

Percentage Yield

The number of microspheres obtained in relation to the microsphere's theoretical content was used to compute the production yield. The % yield was calculated using the following formula: (Yadav and Jain, 2011)

$$\text{Yield (\%)} = \frac{Quantity\ of\ microspheres\ produced}{Theoretical\ content}\ x\ 100$$

Swelling Index

To study the swelling behaviour of the microspheres, they were immersed in simulated gastric fluid (SGF). Initially, a known quantity of dry microspheres was weighed and recorded. These microspheres were then placed in SGF at a controlled temperature to mimic the conditions of the stomach. At specific time intervals, the microspheres were carefully removed from the SGF, gently blotted to remove excess fluid, and weighed again. This process was repeated over a series of time points to monitor the weight changes as the microspheres absorbed the fluid and swelled. The swelling index was calculated using the formula (Shivanand et al., 2010):

Swelling Index = We -W_O/ W_O

Where, Wo = Initial weight of the dry microspheres,

We = weight of the swollen microspheres at equilibrium swelling in the media.

This swelling behaviour provided insights into the mucoadhesive and gastroretentive properties of the microspheres. Increased swelling indicated enhanced adhesion to the gastric mucosa, which is crucial for ensuring the microspheres stay in the stomach for prolonged periods, thereby improving drug release and absorption.

In Vitro Mucoadhesion Study

To evaluate the mucoadhesive strength of the microspheres, a modified in vitro mucoadhesion test was conducted. Freshly excised gastric mucosa was obtained and prepared for the experiment. The mucosa was carefully washed with saline solution to remove any residual contents and then mounted on a glass slide or a similar stable surface to create a smooth, uniform layer. A known quantity of the prepared microspheres was then placed on the mucosal surface. The setup was inclined or positioned to apply gentle shear forces, simulating the conditions in the gastrointestinal tract where peristaltic movements would act on the microspheres. The system was subjected to these shear forces, and the time taken for the microspheres to detach from the mucosal surface was recorded. This adhesion time provided a measure of the mucoadhesive strength of the microspheres. The longer the microspheres adhered to the gastric mucosa, the stronger their mucoadhesive properties were considered to be. This test was crucial for ensuring that the microspheres could remain in the stomach for extended periods, enhancing their gastroretentive properties and improving the effectiveness (Hardenia et al., 2011).

$$\text{Mucoadhesion \%} = \frac{\text{weight of adhered microspheres}}{\text{weight of applied microspheres}} \times\ 100$$

In Vitro Drug Release Study

The release profile of Oxcarbazepine from the microspheres was assessed using a USP Type II dissolution apparatus, also known as a paddle apparatus. Initially, a specified amount of microspheres was placed in the dissolution medium, which consisted of simulated gastric fluid (SGF) maintained at a constant temperature of 37°C to replicate the conditions within the human stomach. The USP Type II dissolution apparatus was set to rotate at a specific speed, typically around 50 to 100 rpm, to ensure uniform mixing and simulate the peristaltic movements in the gastrointestinal tract. At regular intervals, samples of the dissolution medium were withdrawn using a syringe or sampling probe, ensuring that the volume removed was immediately replaced with fresh SGF to maintain a constant volume. The collected samples were then analyzed using UV-Visible spectrophotometry. The absorbance of each sample was measured at the predetermined λmax for Oxcarbazepine, typically around 254 nm. By comparing the absorbance values to a previously established calibration curve of known Oxcarbazepine concentrations, the amount of drug released at each time point was quantified. The cumulative drug release data was then plotted against time to generate the release profile of Oxcarbazepine from the microspheres. This profile helped in determining the controlled release characteristics of the microspheres, illustrating how effectively they could sustain drug release over an extended period. This study was essential for verifying that the microspheres provided a consistent and prolonged therapeutic effect, enhancing the overall efficacy and patient compliance with the medication regimen (Shivanand et al., 2010).

