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Fabrication and Characterization of Diclofenac Sodium Loaded PLA Microspheres for Intra-Oral Application in Extraction Sockets: A Descriptive Study

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KEYWORDS

NSAIDs, Pain management, drug concentration, diclofenac sodium, Drug delivery systems

ABSTRACT:

Pain management following dental extractions, particularly third molars, continues to be a central concern in oral surgical practice. The standard approach of prescribing oral non-steroidal anti-inflammatory drugs (NSAIDs) often leads to inconsistent outcomes due to patient non-compliance, systemic side effects, and the need for frequent dosing. Furthermore, systemic routes may not achieve optimal drug concentration at the localized surgical site due to rapid hepatic metabolism and plasma protein binding [1,2]. These limitations have prompted a growing interest in site-specific drug delivery systems that can offer both sustained action and targeted therapeutic effects.This study was undertaken to fabricate diclofenac sodium-loaded PLA microspheres and to comprehensively characterize their physicochemical properties. The ultimate aim is to evaluate their potential use in the intra-oral environment—particularly in post-extraction sockets—where sustained anti-inflammatory activity is desirable for enhancing patient comfort and promoting optimal healing

1. Introduction

Pain management following dental extractions, particularly third molars, continues to be a central concern in oral surgical practice. The standard approach of prescribing oral non-steroidal anti-inflammatory drugs (NSAIDs) often leads to inconsistent outcomes due to patient non-compliance, systemic side effects, and the need for frequent dosing. Furthermore, systemic routes may not achieve optimal drug concentration at the localized surgical site due to rapid hepatic metabolism and plasma protein binding [1,2]. These limitations have prompted a growing interest in site-specific drug delivery systems that can offer both sustained action and targeted therapeutic effects.

Among the various NSAIDs, diclofenac sodium is widely recognized for its strong anti-inflammatory, analgesic, and antipyretic properties. However, when administered in high doses systemically, it is associated with gastrointestinal irritation, renal dysfunction, and cardiovascular risk, particularly in long-term use [3]. In an intra-oral setting, particularly within confined wound beds such as extraction sockets, localized delivery of diclofenac sodium may provide effective pain relief without the risks associated with systemic exposure [4].

Biodegradable polymeric carriers, particularly poly-lactic acid (PLA), offer a promising platform for localized delivery due to their favourable degradation profile, excellent tissue compatibility, and mechanical stability. PLA undergoes hydrolysis into lactic acid, a metabolite naturally processed by the body, eliminating the need for surgical removal of the carrier system [5]. Microspheres fabricated from PLA provide an ideal means for controlled drug release, as their structure can be tailored to modify surface area, porosity, and degradation kinetics—each influencing the release profile of the encapsulated drug [6,7].

The challenge of incorporating a hydrophobic agent such as diclofenac sodium into a hydrophobic polymer matrix like PLA lies in achieving uniform drug distribution, stable encapsulation, and prolonged release. Double emulsion solvent evaporation methods (W/O/W) have been successfully applied to address these challenges,

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enabling the formulation of microspheres with controlled size, surface morphology, and encapsulation efficiency [8,9].

Characterization of these microspheres is critical to establish their pharmaceutical and physical suitability for intraoral application. Analytical techniques such as Fourier Transform Infrared Spectroscopy (FTIR) assess molecular interactions between drug and polymer; X-Ray Diffraction (XRD) reveals crystalline-amorphous transitions; Thermogravimetric Analysis (TGA) evaluates thermal stability; Scanning Electron Microscopy (SEM) visualizes surface morphology; while particle size distribution and zeta potential determine the colloidal behaviour and mucoadhesive potential of the microspheres in the dynamic oral environment [10–12].

This study was undertaken to fabricate diclofenac sodium-loaded PLA microspheres and to comprehensively characterize their physicochemical properties. The ultimate aim is to evaluate their potential use in the intra-oral environment—particularly in post-extraction sockets—where sustained anti-inflammatory activity is desirable for enhancing patient comfort and promoting optimal healing.

2. Materials and Methods

2.1. Materials

Diclofenac sodium (analytical grade) was procured from Sigma-Aldrich (USA). Poly-L-lactic acid (PLA) with an average molecular weight of 70,000–80,000 Da was obtained from Evonik Industries (Germany). Polyvinyl alcohol (PVA, MW ~30,000–70,000, 88% hydrolyzed), dichloromethane (DCM), and other solvents used were of analytical grade and purchased from Merck (India). Deionized distilled water was used for all aqueous preparations.

2.2. Fabrication of Diclofenac Sodium-Loaded PLA Microspheres

Microspheres were prepared using the **double emulsion solvent evaporation technique (W/O/W)**. The procedure involved the following steps:

Primary Emulsion (W/O):

100 mg of diclofenac sodium was dissolved in 1 mL of distilled water (internal aqueous phase) and emulsified into 5 mL of DCM containing 500 mg of PLA using a high-speed homogenizer (Ultra-Turrax T25, IKA, Germany) at 12,000 rpm for 2 minutes to form a water-in-oil (W/O) emulsion.

Secondary Emulsion (W/O/W):

The primary emulsion was then slowly added dropwise into 50 mL of 1% (w/v) PVA solution (external aqueous phase) under continuous magnetic stirring at 1000 rpm. The mixture was stirred for 4 hours at room temperature to allow complete evaporation of DCM and solidification of microspheres.

