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Research Article

# Acarbose-Loaded PLGA Microspheres: Efficient Encapsulation and Controlled Release

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## Abstract

Acarbose, a locally administered oral anti-diabetic agent, also experiences bioavailability and controlled release difficulties. To overcome such limitations, Acarbose-loaded microspheres were designed to ensure a higher therapeutic efficacy through controlled release of the drug and increased stability. Microspheres were prepared using the solvent evaporation process with different ratios of drug and polymer. The best drug release profile was selected, and optimization of the formulation was done further. Encapsulation efficiency, particle size, surface topography, and drug release rates were considered critical parameters to test. Characterization of the microspheres was conducted through Scanning Electron Microscopy (SEM), Differential Scanning Calorimetry (DSC), and Fourier Transform Infrared Spectroscopy (FTIR) to determine morphology, drug-polymer interaction, and physical state of Acarbose. Particle size distribution and zeta potential were also investigated to determine the stability of the formulation. The microspheres obtained using a 1:4 (Acarbose: PLGA) ratio showed high encapsulation efficiency (95.7%) and sustained release of drug for 24 hours. The optimized formulation showed smooth spherical morphology, particle size of 165.4 µm, and good flow properties. The zeta potential of the formulation showed excellent dispersion stability. The findings indicate that the 1:4 Acarbose: PLGA microspheres offer a promising drug delivery system with controlled release, improved stability, and good dispersion characteristics. These results underscore the possibility of enhancing the bioavailability and therapeutic activity of Acarbose, opening the door for additional in vivo investigations and clinical use.

**Keywords:** Acarbose, microspheres, solvent evaporation, PLGA, drug release, encapsulation efficiency, particle size distribution, zeta potential, SEM, DSC, FTIR, drug delivery system.

## INTRODUCTİON

Diabetes mellitus is a chronic metabolic disorder that affects millions globally, characterized by persistent hyperglycemia.[1,2] Acarbose, an alpha-glucosidase inhibitor, slows the digestion of carbohydrates in the intestine, thereby managing postprandial blood glucose levels.[3,4] However, its short biological half-life and limited bioavailability necessitate frequent administration, which can reduce patient compliance. Controlled-release drug delivery systems such as microspheres can overcome these challenges.[5,6] This study aims to formulate and evaluate Acarbose-loaded PLGA microspheres using solvent evaporation, optimizing formulation parameters, and characterizing the microspheres for improved drug release.

## MATERİAL, METHODS AND RESULTS

### Material

Acarbose, an antidiabetic agent, was procured as a gift sample from Octavius Pharmaceuticals, Gujarat, India. This drug was selected for its proven efficacy in managing Type II diabetes and its suitability for sustained-release formulations.The microsphere formulation utilized biodegradable and biocompatible polymers, including Poly(lactic-co-glycolic acid) (PLGA), Chitosan, and Ethylcellulose, all sourced from Sigma-Aldrich. Polyvinyl alcohol (PVA), also from Sigma-Aldrich, served as a stabilizer, maintaining emulsion stability during the solvent evaporation process. Dichloromethane (DCM), obtained from Sigma-Aldrich, was used as an organic solvent for polymer and drug dissolution. Ethanol, used for microsphere washing and purification, was procured from Fine Chemicals. Calcium chloride ($CaCl_2$) and Phosphate-buffered saline (PBS), essential for cross-linking studies and drug release evaluation, were supplied by Sisco Research Laboratories Pvt. Ltd. (SRL). Distilled water was used for all aqueous preparations, ensuring consistent purity and formulation integrity.

### Preparation Method

Microspheres containing Acarbose were successfully formulated using the solvent evaporation method, optimizing various parameters to achieve high encapsulation efficiency, controlled drug release, and stable morphology.[7–9] The drug-to-polymer ratio (1:1, 1:2, 1:3, 1:4, and 1:5) was varied to evaluate its impact on particle size, drug retention, and release behavior. The microspheres were smooth and spherical, confirming efficient emulsification and polymer solidification. Among all the prepared batches, the F4 (1:4 drug-to-polymer ratio) formulation was identified as the best based on its superior characteristics. This batch exhibited high encapsulation efficiency, smooth and spherical morphology, and a sustained drug release profile over 24 hours. The optimized formulation used 100 mg of Acarbose and 400 mg of PLGA, with 1% PVA as a stabilizer, maintaining stirring at 1200 rpm for 5 hours and incorporating a brief sonication step (Table 1).

**Table 1: Formulation table for Acarbose Microspheres**

| Batch Code | Drug : Polymer Ratio | Acarbose (mg) | PLGA (mg) | DCM (mL) | PVA Concentration (% w/v) | Aqueous Phase Volume (mL) | Stirring Speed (rpm) | Stirring Time (h) |
|---|---|---|---|---|---|---|---|---|
| F1 | 01:01 | 100 | 100 | 5 | 1% | 100 | 1200 | 5 |
| F2 | 01:02 | 100 | 200 | 5 | 1% | 100 | 1200 | 5 |
| F3 | 01:03 | 100 | 300 | 5 | 1% | 100 | 1200 | 5 |
| F4 | 01:04 | 100 | 400 | 5 | 1% | 100 | 1200 | 5 |
| F5 | 01:05 | 100 | 500 | 5 | 1% | 100 | 1200 | 5 |

## Yield of Microspheres

The percentage yield of Acarbose microspheres was calculated to assess the efficiency of the solvent evaporation method. The theoretical yield was determined by adding the initial weights of drug and polymer, while the practical yield was recorded after drying and recovering the microspheres. The yield increased progressively with polymer concentration, ranging from 72.5% (F1) to 91.8% (F5). This trend indicates improved microsphere formation and reduced material loss at higher polymer levels.(Table 2).