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was conducted to identify any potential chemical interactions between Oxcarbazepine and the polymers used in the formulation. The spectra of the pure drug, polymers, and drug-loaded microspheres were compared to detect any shifts or changes in functional groups.

Statistical analysis

In this study, statistical analysis was performed using GraphPad Prism software. A One-Way Analysis of Variance (ANOVA) assessed variability and significance among multiple groups, followed by Tukey's tests as post hoc for specific group comparisons. Data were presented as mean values ± standard deviation (SD). A significance level of $p < 0.05$ was set.

RESULTS AND DISCUSSION

Fabrication of microsphere formulations, Encapsulation efficiency and Drug loading

The drug loading capacity for the formulations ranges from 40.20 to 43.09. This indicates that the formulations have a relatively consistent loading capacity, with slight variations. The highest drug loading capacity is observed in OXCF-4 (43.09), while the lowest is in OXCF-1 and OXCF-5 (40.20). Encapsulation efficiency varies between 90.62 and 93.98, which indicates a high level of consistency in the encapsulation process. OXCF-6 shows the highest encapsulation efficiency at 93.98%, while OXCF-4 has the lowest at 90.62%. The formulations demonstrate a narrow range of values for both drug loading capacity and encapsulation efficiency, indicating a reliable and reproducible formulation process. OXCF-1 and OXCF-5 have identical LC values (40.20) but differ slightly in EE (93.25 and 91.25, respectively), suggesting that minor variations in the formulation process could influence encapsulation efficiency without affecting the drug loading capacity. OXCF-6 emerges as the most optimal formulation, achieving both a high LC (41.65) and the highest EE (93.98). This formulation

strikes a balance between high drug loading and efficient encapsulation, making it potentially the most effective. The slight decrease in encapsulation efficiency observed in formulations with higher drug loading capacities (e.g., OXCF-4) suggests a potential trade-off between these two parameters. As the drug loading capacity increases, the encapsulation efficiency may slightly decrease, likely due to the limitations in the formulation matrix to accommodate higher drug content while maintaining encapsulation efficiency. The analysis of the formulations OXCF-1 to OXCF-6 shows a consistent performance in terms of drug loading capacity and encapsulation efficiency. OXCF-6 stands out as the most optimal formulation with the highest encapsulation efficiency, while OXCF-4, despite having the highest drug loading capacity, shows a slight reduction in encapsulation efficiency (Table 2 and Figure 1).

Table 2. Encapsulation efficiency and drug loading capacity.

Formulation code	Drug loading capacity (LC)	Encapsulation Efficiency (EE)
OXCF-1	40.20	93.25
OXCF-2	41.65	92.67
OXCF-3	42.65	91.99
OXCF-4	43.09	90.62
OXCF-5	40.20	91.25
OXCF-6	41.65	93.98