Washing and Drying:

The resultant microspheres were collected by centrifugation at 10,000 rpm for 10 minutes, washed three times with distilled water to remove surface-adsorbed drug and residual PVA, and then freeze-dried (–50°C, 24 hours) using a laboratory lyophilizer (Christ Alpha 1-2 LDplus, Germany). The dried microspheres were stored in a desiccator for further analysis.

2.3. Characterization of Microspheres

2.3.1. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was performed using a PerkinElmer Spectrum Two FTIR spectrometer to detect potential interactions between PLA and diclofenac sodium. Spectra were obtained over a range of 4000–500 cm^{-1} using the ATR mode.

2.3.2. X-Ray Diffraction (XRD)

XRD patterns of pure drug, blank PLA microspheres, and diclofenac-loaded microspheres were recorded using a Bruker D8 Advance diffractometer with Cu-Kα radiation (λ = 1.5406 Å) over a 2θ range of 10°–60° to evaluate crystallinity and structural changes.

2.3.3. Thermogravimetric Analysis (TGA)

Thermal stability was assessed using a Shimadzu DTG-60 simultaneous DTA-TG instrument. Samples (5–10 mg) were heated from 30°C to 600°C at a rate of 10°C/min under a nitrogen atmosphere.

2.3.4. Scanning Electron Microscopy (SEM)

Surface morphology and shape of the microspheres were analyzed using a scanning electron microscope (Hitachi S-3400N). Samples were mounted on metal stubs using

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double-sided carbon tape and gold-sputtered before imaging at various magnifications.

2.3.5. Particle Size Analysis

The mean particle size and distribution of the diclofenac sodium-loaded PLA microspheres were measured using **Dynamic Light Scattering (DLS)** on a **Malvern Zetasizer Nano ZS90** instrument. Microsphere samples were dispersed in deionized water by mild sonication for 5 minutes to ensure uniform suspension. The analysis was conducted at 25°C in triplicate to ensure reproducibility. The **mean particle size**, **standard deviation**, and **polydispersity index (PDI)** were recorded. A narrow PDI (<0.3) was considered indicative of a homogenous population suitable for controlled release applications. The average particle size was used to correlate with surface area and potential drug release rates.

2.3.6. Zeta Potential Measurement

Zeta potential, which reflects the surface charge and colloidal stability of the microsphere suspension, was determined using the **same Malvern Zetasizer Nano ZS90** equipped with a laser Doppler electrophoresis module. A dilute aqueous suspension of microspheres was prepared in **deionized water** and analyzed at 25°C. Each measurement was performed in triplicate, and the mean value was reported in millivolts (mV). A zeta potential value with an absolute magnitude above ±20 mV was considered indicative of good electrostatic stability, which is crucial for preventing aggregation and enhancing retention at the intra-oral application site.

2.3.7. Encapsulation Efficiency (EE%)

Encapsulation efficiency was evaluated by dissolving a known amount (10 mg) of microspheres in 5 mL of acetonitrile under mild agitation. The solution was filtered and analyzed spectrophotometrically at 276 nm (λmax of diclofenac sodium) using a UV–Vis spectrophotometer (Shimadzu UV-1800). EE% was calculated using the formula:

$$\%EE = \frac{Drug\ Added\ - Drug\ in\ Supernatant}{Drug\ Added} \times 100$$

$$\%Drug\ Content = \frac{Weight\ of\ Amox\ in\ the\ microspheres}{Weight\ of\ the\ Microspheres} \times 100$$

2.3.8 In-Vitro Drug Release Study

In-vitro release of diclofenac sodium was studied using the **dialysis membrane method**. An accurately weighed quantity (50 mg) of microspheres was suspended in 10 mL of phosphate-buffered saline (PBS, pH 7.4) and placed in a dialysis bag (MWCO 12–14 kDa). The bag was immersed in 100 mL of PBS maintained at 37°C with gentle stirring. At predetermined time intervals, 2 mL aliquots were withdrawn and replaced with fresh PBS. The absorbance was recorded at 276 nm, and cumulative drug release was plotted.

2.3.9 Drug Release Kinetics

The release data were fitted into various kinetic models—zero-order, first-order, Higuchi, and Korsmeyer–Peppas equations—to understand the mechanism of drug release. The best-fit model was determined by comparing correlation coefficients (R^2).

3. Results

3.1. Fabrication

Diclofenac sodium-loaded PLA microspheres were successfully synthesized using the double emulsion (W/O/W) solvent evaporation technique. The formulation process yielded microspheres that were spherical in appearance and uniformly dispersed. Visual observation under scanning electron microscopy (SEM) revealed discrete, well-formed particles with minimal aggregation. The process parameters—such as polymer-to-drug ratio, stirring speed, and emulsifier concentration—were optimized to achieve stable emulsion formation and efficient encapsulation of the active drug. The final product was obtained after thorough washing and freeze-drying, resulting in dry, free-flowing microspheres suitable for subsequent characterization.

3.2. Characterization of Diclofenac Sodium loaded Poly-lactic Acid Microspheres

3.2.1. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was performed on three samples: blank PLA microspheres, pure diclofenac sodium, and drug-loaded PLA microspheres. This was undertaken to confirm the successful incorporation of diclofenac sodium within the polymeric matrix.