**Table 2: Percentage yield of Acarbose microspheres**

| Drug: Polymer Ratio | Drug (g) | Polymer (g) | Theoretical Yield (g) | Practical Yield (Acarbose) (g) | % Yield (Acarbose) |
|---|---|---|---|---|---|
| F1 | 1 | 1 | 2 | 1.45 | 72.50% |
| F2 | 1 | 2 | 3 | 2.21 | 73.70% |
| F3 | 1 | 3 | 4 | 3.1 | 77.50% |
| F4 | 1 | 4 | 5 | 4.41 | 88.30% |
| F5 | 1 | 5 | 6 | 5.51 | 91.80% |

The increase in yield with higher polymer ratios is attributed to more efficient encapsulation and reduced loss during processing. The F4 batch showed a high yield of 88.3%, confirming the reliability and reproducibility of the process. This batch provided the best balance of yield, formulation quality, and material efficiency, and was thus selected for further development.

## Evaluation of Microspheres

### *Physical Properties*

### Bulk Density and Tap Density

The bulk and tapped density measurements of Acarbose microspheres were carried out to evaluate their flow behavior and compressibility (Tables 3 and 4). [10] The bulk density was determined by loosely filling a pre-weighed 50 mL graduated cylinder with microspheres, while tapped density was obtained after tapping the cylinder 500 times. The bulk density of Acarbose microspheres decreased as the polymer concentration increased, suggesting that higher polymer amounts produced more porous and larger particles. The tapped density values were consistently higher than the corresponding bulk densities, indicating that tapping allowed better packing of microspheres. The difference between the two densities was more noticeable at higher polymer concentrations (F4 and F5), pointing to increased void spaces and reduced packing efficiency.

**Table 3: Observations for the Bulk Density**

| Batch Code | Mass of Acarbose Microspheres (g) | Bulk Density (Acarbose) ($g/cm^3$) | Bulk Volume (Acarbose) (mL) |
|---|---|---|---|
| F1 | 26 | 0.52 | **50** |
| F2 | 24 | 0.48 | **50** |
| F3 | 22.5 | 0.45 | **50** |
| F4 | 21 | 0.42 | **50** |
| F5 | 19.5 | 0.39 | **50** |

**Table 4: Observations for the Tap Density**

| Batch Code | Mass of Acarbose Microspheres (g) | Tapped Volume (Acarbose) (mL) | Tapped Density (Acarbose) ($g/cm^3$) |
|---|---|---|---|
| F1 | 26 | 44.8 | 0.58 |
| F2 | 24 | 43.7 | 0.55 |
| F3 | 22.5 | 42.9 | 0.52 |
| F4 | 21 | 42.5 | 0.49 |
| F5 | 19.5 | 41.2 | 0.47 |

### Carr's Index and Hausner's Ratio

Carr's Index and Hausner's Ratio as shown in Table 4 were calculated to further assess flow properties.[11] The Carr's Index for Acarbose microspheres ranged from 10.34% to 15.22%, indicating good to fair flowability. Hausner's Ratio values ranged from 1.11 to 1.18, consistent with moderate flowability. Higher polymer concentrations (especially F4 and F5) exhibited slightly poorer flow, attributed to larger, more porous microspheres with greater interparticle voids.

**Table 4: Observations of Carr's Index and Hausner's Ratio**

| Batch Code | Carr's Index (Acarbose) (%) | Hausner's Ratio (Acarbose) |
|---|---|---|
| F1 | 10.34 | 1.11 |
| F2 | 12.72 | 1.15 |
| F3 | 13.46 | 1.16 |
| F4 | 14.29 | 1.17 |
| F5 | 15.22 | 1.18 |

### Angle of Repose

Acarbose microspheres showed a clear trend of decreasing angle of repose with increasing polymer concentration, as shown in Table 5. [12] Microspheres with a 1:1 drug-to-polymer ratio had the highest angle of repose at 39.2°, indicating moderate flowability due to smaller particle size and higher cohesion. As the polymer concentration increased, the angle of repose progressively decreased, reaching 30.9° at the 1:5 ratio, suggesting improved flow behavior. This improvement can be attributed to larger microsphere size and smoother surfaces at higher polymer concentrations, which reduce inter-particle friction. From a formulation standpoint, microspheres from the F4 and F5 batches exhibit better flow properties, making them more appropriate for manufacturing processes like capsule filling and tableting.