Where LC= Loading capacity, EE= Encapsulation efficiency

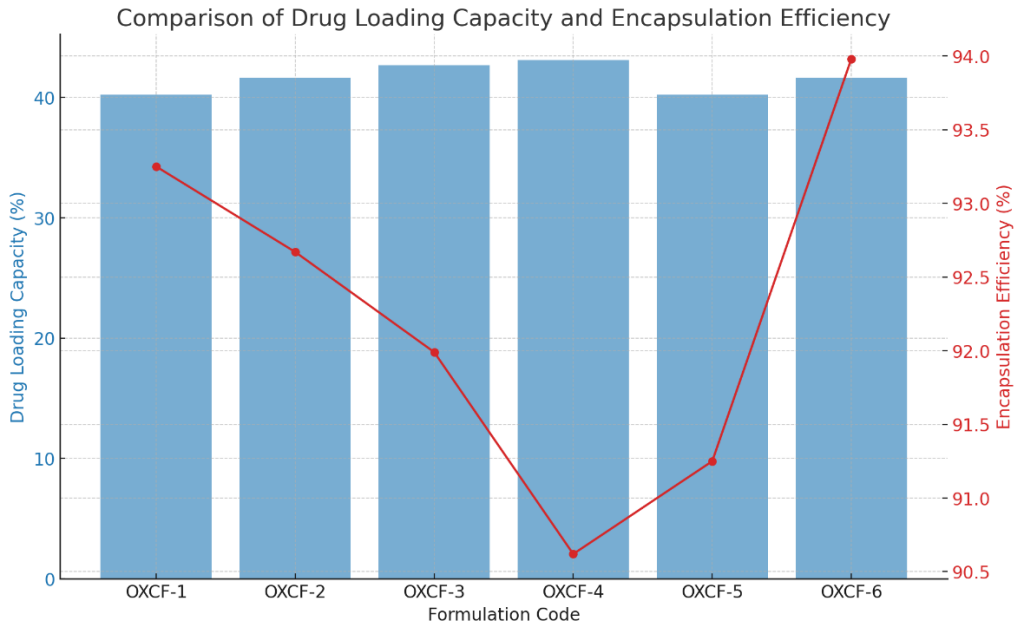

Figure 1. Depicting the Encapsulation efficiency and drug loading capacity.

Characterization of the formulated microspheres

Scanning Electron Microscopy (SEM) & Particle size analysis

The SEM images provide valuable insights into the morphology and size distribution of the microspheres (Figure 2 and Table 3). The right image shows a more consistent and refined formulation with uniform particle size and smoother surfaces, which is generally desirable for controlled drug delivery systems. The left image, with its broader size distribution and attached smaller particles, indicates areas where the formulation process could be improved to achieve better uniformity and potentially more predictable drug release profiles. These observations can guide further optimization and quality control in the production of such microspheres.

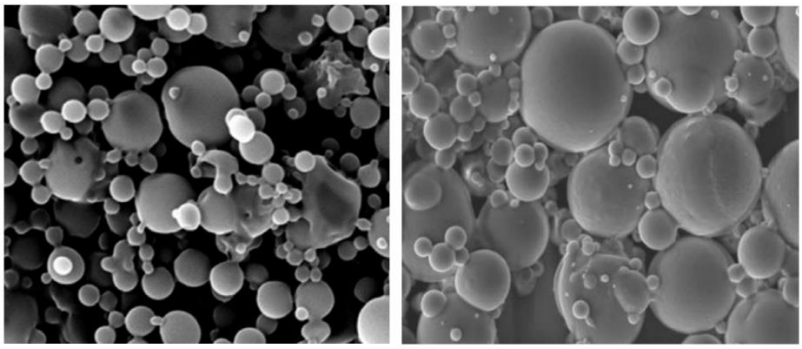

Figure 2. SEM Photograph of formulation

The analysis of particle size and shape for formulations OXCF-1 to OXCF-6 reveals that spherical particles with medium sizes (e.g., OXCF-2, OXCF-4, OXCF-6) are likely to offer better drug delivery performance. These formulations are expected to provide more controlled and predictable drug release profiles, while non-spherical particles may present challenges in terms of flow properties, packing density, and stability. The insights gained from this analysis can guide the optimization of particle morphology to achieve desired therapeutic outcomes.

Table 3. Particle size and shape of microspheres

Formulation Code	Particle size (µm) ± SD	Shape
OXCF-1	5.54±0.19	Non spherical
OXCF-2	4.61±0.21	Spherical
OXCF-3	4.58±0.18	Non spherical
OXCF-4	5.45±0.16	Spherical
OXCF-5	3.51±0.19	Non spherical
OXCF-6	5.11±0.18	Spherical

Yield percentage and Swelling index

The yield percentage varies between 83.18% and 92.30%, indicating the efficiency of the formulation process in producing the final product. OXCF-2 and OXCF-6 indicated highest yield percentage at 92.30% ± 3.21, which indicated a highly efficient formulation process with minimal loss of material. OXCF-3 revealed lowest yield percentage at 83.18% ± 3.33, which suggested some inefficiencies or losses during the formulation process.