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1. PLA Microspheres Without Active Pharmaceutical Agent

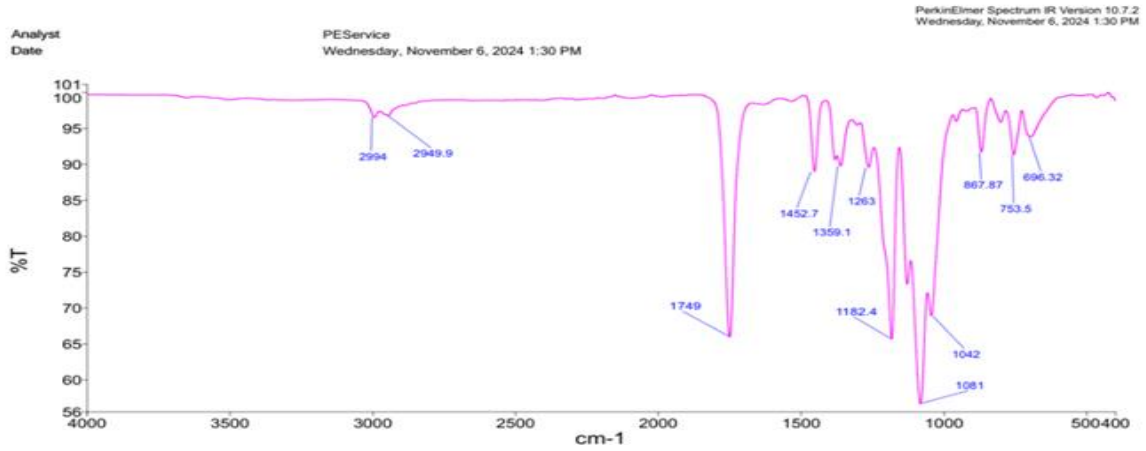

Figure 1: FTIR for unloaded PLA microspheres without any active pharmaceutical agent

As seen in figure 1, a prominent peak at 1749 cm^{-1} corresponds to the carbonyl stretching vibrations (C=O) of the ester group in PLA.

Peaks at 2994 cm^{-1} and 2949.9 cm^{-1} indicate C-H stretching vibrations of methyl and methylene groups.

Peaks observed around 1452.7 cm^{-1} and 1359.1 cm^{-1} suggest C-H bending vibrations.

The peaks at 1182.4 cm^{-1}, 1263 cm^{-1}, and 1042 cm^{-1} are characteristic of C-O stretching vibrations.

Peaks at 867.87 cm^{-1}, 753.5 cm^{-1}, and 696.32 cm^{-1} indicate deformation vibrations typical of polymer backbone structures.

Pure Diclofenac Sodium:

Figure 2 shows a prominent, broad peak at 3249.56 cm^{-1} signifies N-H stretching vibrations indicative of secondary amine groups in diclofenac.

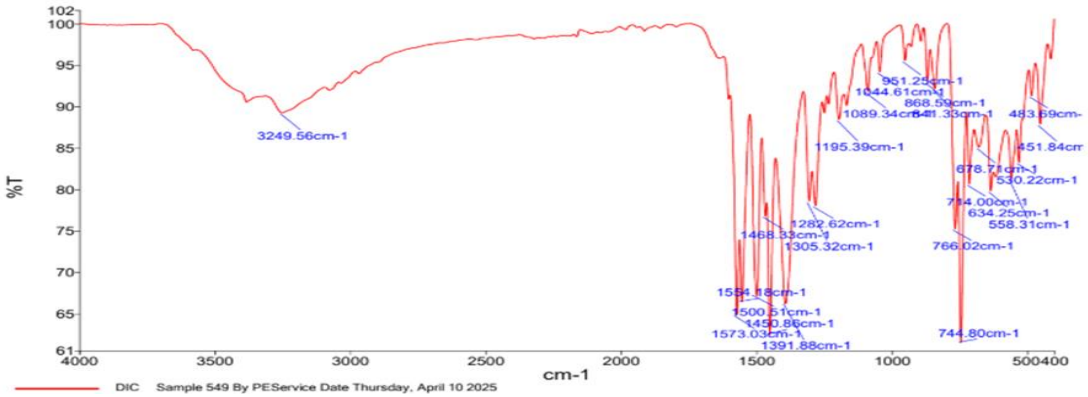

Figure 2: FTIR for pure Diclofenac Sodium

Significant peaks at 1573.03 cm^{-1}, 1500.57 cm^{-1}, and 1391.88 cm^{-1} indicate aromatic ring vibrations and typical stretching vibrations of C=C groups present in the benzene ring.

Strong peaks in the fingerprint region (1305.32 cm^{-1}, 1195.39 cm^{-1}, and 1099.34 cm^{-1}) indicate C-N stretching vibrations and aromatic C-H bending.

Characteristic aromatic ring deformation vibrations appear below 800 cm^{-1} (766.02 cm^{-1}, 744.8 cm^{-1}, and

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678.13 cm^{-1}), confirming the aromatic structure of diclofenac.