**Table 5: Observations for the Angle of Repose**

| Batch Code | Height (Acarbose) (cm) | Base Radius (Acarbose) (cm) | Angle of Repose (Acarbose) (°) |
|---|---|---|---|
| F1 | 4.2 | 5.1 | 39.2° |
| F2 | 4 | 5.3 | 37.5° |
| F3 | 3.8 | 5.5 | 34.6° |
| F4 | 3.6 | 5.7 | 32.8° |
| F5 | 3.4 | 5.9 | 30.9° |

### Optimization of the Batch (Based on Flow Property)

The optimization of Acarbose microsphere batches was based on the evaluation of flow properties, including bulk density, tapped density, Carr's Index, Hausner's Ratio, and angle of repose. Bulk density and tapped density measurements showed a gradual decrease as the polymer concentration increased, indicating that higher polymer content produced microspheres with more interstitial spaces and lower packing efficiency. The Carr's Index values for Acarbose microspheres ranged between 10.34% and 15.22%, and Hausner's Ratio values were between 1.11 and 1.18. These findings suggest good to moderate flow characteristics across all batches. The angle of repose decreased from 39.2° in the F1 batch to 30.9° in the F5 batch, demonstrating better flow behavior with increasing polymer concentration. Although the F5 batch showed the lowest angle of repose (30.9°), it exhibited a relatively higher Carr's Index (15.22%), indicating slightly higher cohesiveness, which could interfere with process efficiency during capsule filling or tableting. The F3 batch showed moderate improvements but was not as balanced. The F 4 drug-to-polymer ratio batch demonstrated a Carr's Index of 14.29%, a Hausner's Ratio of 1.17, and an angle of repose of 32.8°, reflecting good flowability with acceptable compressibility and handling properties. Therefore, based on overall flow behavior, the F4 batch was selected as the optimized batch for further studies on encapsulation efficiency, drug release, and stability analysis.

### Morphological Studies (SEM Analysis)

The surface morphology of the optimized Acarbose microsphere formulation (1:4 polymer ratio) was examined using scanning electron microscopy (SEM), as depicted in Figure 01. The microspheres demonstrated a generally spherical shape with a moderately rough and porous surface. The presence of surface pores, varying in size and distribution, suggests the formation of a porous polymeric network during solvent evaporation. These pores, though clearly visible, were relatively uniform and did not compromise the structural integrity of the microspheres. Such porosity plays a crucial role in facilitating the controlled release of the drug, allowing for gradual diffusion while preventing rapid drug discharge or burst release. In comparison to lower polymer ratio formulations that may show irregular shapes and fragile morphology, the 1:4 batch achieved an optimal balance between robustness and porosity.

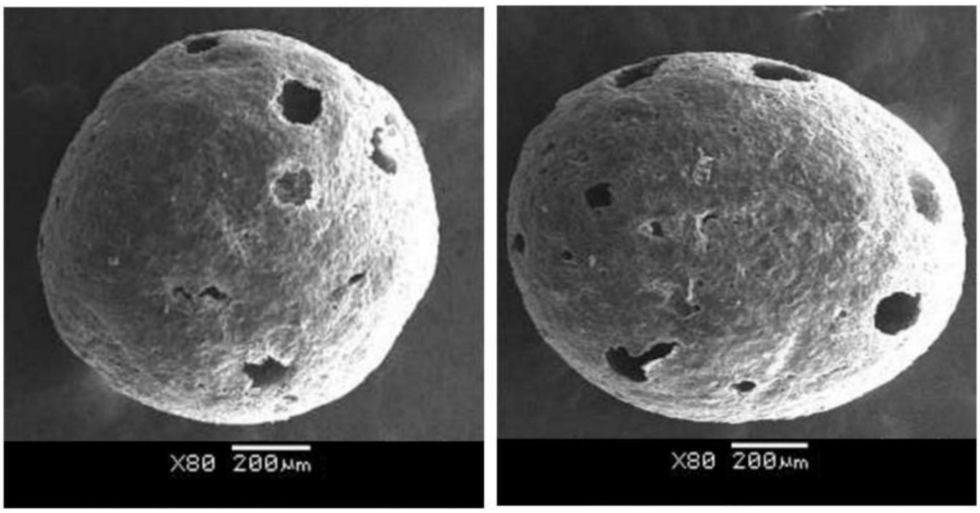


**Figure 1: Scanning Electron Microscopy (SEM) images of the Acarbose microsphere formulations at X80 magnification with a scale of 200 µm**

### Particle Size Analysis

The particle size distribution of Acarbose microspheres was analyzed using a laser diffraction particle size analyzer (Zetasizer Pro, Malvern Panalytical) as presented in Table 6.[13] Each formulation was dispersed in distilled water, followed by sonication to ensure a uniform suspension before analysis. The mean particle size increased with increasing polymer concentration, ranging from 120.5 µm in the F1 formulation to 180.3 µm in the F5 formulation. This trend suggests that higher polymer content resulted in thicker polymer coatings around the drug core. Polydispersity index (PDI) values for all Acarbose batches remained below 0.3, confirming a narrow and acceptable size distribution.

**Table 6: Particle size of Acarbose microspheres**

| Batch Code | Mean Particle Size (Acarbose) (µm) | PDI (Acarbose) |
|---|---|---|
| F1 | 120.5 | 0.21 |
| F2 | 135.2 | 0.23 |
| F3 | 150.8 | 0.25 |
| F4 | 165.4 | 0.27 |
| F5 | 180.3 | 0.3 |

The F 4 batch showed an ideal particle size of 165.4 µm with a moderate PDI of 0.27, indicating uniform particle distribution suitable for controlled drug release. The F5 batch had a slightly larger particle size but a higher PDI (0.30), suggesting increased variability. The smaller microspheres in the F1 and F2 batches may lead to faster drug release due to thinner polymer coatings. Thus, the F4 batch was selected as the optimized formulation for further studies.