The swelling index varies significantly between the formulations, ranging from 0.22 to 0.98. The swelling index indicates the ability of the microspheres to swell in the presence of a solvent, which is critical for drug release kinetics. OXCF-1, OXCF-3, and OXCF-5 demonstrated high swelling index values (0.96 to 0.98). These formulations are likely to swell

significantly, which can facilitate faster drug release. The high swelling index may lead to a burst release of the drug, which might not be desirable for controlled release formulations. OXCF-2, OXCF-4, and OXCF-6 demonstrated low swelling index values (0.22 to 0.24).These formulations swell less, suggesting a more controlled and sustained drug release profile. Lower swelling index values are beneficial for formulations where a slow and controlled drug release is required.

Formulations with the highest yield percentages (OXCF-2 and OXCF-6) also have the lowest swelling indices, indicating that these formulations are not only efficient to produce but also provide controlled swelling properties. OXCF-2 and OXCF-6 appear to be optimal formulations due to their high yield and low swelling index. This combination is advantageous for ensuring efficient production and achieving controlled drug release. OXCF-3, with the lowest yield and high swelling index, indicates a need for process optimization to improve both production efficiency and control over the drug release mechanism. The analysis of the yield percentage and swelling index for formulations OXCF-1 to OXCF-6 reveals that OXCF-2 and OXCF-6 are the most efficient and optimal formulations. They exhibit high yield percentages and low swelling indices, indicating a well-controlled production process and desirable drug release profiles. In contrast, formulations with high swelling indices (OXCF-1, OXCF-3, and OXCF-5) are likely to release the drug more rapidly, which may not be suitable for controlled release applications (Table 4 and Figure 3). These insights can guide further formulation development to enhance efficiency and achieve the desired therapeutic outcomes.

Table 4. Swelling Index and yield percentage

Formulation code	Yield % (Adjusted)	Swelling index
OXCF-1	85.26±2.76	0.98±0.002
OXCF-2	92.30±3.21	0.23±0.001
OXCF-3	83.18±3.33	0.96±0.002
OXCF-4	84.29±3.63	0.24±0.001
OXCF-5	85.26±2.76	0.97±0.002
OXCF-6	92.30±3.21	0.22±0.001

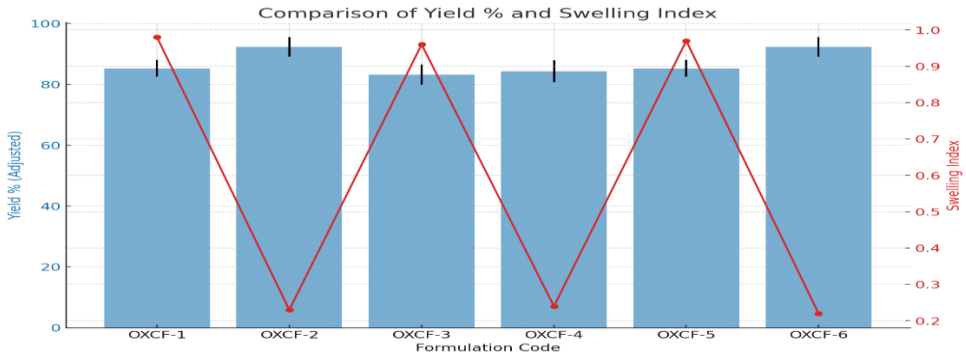

Figure 3. Depicting the comparison of Swelling Index and yield percentage

Mucoadhesive property

The data presented in Table 5 highlights the mucoadhesive properties of various formulations (OXCF-1 to OXCF-6) over a 10-hour period, showcasing the effectiveness of each formulation in adhering to mucosal surfaces. Mucoadhesion percentage is a critical parameter for formulations intended for prolonged mucosal contact, influencing the sustained release and