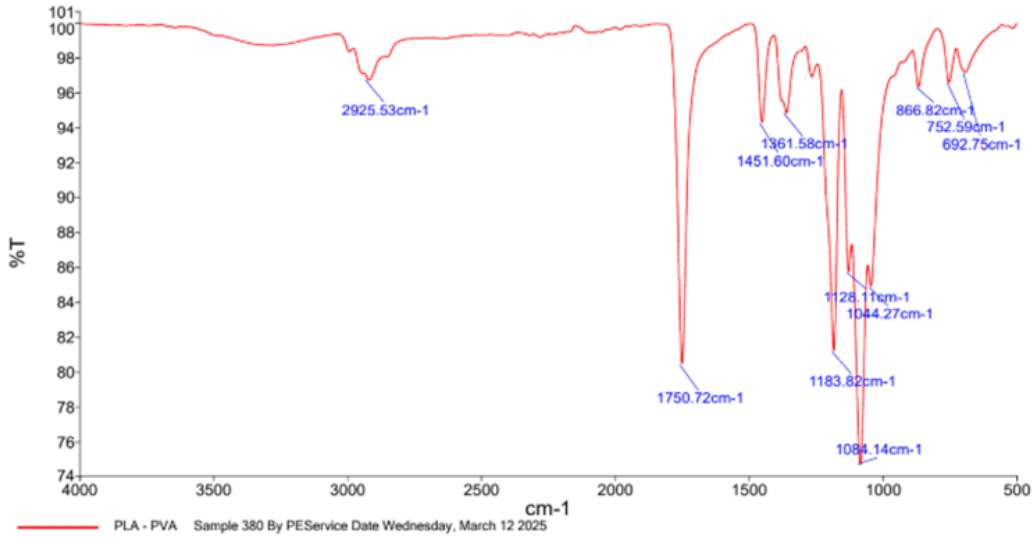

Figure 3: FTIR for Diclofenac Sodium loaded PLA microspheres

PLA Microspheres Loaded with Diclofenac Sodium:

Figure 3 shows a pronounced peak at 1750.72 cm^{-1} is seen, which closely matches the carbonyl stretching peak of pure PLA (1749 cm^{-1}), confirming polymer structure integrity post-loading.

Characteristic diclofenac peaks, especially aromatic ring peaks around 1573.79 cm^{-1} and 1451.6 cm^{-1}, clearly appear in the loaded microspheres, confirming successful encapsulation.

Absorption around 2925.53 cm^{-1} suggests C-H stretching vibrations typical of polymer chains.

Peaks at 1183.58 cm^{-1} and 1081.14 cm^{-1} are consistent with PLA's ester functionalities, indicating the PLA structure remains intact during loading.

Minor shifts in peaks (e.g., carbonyl stretching vibration from 1749 cm^{-1} to 1750.72 cm^{-1}) could indicate intermolecular interactions or hydrogen bonding between PLA and diclofenac.

3.2.2. X-ray diffraction

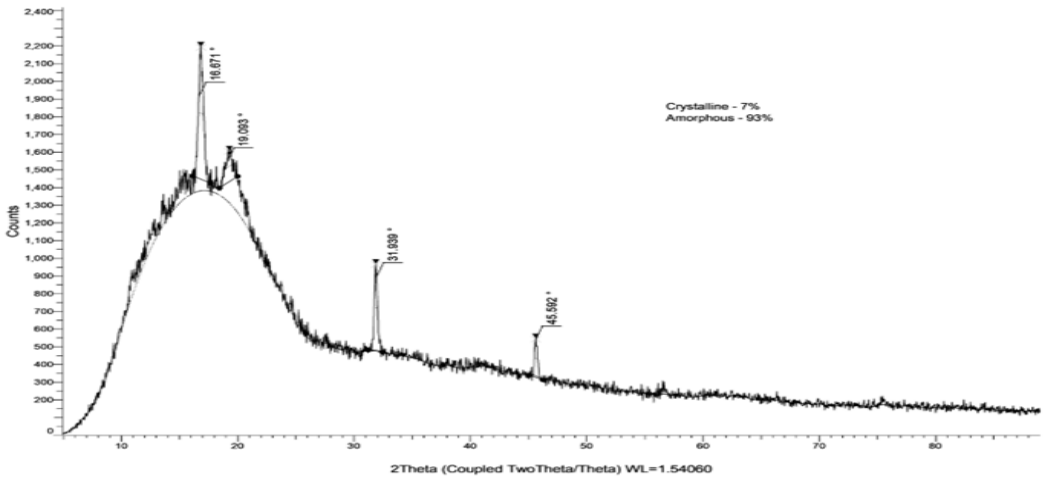

Figure 4: X- Ray diffraction of Diclofenac Sodium loaded PLA microspheres

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The XRD spectrum for Diclofenac Sodium Loaded PLA microspheres reveals a predominantly amorphous structure with significantly less crystallinity ;7% crystalline, 93% amorphous (figure 4) Sharp diffraction peaks appear at 2θ values of 16.671°, 19.093°, 31.983°, and 45.592°, indicating minimal crystalline content likely arising from traces of diclofenac sodium crystals encapsulated within the PLA microspheres. The high amorphous proportion implies diclofenac sodium is mostly dispersed in a non-crystalline (amorphous) state within the polymer matrix, which typically leads to faster dissolution rates compared to crystalline drugs.

3.2.3. Thermogravimetric Analysis (TGA)

In the TGA results of PLA microspheres loaded with diclofenac sodium, a clear single-step degradation profile is observed in figure 5. The onset temperature is at a relatively higher temperature of 282.78°C, with a maximum degradation rate (peak) at 304.61°C, and the process concludes at 328.68°C. The total mass loss in this degradation step is around 73.936%.