### Zeta Potential Analysis

The zeta potential of Acarbose microspheres was measured using a Zetasizer Pro via electrophoretic light scattering (ELS) [14,15], as shown in Table 7. Microspheres were dispersed in distilled water, and measurements were conducted to assess colloidal stability. Zeta potential is a key parameter indicating the degree of electrostatic repulsion between particles. A more negative or positive value (typically beyond ±30 mV) reflects better dispersion stability. For Acarbose microspheres, the zeta potential values became increasingly negative with higher polymer concentrations.

**Table 7: Zeta Potential of Acarbose Microspheres**

| Batch Code | Zeta Potential (Acarbose) (mV) |
|---|---|
| F1 | -12.8 |
| F2 | -19.8 |
| F3 | -22.3 |
| F4 | -26.7 |
| F5 | -27.9 |

The F 1 and F 2 batches showed lower zeta potentials (−12.8 mV and −19.8 mV), suggesting reduced electrostatic stabilization and a greater chance of particle aggregation. The 1:3 batch marked an improvement (−22.3 mV), while the 1:4 formulation achieved a near-optimal zeta potential of −26.7 mV, indicating excellent colloidal stability. The F5 batch reached −27.9 mV, further enhancing stability but potentially affecting viscosity and flow behavior. Hence, the 1:4 drug-to-polymer batch was considered optimal for Acarbose microspheres, balancing good dispersion stability with practical handling properties for further development (Figure 2).

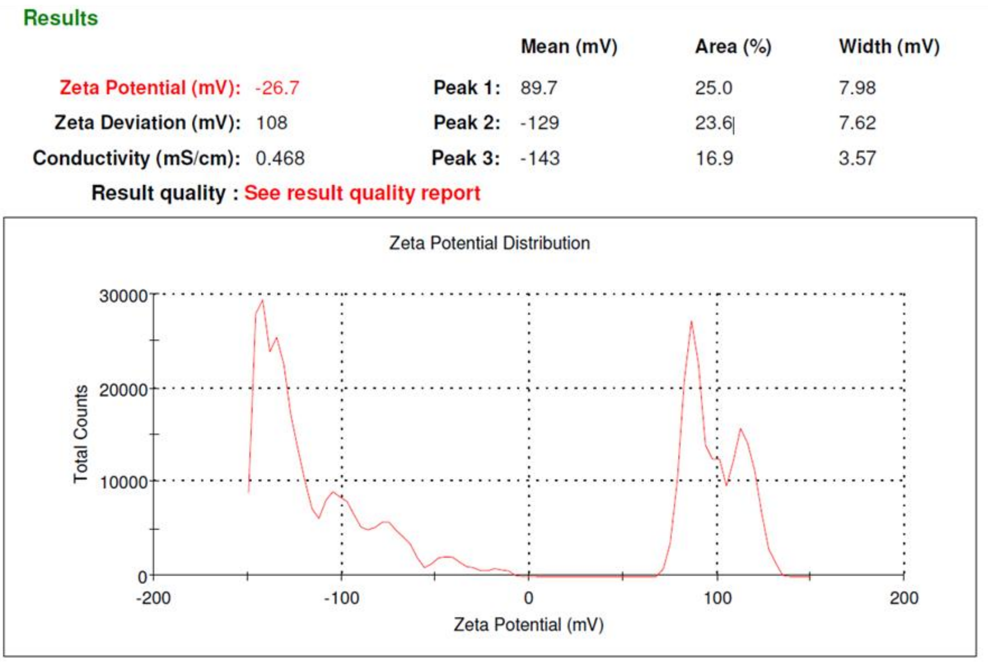


**Figure 2: Zeta Potential results of Acarbose microspheres formulation**

### Encapsulation Efficiency and Drug Content

The encapsulation efficiency (EE%) and drug content (DC%) of Acarbose microspheres were calculated across five drug-to-polymer ratios. [16,17] A 10 mg sample of each formulation was dissolved, and drug content was analyzed using UV spectrophotometry based on the calibration equation $y = 0.0599x + 0.003$. The actual amount of drug detected was compared with the theoretical loading to calculate EE% and DC%. As the polymer concentration increased from Batch F1 to F5, encapsulation efficiency improved due to better entrapment within the polymeric matrix. However, drug content (%) declined, reflecting reduced drug loading as a result of polymer dilution (Table 8).