efficacy of the drug. The formulations exhibit varying degrees of mucoadhesion, ranging from 67.99% to 77%, with the precision of the measurements reflected in the standard deviation of ±1.13. Formulation OXCF-6 demonstrates the highest mucoadhesion at 77% ± 1.13, indicating its superior potential for applications requiring extended mucosal contact. Similarly, OXCF-2 shows a comparable performance with a mucoadhesion percentage of 76.67% ± 1.13. These formulations, with their higher adhesive properties, suggest a robust capability for enhancing drug residence time at the target site, which is crucial for improving therapeutic outcomes. In contrast, formulations OXCF-4 and OXCF-5 exhibit the lowest mucoadhesion values at 67.99% ± 1.13 and 69.82% ± 1.13, respectively. Despite being lower, these values still reflect a significant level of mucoadhesion, ensuring a degree of efficacy for applications where less prolonged adhesion is acceptable. The differences in mucoadhesion percentages among the formulations can be attributed to variations in their composition. Factors such as the type and concentration of mucoadhesive polymers, excipients, and the physical form of the formulation play a significant role in determining the adhesion capability. Understanding these differences is essential for optimizing formulations to achieve the desired level of mucoadhesion. The data underscores the importance of formulation components and their interactions in enhancing or limiting mucoadhesive properties (Table 5 and Figure 4).

Applications of formulations with high mucoadhesive properties are vast, including buccal, nasal, vaginal, and gastrointestinal drug delivery systems. These formulations can improve the residence time at the application site, enhance drug absorption, and ensure better therapeutic outcomes. Further research into the specific components and mechanisms contributing to the high mucoadhesive properties of OXCF-6 and OXCF-2 could provide insights for developing even more effective formulations. Additionally, assessing the in vivo performance of these formulations would be essential to confirm their practical applicability and effectiveness. In inference, the data on mucoadhesive properties of various formulations provides valuable insights for the development of efficient drug delivery systems. Formulations OXCF-6 and OXCF-2 emerge as the most effective, highlighting their potential for prolonged mucosal adhesion. Understanding and optimizing the factors contributing to mucoadhesion can lead to the development of superior formulations, ensuring improved therapeutic outcomes. Further research and optimization efforts can enhance the performance of less effective formulations, broadening the scope of their applications in pharmaceutical sciences.

Table 5. Mucoadhesive property

Formulation code	**% Mucoadhesion at 10 hour**
OXCF-1	71.89±1.13
OXCF-2	76.67±1.13
OXCF-3	70.45±1.13
OXCF-4	67.99±1.13
OXCF-5	69.82±1.13
OXCF-6	77±1.13