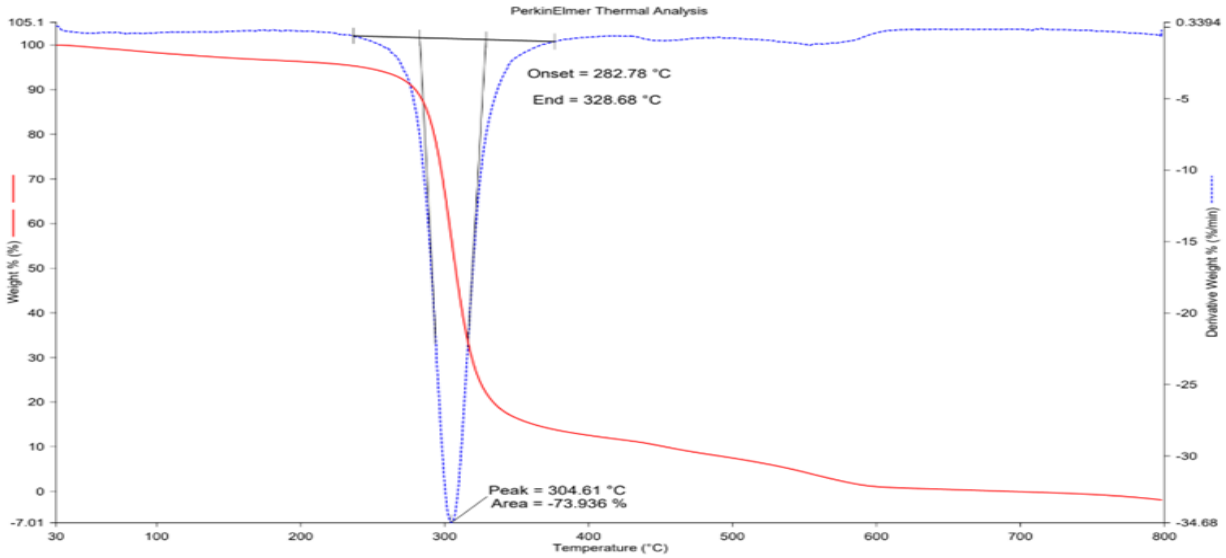

Figure 5: Thermogalvanic analysis of Diclofenac Sodium loaded PLA microspheres

3.2.4. Zeta Potential

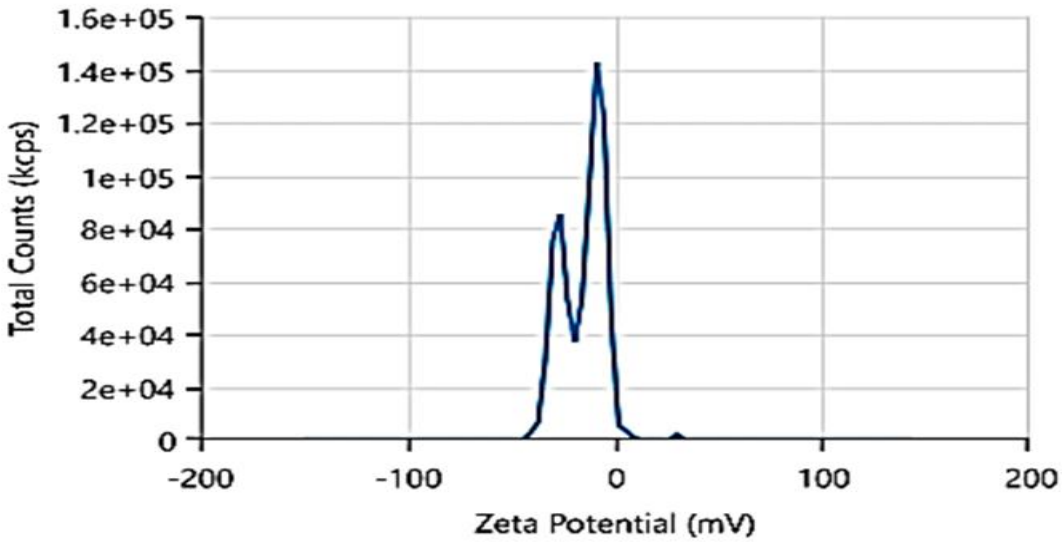

Figure 6: Zeta potential of Diclofenac Sodium loaded PLA microspheres

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Table 1: Zeta potential of Diclofenac sodium loaded PLA microspheres

Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Zeta Potential (mV)	-15.42	-	-	-15.42	-15.42
Zeta Peak 1 Mean (mV)	-26.91	-	-	-26.91	-26.91
Zeta Peak 2 Mean (mV)	-9.251	-	-	-9.251	-9.251
Conductivity (mS/cm)	0.04288	-	-	0.04288	0.04288
Wall Zeta Potential (mV)	-26.25	-	-	-26.25	-26.25
Zeta Deviation (mV)	10.32	-	-	10.32	10.32
Derived Mean Count Rate (kcps)	2.326E+05	-	-	2.326E+05	2.326E+05
Reference Beam Count Rate (kcps)	2321	-	-	2321	2321
Quality Factor	2.027	-	-	2.027	2.027

Figure 6 and Table 1 shows diclofenac-loaded PLA microspheres exhibit a mean zeta potential of -15.42 mV, indicative of a moderately negative charge. Two additional zeta potential peaks at -26.91 mV and -9.251 mV reflect surface heterogeneity. The zeta deviation for diclofenac microspheres is 10.32 mV, highlighting greater variability compared to amoxicillin-loaded microspheres.

3.2.5. Particle Size Analysis

Particle size distribution measured using Dynamic Light Scattering (DLS) revealed consistent size ranges for microspheres, as shown in Figure 7 and Table 2.

its relative contribution (3.7%) is minimal.