**Table 8: Encapsulation Efficiency and Drug Content of Acarbose Microspheres Formulation**

| Batch Code | Theoretical EE (%) | Theoretical Drug Content for both Formulation (10 mg formulation) | Acarbose | | |
|---|---|---|---|---|---|
| | | | Actual Drug Content (mg) for 10 mg formulation | EE (%) | Drug Content (%) |
| F1 | 50 | 5 | 4.425 | 88.5 | 44.25 |
| F2 | 33.33 | 3.333 | 3.0096 | 90.3 | 30.0969 |
| F3 | 25 | 2.5 | 2.3 | 92 | 23 |
| F4 | 20 | 2 | 1.914 | 95.7 | 19.14 |
| F5 | 16.67 | 1.667 | 1.6203 | 97.2 | 16.203 |

The F4 batch achieved a high encapsulation efficiency of 95.7% with a drug content of 19.14%, representing the best balance between drug entrapment and loading. While the F5 batch showed slightly higher EE%, its drug content (16.20%) was relatively low. In contrast, the F1 batch had the highest drug load but lower EE%, indicating insufficient polymer coverage. Thus, the 1:4 formulation was selected as the optimized batch for Acarbose microspheres.

### DSC

The DSC thermogram of Acarbose-loaded microspheres exhibited distinct thermal transitions that reflect the physical state and successful incorporation of the drug within the microsphere matrix. A small endothermic peak was observed at approximately 70°C, which corresponds to the melting of the lipid or polymeric matrix material used for microsphere formulation. A broad endothermic transition was noted at approximately 160°C, which is significantly lower than the melting point of crystalline Acarbose (which normally melts above 200°C). This shift and broadening of the drug melting peak suggests that Acarbose is present in an amorphous or molecularly dispersed form within the microspheres. The absence of a sharp crystalline drug peak strongly indicates that the drug has lost its crystallinity during microsphere formation and is uniformly distributed within the matrix. Such a transition is desirable as the amorphous state generally enhances the solubility and bioavailability of the drug. At higher temperatures, a gradual endothermic event starting around 300°C was observed, which can be attributed to the thermal decomposition of the formulation. This peak indicates the onset of degradation of both the polymeric matrix and the drug at elevated temperatures, which is typical in thermogravimetric profiles of complex formulations. Overall, the thermogram confirms the successful entrapment of Acarbose within the microsphere system with transformation from crystalline to amorphous state, which is crucial for enhancing the drug release profile and stability. The absence of sharp crystalline peaks and the presence of broad transitions validate the effective encapsulation and dispersion of the drug (Figure 3)

### FTIR

The FTIR spectrum of Acarbose Microsphere Formulation reveals characteristic vibrational bands indicating successful drug encapsulation within the polymer matrix. A broad absorption band at 3740–3600 $cm^{-1}$ corresponds to O–H stretching vibrations, signifying hydrogen bonding. Bands at 2883 $cm^{-1}$ reflect C–H stretching of aliphatic chains, while a sharp peak at 1735 $cm^{-1}$ indicates ester carbonyl (C=O) stretching from the polymer matrix. The region of 1500–1000 $cm^{-1}$ shows C–O stretching, aromatic C=C, and N–H bending, confirming the integrity of Acarbose. Peaks at 1280–1140 $cm^{-1}$ denote glycosidic linkages, while those below 1000 $cm^{-1}$, including 954 $cm^{-1}$ and 721 $cm^{-1}$, correspond to C–H bending, indicating intact saccharide structures. The analysis confirms Acarbose's physical dispersion within the polymer without chemical modification, with evidence of hydrogen bonding interactions (Figure 4).