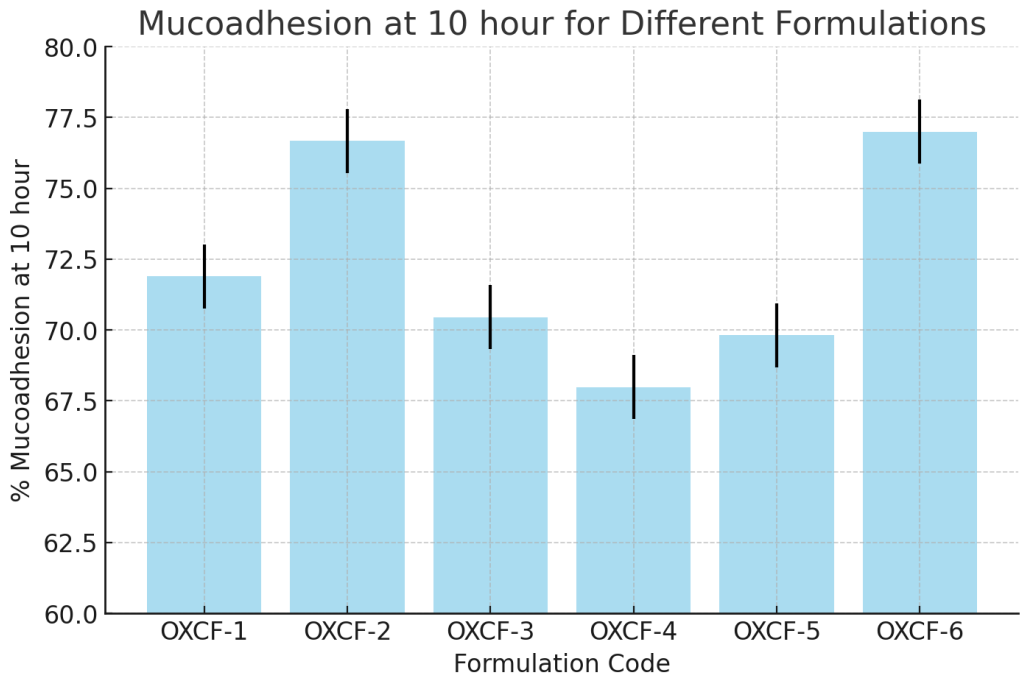

Figure 4. Percentage Mucoadhesion at 10 hours for different formulations

In vitro drug release

The data from Table 6 presents the results of an in vitro drug release study at pH 1.2 for various formulations (OXCF-1 to OXCF-6) over a 12-hour period (Table 6 and Figure 5). The study measures the percentage of drug released from each formulation at hourly intervals, providing insight into the efficiency and potential application of each formulation in drug delivery systems. In the initial phase (1-2 hours), OXCF-1 shows the highest release with 19.37% ± 0.42 at the 1-hour mark and 30.94% ± 0.54 at the 2-hour mark. This indicates a rapid release rate early on. In contrast, OXCF-6 has the lowest release initially, with 15.96% ± 0.31 at 1 hour and 26.21% ± 0.41 at 2 hours, suggesting a slower release rate. This trend continues into the midpoint of the study (3-6 hours), where OXCF-1 consistently maintains the highest release percentages, reaching 56.78% ± 0.81 by the 6-hour mark. Conversely, OXCF-6 continues to release the drug more slowly, showing 49.09% ± 0.67 at the 6-hour mark. In the later phase (7-12 hours), OXCF-1 reaches the highest cumulative release of 71.69% ± 1.01 at 9 hours and nearly completes the release at 12 hours with 98.80% ± 1.39. OXCF-2 follows closely with 77.57% ± 1.09 at 10 hours and 96.02% ± 1.35 at 12 hours. OXCF-6 shows a slower and more controlled release, achieving 92.55% ± 1.29 by the end of the 12-hour period, indicating its potential for applications requiring sustained drug release.

The varying release rates among the formulations are likely due to differences in their compositions, particularly the type and concentration of polymers and excipients used. These components play a significant role in influencing the drug release mechanisms, such as diffusion, erosion, or swelling. OXCF-1's rapid release profile suggests it is suitable for applications where immediate drug action is necessary, such as in acute treatment scenarios or pain relief. On the other hand, the slower, more controlled release profiles of OXCF-6 and OXCF-4 make them ideal for chronic conditions where sustained medication levels are required, enhancing patient compliance by reducing the frequency of dosing. For formulations needing quicker drug release, modifications such as adjusting polymer concentration or

incorporating more hydrophilic excipients could be explored. Conversely, to achieve a slower release rate, incorporating more hydrophobic polymers or altering the matrix structure could be beneficial. The study highlights the importance of understanding the release dynamics to design effective drug delivery systems tailored to specific therapeutic needs. In assumption, the in vitro drug release study at pH 1.2 provides valuable insights into the release profiles of various formulations. OXCF-1 exhibits the fastest release, suitable for immediate-release applications, while OXCF-6 and OXCF-4 demonstrate slower, controlled release profiles ideal for sustained-release applications. Understanding these dynamics is crucial for developing effective drug delivery systems, and further optimization can enhance the performance and applicability of these formulations