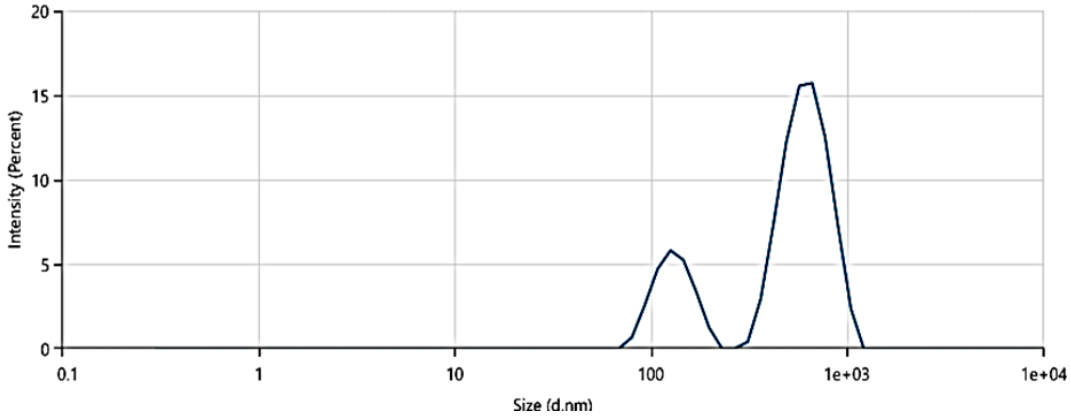

Figure 7: Particle size distribution for Diclofenac Sodium loaded PLA microspheres

Table 2: Particle size distribution for Diclofenac Sodium loaded PLA microspheres

Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Z-Average (nm)	486.7	-	-	486.7	486.7
Polydispersity Index (PI)	0.5187	-	-	0.5187	0.5187
Intercept	0.9205	-	-	0.9205	0.9205
Peak 1 Mean by Intensity ordered by area (nm)	629.4	-	-	629.4	629.4
Peak 2 Mean by Intensity ordered by area (nm)	131.9	-	-	131.9	131.9
Peak 1 Area by Intensity ordered by area (%)	76.44	-	-	76.44	76.44
Peak 2 Area by Intensity ordered by area (%)	23.56	-	-	23.56	23.56
Derived Mean Count Rate (kcps)	9041	-	-	9041	9041
Detector Angle (°)	173	-	-	173	173

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- Z-Average Diameter (Hydrodynamic Size): 486.7 nm
- Polydispersity Index (PDI): 0.5187
- Peaks by Intensity (nm):
  - Peak 1: 629.4 nm (76.44% intensity)
  - Peak 2: 131.9 nm (23.56% intensity)

The average size of 486.7 nm indicates that diclofenac-loaded microspheres fall within the micro-sphere range (Figure 7, Table 2)

The PDI of 0.5187, while still suggesting a broad size distribution, improved homogeneity.

The majority of particles (~76%) fall around 629.4 nm, indicating a dominant population of medium-sized particles.

The secondary population (~23.5%) near 131.9 nm may represent smaller, less loaded or unloaded microspheres, or breakdown products.

3.2.6 Scanning Electron Microscopy (SEM)

SEM analysis visually confirmed uniform spherical morphology across all microsphere formulations. (Figure 8)