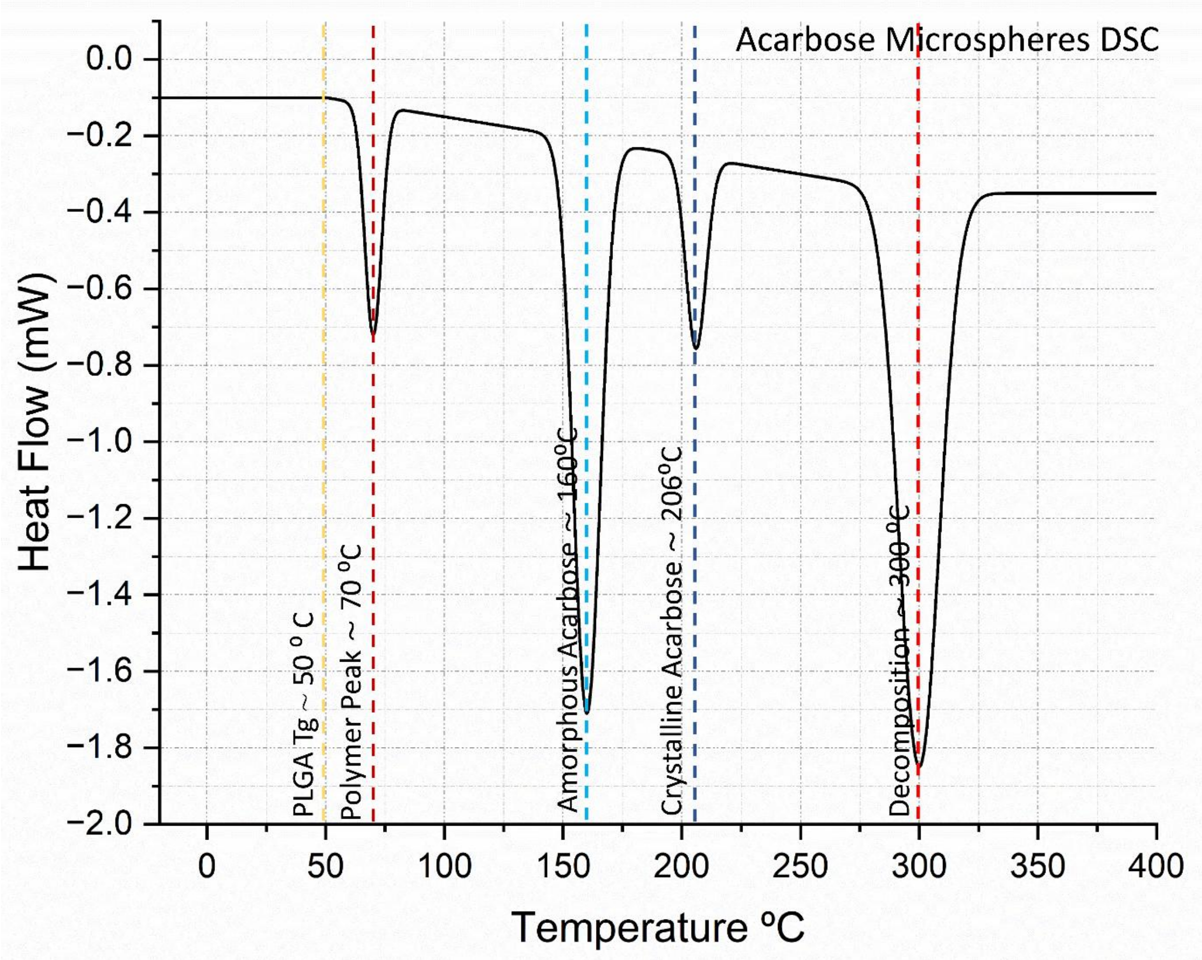


**Figure 3: DSC thermogram for Acarbose microspheres formulation**

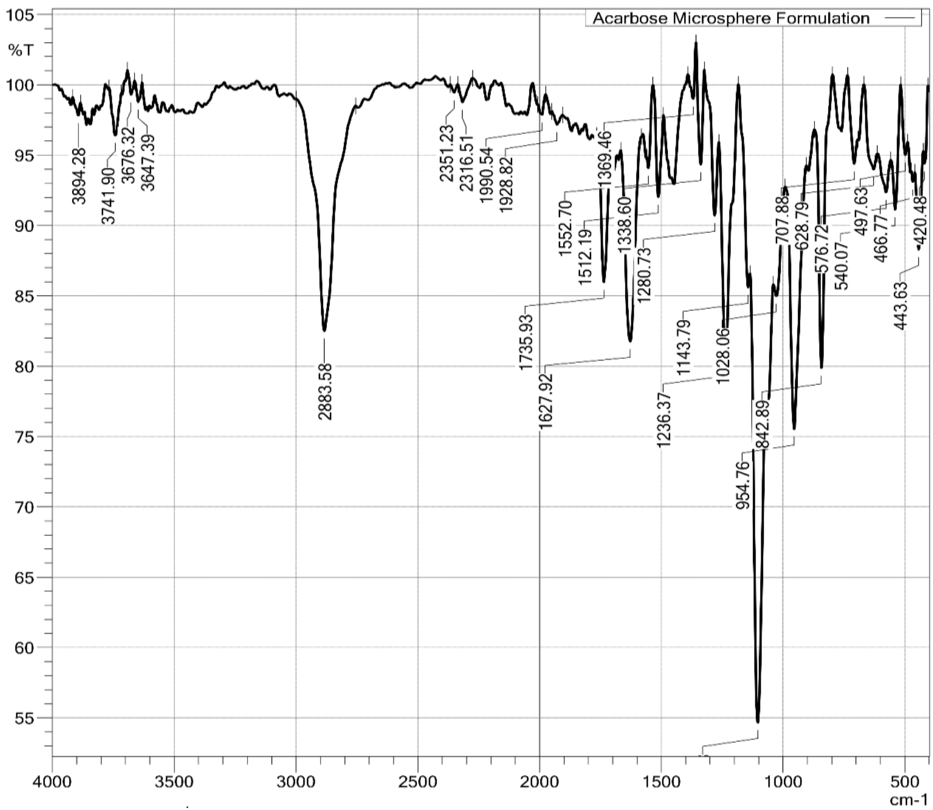


**Figure 4: FTIR spectra of Acarbose microspheres formulation**

**In Vitro Drug Release Studies**

***Drug release study of Acarbose microsphere***

The in vitro drug release study of Acarbose-loaded microsphere formulations was conducted over 24 hours to assess the sustained release potential across varying drug-to-polymer ratios. [18,19]The results, expressed as Mean ± SD, demonstrate a clear pattern correlating polymer concentration with drug release rate and extent. At the initial time point (0.5 h), all batches exhibited a controlled release of Acarbose, ranging from 11.6% (F1) to 17.9% (F4). This suggested minimal burst effect, with the F4 formulation showing a slightly higher early release, possibly due to better hydration and surface-associated drug release. By 1 h, release percentages increased gradually, with the F4 formulation reaching 28.8%, the highest among all, while F1 and F5 showed 20.6% and 24.5%, respectively. The sustained release trend became more prominent as the duration extended. At 4 h, the drug release for the F4 batch was 53.0%, significantly higher than 39.4% for F1 and 43.8% for F5. Notably, the F4 batch consistently exhibited higher release throughout all time points, indicating superior polymer matrix integrity and diffusion-facilitated drug transport. By 12 hours, the 1:4 formulation released 86.7%, closely followed by the 1:3 (75.3%) and 1:5 (72.8%) formulations. The F1 and F2 batches