Table 6. Results of In vitro drug release study at pH 1.2

Formulation Code	**OXCF-1**	**OXCF-2**	**OXCF-3**	**OXCF-4**	**OXCF-5**	**OXCF-6**
1hr	19.37 ± 0.42	17.01 ± 0.37	15.97 ± 0.32	16.15 ± 0.29	16.71 ± 0.34	15.96 ± 0.31
2hr	30.94 ± 0.54	28.58 ± 0.47	27.60 ± 0.45	26.40 ± 0.39	26.96 ± 0.42	26.21 ± 0.41
3hr	35.69 ± 0.59	32.90 ± 0.52	31.30 ± 0.50	31.51 ± 0.49	32.07 ± 0.53	31.32 ± 0.48
4hr	38.79 ± 0.61	37.43 ± 0.57	37.07 ± 0.55	36.30 ± 0.53	36.86 ± 0.56	36.11 ± 0.51
5hr	48.11 ± 0.72	45.91 ± 0.66	40.48 ± 0.59	39.73 ± 0.58	40.29 ± 0.61	39.54 ± 0.57
6hr	56.78 ± 0.81	54.88 ± 0.77	52.95 ± 0.74	49.28 ± 0.68	49.84 ± 0.70	49.09 ± 0.67
7hr	61.67 ± 0.88	60.23 ± 0.84	59.95 ± 0.83	59.31 ± 0.81	59.87 ± 0.82	59.12 ± 0.79
8hr	66.25 ± 0.95	65.03 ± 0.93	65.08 ± 0.94	62.85 ± 0.89	63.41 ± 0.91	62.66 ± 0.88
9hr	71.69 ± 1.01	69.01 ± 0.98	68.20 ± 0.97	68.19 ± 0.96	68.75 ± 0.98	68.00 ± 0.95
10hr	79.36 ± 1.12	77.57 ± 1.09	74.53 ± 1.04	74.43 ± 1.03	74.99 ± 1.05	74.24 ± 1.02
11hr	87.80 ± 1.24	85.02 ± 1.20	83.65 ± 1.18	83.75 ± 1.19	84.31 ± 1.21	83.56 ± 1.17
12hr	98.80 ± 1.39	96.02 ± 1.35	94.19 ± 1.32	92.74 ± 1.30	93.30 ± 1.31	92.55 ± 1.29