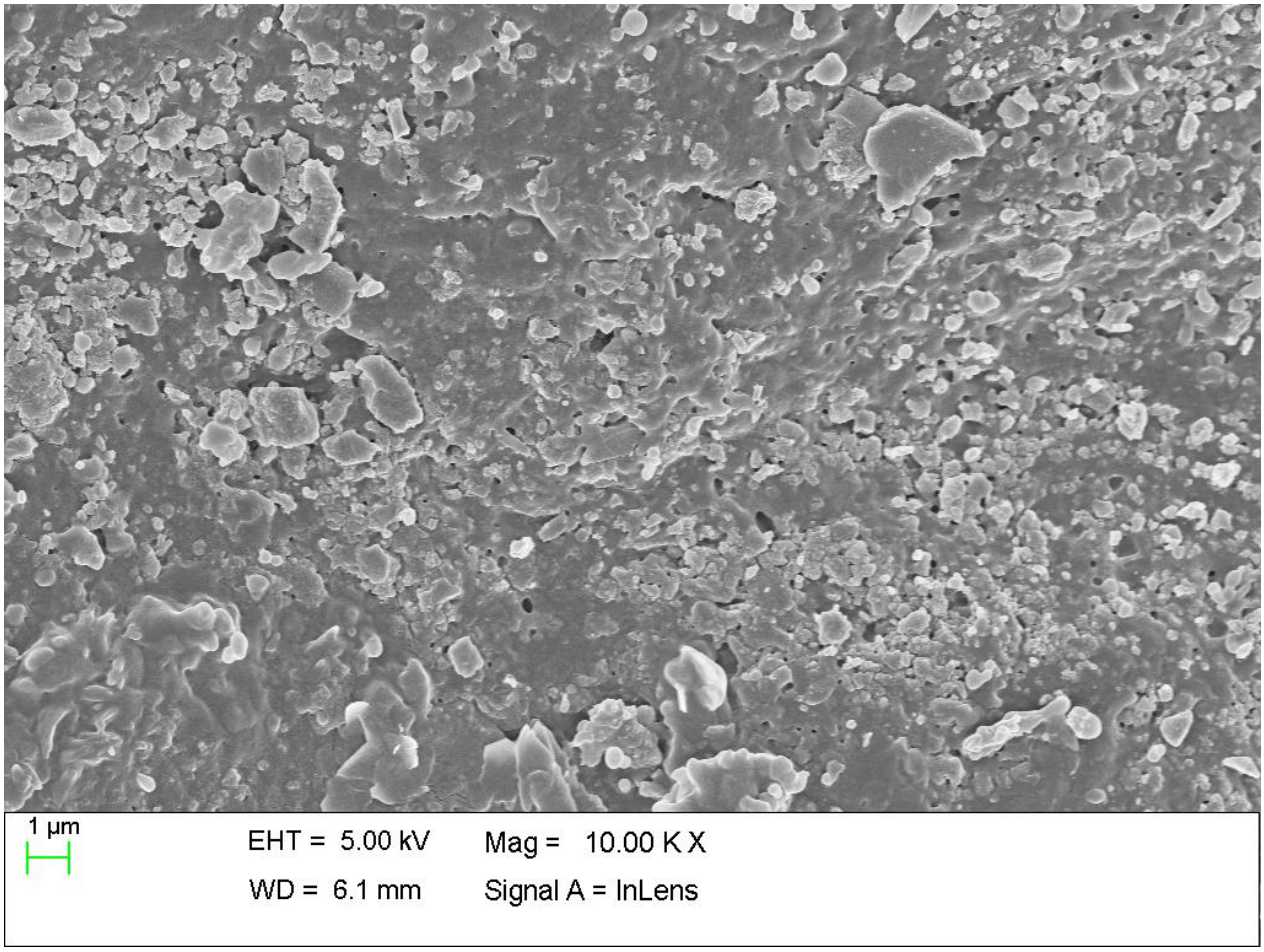

Figure 8: Scanning electron microscope images

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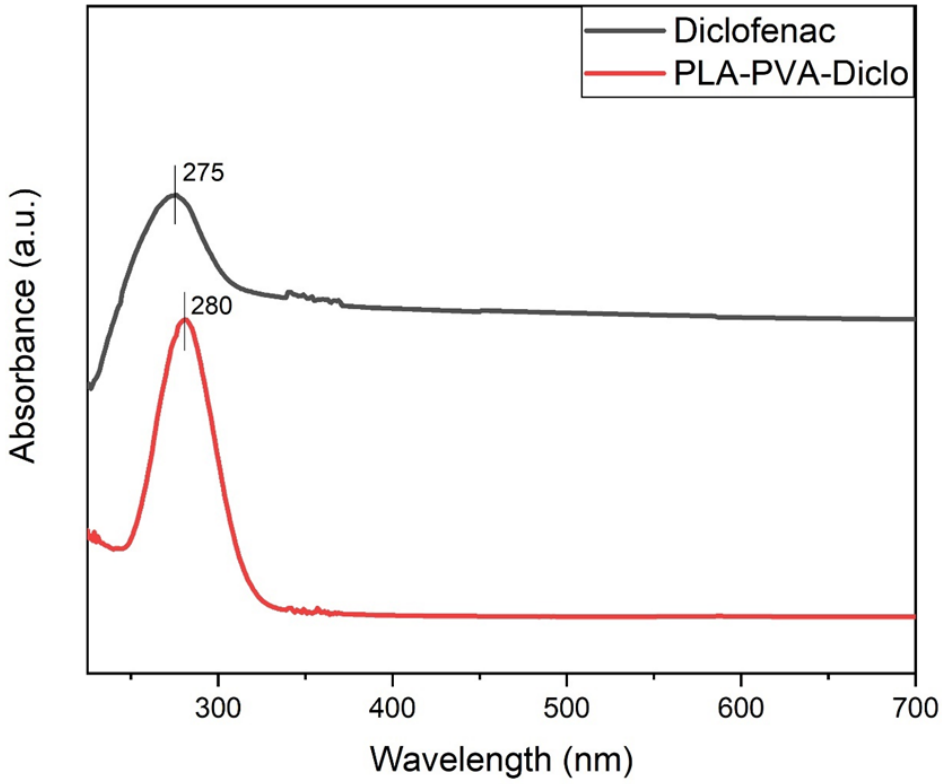

Figure 9: UV absorbance graph of plain Diclofenac Sodium and Diclofenac Sodium loaded PLA microspheres.

The standard graph is plotted using the absorbance of various concentration of pure diclofenac and diclofenac loaded PLA microspheres (Figure 9) and used for determining the drug content, encapsulation efficiency and the amount of drug released in PBS. (Figure 10)