lagged, releasing 67.9% and 69.9%, respectively. Ultimately, at the 24-hour mark, the F4 batch achieved the highest cumulative release of 98.8%, demonstrating an almost complete release of the drug in a sustained manner. In contrast, the F1 and F5 batches released 75.7% and 82.8%, respectively. The data establishes the F4 polymer ratio as the most optimized batch in terms of controlled and extended drug release. The enhanced performance may be attributed to the optimal balance between polymer density and porosity, allowing for sustained hydration, drug diffusion, and erosion over time. The low standard deviation values across replicates reinforce the reproducibility and consistency of the formulation behavior (Table 9) (Figure 5).

**Table 9: In vitro cumulative % drug release of Acarbose microsphere formulations**

| Time (h) | F1 (Mean ± SD) | F2 (Mean ± SD) | F3 (Mean ± SD) | F4 (Mean ± SD) | F5 (Mean ± SD) |
|---|---|---|---|---|---|
| **0.5** | 11.6 ± 0.73 | 13.9± 0.71 | 17.1 ± 0.56 | 17.9 ± 0.60 | 14.6 ± 1.00 |
| **1** | 20.6 ± 0.46 | 24.8± 0.70 | 26.2 ± 0.07 | 28.8 ± 0.77 | 24.5 ± 0.66 |
| **2** | 29.9 ± 1.25 | 31.7 ± 0.31 | 35.7 ± 0.85 | 40.4 ± 0.55 | 34.2 ± 0.34 |
| **4** | 39.4 ± 0.63 | 42.7 ± 0.88 | 46.5 ± 0.67 | 53.0 ± 0.17 | 43.8 ± 0.84 |
| **6** | 48.8 ± 0.41 | 51.6 ± 0.46 | 54.8 ± 0.30 | 63.7 ± 0.18 | 53.3 ± 0.57 |
| **8** | 58.4 ± 1.39 | 61.1 ± 0.57 | 65.4 ± 0.64 | 75.5 ± 1.14 | 64.2 ± 1.77 |
| **12** | 67.9 ± 0.89 | 69.9 ± 1.05 | 75.3 ± 0.84 | 86.7 ± 0.30 | 72.8 ± 0.65 |
| **24** | 75.7 ± 0.77 | 79.2 ± 0.64 | 84.2 ± 0.05 | 98.8 ± 0.89 | 82.8 ± 0.48 |