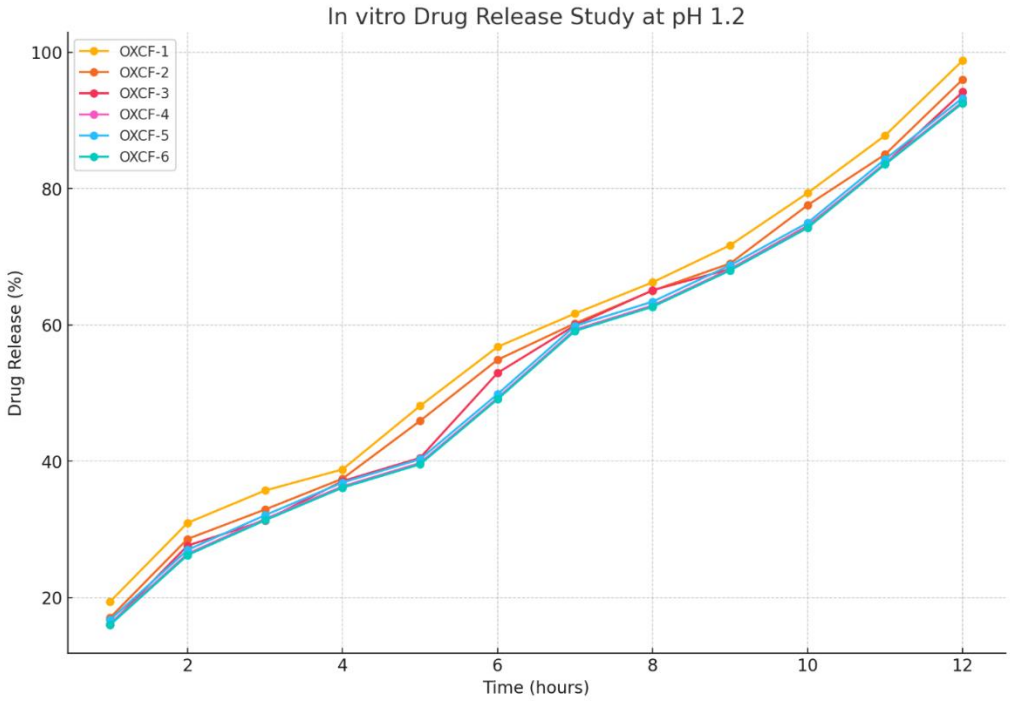

Figure 5. In vitro drug release at pH 1.2

Kinetic Modelling

The table below presents the results of fitting the in vitro drug release data for each formulation (OXCF-1 to OXCF-6) to various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. The parameters for each model, along with their respective R-squared values, are shown to indicate the goodness of fit. All formulations exhibited high R-squared values (~0.991-0.992) for the zero-order model, indicating a consistent and reliable fit. This suggests that these formulations generally follow zero-order kinetics, where the drug release rate is constant over time. This is desirable for achieving steady therapeutic levels.The first-order model showed slightly lower R-squared values (~0.922-0.935) compared to the zero-order model. This model, which assumes a concentration-dependent release rate, was less fitting for the formulations, suggesting that the drug release does not primarily follow first-order kinetics. The Higuchi model, which describes release as a function of the square root of time, had the lowest R-squared values (~0.895-0.915) among the models tested. This indicates that while diffusion may play a role, it is not the predominant release mechanism for these formulations. The Korsmeyer-Peppas model provided very good fits with high R-squared values (~0.981-0.986). The release exponent n values ranged from 0.71 to 0.79, indicating an anomalous transport mechanism (non-Fickian diffusion), suggesting a combination of diffusion and erosion processes (Table 7). Overall, the zero-order and Korsmeyer-Peppas models provide the best fits for the drug release data of these formulations. The zero-order model indicates a constant release rate, while the Korsmeyer-Peppas model suggests a complex release mechanism involving both diffusion and erosion. This information is valuable for optimizing and tailoring drug delivery systems to achieve desired release profiles.

Table 7. Kinetic modelling of the drug release data

Formulation	Zero-order R-squared	First-order R-squared	Higuchi R-squared	Korsmeyer-Peppas Parameters	Korsmeyer-Peppas R-squared
OXCF-1	0.991	0.930	0.922	kP: 15.77, n: 0.71	0.981
OXCF-2	0.992	0.935	0.915	kP: 14.36, n: 0.74	0.986
OXCF-3	0.990	0.929	0.902	kP: 13.29, n: 0.77	0.983
OXCF-4	0.992	0.922	0.896	kP: 12.62, n: 0.78	0.984
OXCF-5	0.992	0.923	0.900	kP: 13.01, n: 0.77	0.984
OXCF-6	0.992	0.922	0.895	kP: 12.49, n: 0.79	

CONCLUSIONS

This study demonstrated the successful formulation and characterization of oxcarbazepine loaded microsphere drug delivery systems. The results from the analysis of formulations OXCF-1 to OXCF-6 highlighted the importance of optimizing drug loading, encapsulation efficiency, particle morphology, and mucoadhesive properties to enhance therapeutic outcomes. Formulations OXCF-2 and OXCF-6 emerged as particularly effective, exhibiting optimal yield, controlled swelling, and superior mucoadhesion, making them ideal candidates for sustained and efficient drug delivery. Additionally, the in vitro drug release studies and kinetic modelling provided valuable insights into the release mechanisms, confirming the suitability of these formulations for applications requiring precise and controlled drug dosing. Future research should focus on in vivo studies to validate these findings and further refine the formulations for clinical applications. This integrated approach ensures the development of reliable and effective drug delivery systems, advancing the field of pharmaceutical mucoadhesive microsphere drug delivery systems.

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