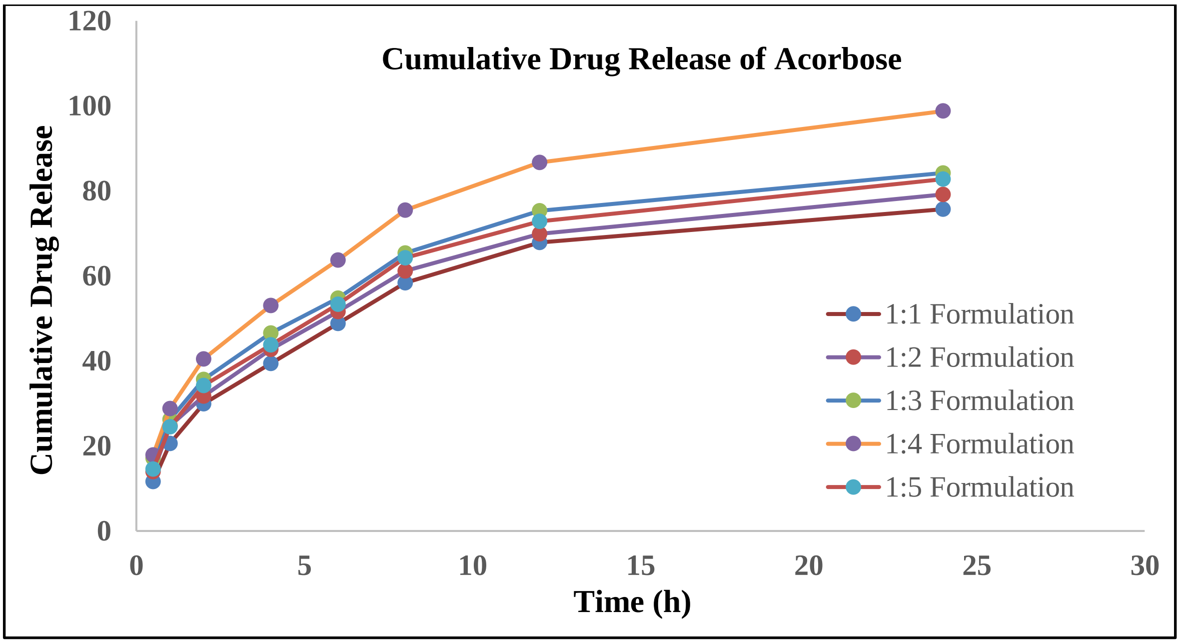


**Figure 5: Graphical representation of the Cumulative Drug Release of Acorbose**

The drug release behavior of Acarbose microsphere formulations was studied by fitting the in vitro cumulative release data to various kinetic models, including Zero-order, First-order, Higuchi, and Korsmeyer Peppas models, to determine the underlying release mechanism and model best describing the data.[20,21] Across all batches, the Zero-order kinetics showed very poor correlation ($R^2 < 0.1$), with even negative values for some batches (F2 to F5). This suggests that Acarbose did not follow a constant drug release rate over time, and zero-order kinetics is not suitable for describing the release behavior from these microspheres. On the other hand, the First-order kinetic model gave significantly better $R^2$ values, ranging from 0.821 to 0.944, with the highest value observed for batch F4 ($R^2$ = 0.944). This indicates that the release of Acarbose is likely concentration-dependent, where the rate of drug release decreases as the drug content within the microspheres is depleted over time. The Higuchi model also exhibited good fit for all batches ($R^2$ values between 0.880 and 0.916), suggesting that the drug release is primarily governed by diffusion through the polymer matrix. Batch F1 showed the best Higuchi fit ($R^2$ = 0.916), reinforcing the role of Fickian diffusion in the release process.

The Korsmeyer–Peppas model yielded the highest $R^2$ values for all formulations ($R^2$ = 0.959–0.971), indicating that this semi-empirical model best explains the drug release behavior. Moreover, the n values for all batches were found to be below 0.45 (ranging from 0.366 to 0.399), which falls within the range of the Fickian diffusion mechanism for spherical matrices. This further supports that the drug release from Acarbose-loaded microspheres is predominantly governed by a diffusion-controlled mechanism (Table 10).

**Table 10: Release order kinetics of Acarbose microsphere formulations**

| Formulation | Zero Order | First Order | Higuchi | Korsmeyer-Peppas | n value |
|---|---|---|---|---|---|
| F1 | 0.054 | 0.839 | 0.916 | 0.959 | 0.399 |
| F2 | -0.102 | 0.821 | 0.898 | 0.968 | 0.379 |
| F3 | -0.215 | 0.844 | 0.88 | 0.97 | 0.366 |
| F4 | -0.076 | 0.944 | 0.906 | 0.971 | 0.382 |
| F5 | -0.075 | 0.86 | 0.903 | 0.968 | 0.382 |

Notably, batch F4 exhibited the best overall fit to all models (especially First-order and Korsmeyer–Peppas), and showed an n value of 0.382, confirming Fickian diffusion as the primary release mechanism. These results, when combined with previous characterization data, reaffirm that the 1:4 drug-to-polymer ratio (Batch F4) is the most optimized formulation in terms of controlled and predictable release behavior.

**Stability Studies**

Stability studies for Acarbose microspheres were conducted for 6 months under two conditions: accelerated (40 ± 2°C / 75 ± 5% RH) and refrigerated (4 ± 2°C), as per ICH guidelines. Drug content was monitored to evaluate the chemical stability of the optimized formulation. Under accelerated storage, a slight but steady decline in drug content was observed, reducing from 98.8% at month 0 to 94.5% at month 6.[22-24]. This corresponds to a total loss of approximately 4.3%, which is within acceptable limits, indicating good short-term chemical stability. Under refrigerated storage, the formulation retained most of its drug content. Acarbose showed only a minor reduction from 98.8% to 98.3% over six months, confirming excellent stability at low temperatures (Table 11).

**Table 11: Drug Content of the Stability Studies of Acarbose Microspheres formulation**

| Time (Months) | Acarbose | |
|---|---|---|
| | Accelerated (%) | Refrigerated (%) |
| 0 | 98.8 | 98.8 |
| 1 | 97.6 | 98.7 |
| 3 | 96.3 | 98.5 |
| 6 | 94.5 | 98.3 |

The formulation remained chemically stable under both conditions. However, refrigerated storage significantly reduced the rate of degradation. The results indicate that while the microspheres are suitable for short-term ambient storage, refrigeration is preferable for long-term preservation.

## CONCLUSİON

Acarbose-loaded PLGA microspheres were effectively formulated with the solvent evaporation method and optimized some formulation parameters to result in high encapsulation efficiency and controlled release of the drug. The research revealed that higher concentration of the polymer enhanced yield, encapsulation efficiency, and stability of particles and that batch F4 (1:4 ratio of drug-to-polymer) was the most optimized form. This batch had higher encapsulation efficiency (95.7%) and controlled drug release profile for 24 hours and thus, is a good potential for sustained-release purposes. Morphological characteristics of the surface through SEM were found to be smooth and porous that enables slow drug release. The F4 batch also had good flow properties with moderate values for Carr's Index and Hausner's Ratio, which shows good handling for manufacturing processes. Zeta potential analysis reaffirmed good colloidal stability, and DSC and FTIR analysis confirmed the entrapped Acarbose within the microspheres to be in an amorphous state, which would increase the solubility and bioavailability. Overall, the use of Acarbose-loaded PLGA microspheres represents a potential approach to improve the limitations of traditional oral drug delivery systems, enhancing patient compliance and therapeutic efficacy in Type II diabetes management. Additional in vivo experiments are needed to verify the long-term safety and efficacy of this system.

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