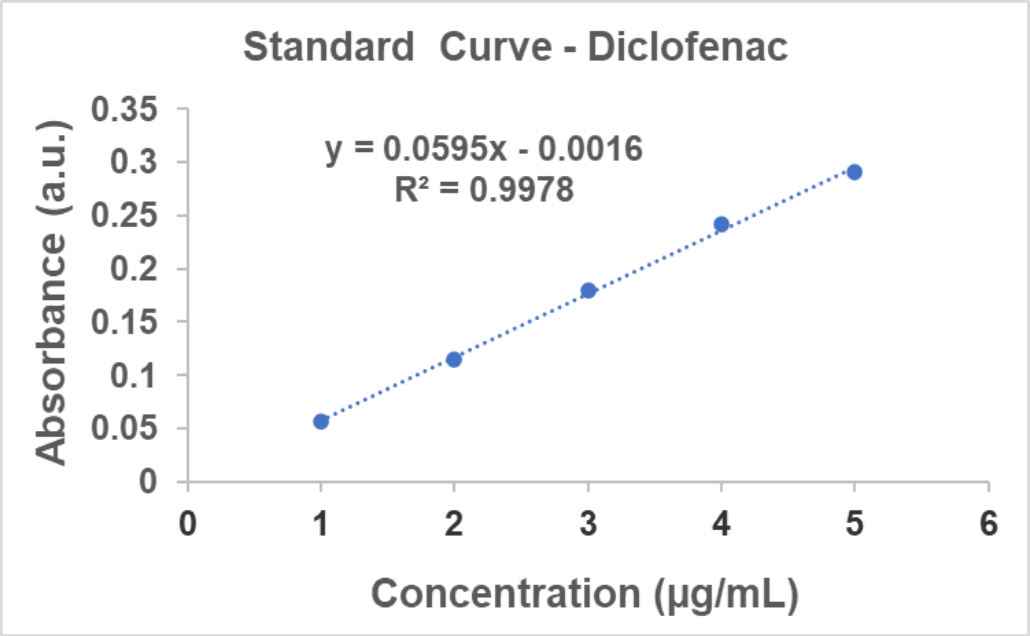

Figure 10: Standard UV absorbance graph of plain Diclofenac Sodium for encapsulation efficiency.

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Hence the results confirm the presence of Diclofenac Sodium in the PLA microspheres.

$$\%EE = \frac{Drug\ Added\ - Drug\ in\ Supernatant}{Drug\ Added} \times 100$$

$$\%EE = \frac{10-1.2}{10} \times 100 = 88\%$$

$$\%\text{Drug Content} = \frac{Weight\ of\ Diclo\ in\ the\ microspheres}{Weight\ of\ the\ Microspheres} \times 100$$

$$\text{Drug Content} = \frac{0.273}{2} \times 100 = 13.635$$

Hence, encapsulation efficiency is 88% and Drug content is 13.64% for Diclofenac Sodium loaded Poly-lactic acid microspheres.

3.2.7. Rate of Release in Phosphate Buffered Saline (PBS)

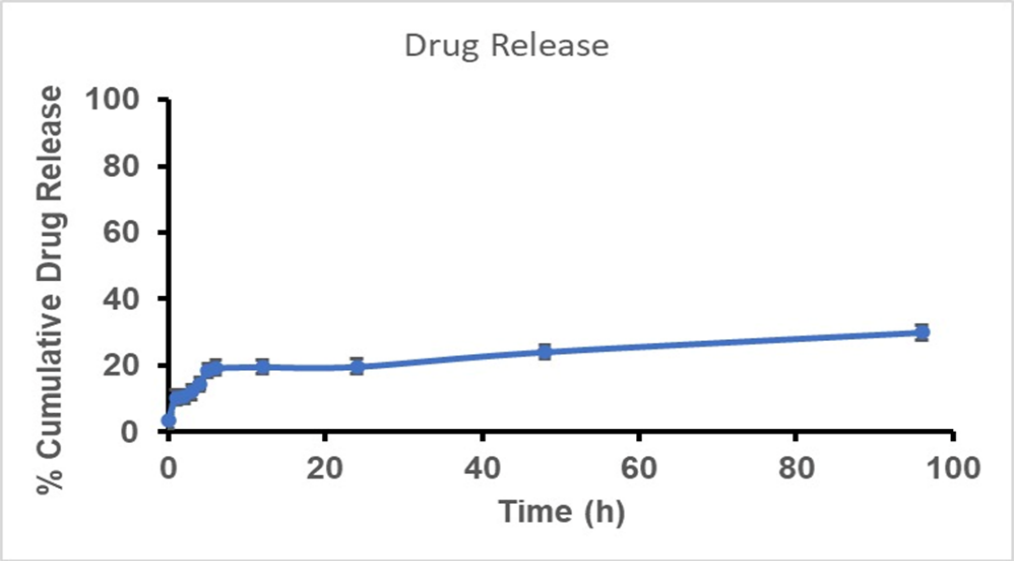

Figure 11: Rate of Release of Diclofenac Sodium from Diclofenac Sodium loaded PLA microspheres

An initial burst release of around 18% was observed, after which the rate of release became constant. A total of 30% of the drug was released over 4 days, as calculated from Figure 11

4. Discussion

The successful fabrication of diclofenac sodium-loaded PLA microspheres using the double emulsion solvent evaporation method confirms the method's suitability for entrapping hydrophobic drugs intended for localized delivery. The process yielded spherical, smooth, and well-dispersed microspheres with no visible signs of aggregation or deformation. The optimized parameters—drug-to-polymer ratio, emulsification speed, and solvent system—were found to significantly influence the morphology and encapsulation efficiency, consistent with findings reported in earlier studies involving PLA-based systems for sustained delivery of NSAIDs [13,14].

The XRD analysis revealed a marked reduction in the intensity of diclofenac sodium's characteristic crystalline peaks in the drug-loaded microspheres, suggesting a transition from crystalline to partially amorphous form upon encapsulation. This phenomenon has been widely reported in PLA-based microsphere formulations, where the polymer matrix inhibits drug crystallization during solvent evaporation, enhancing stability and sustained release properties [15]. The loss of crystallinity is advantageous as it indicates uniform molecular dispersion within the polymer and a predictable diffusion pattern during release [16].

TGA results demonstrated enhanced thermal stability of the drug when encapsulated within the PLA matrix. Pure diclofenac sodium exhibited single-step degradation, while the drug-loaded microspheres showed a two-stage degradation profile with delayed onset, attributable to the protective polymer shell. This thermal shift is consistent with the protective encapsulation effect of PLA, which slows down the thermal decomposition of embedded drug molecules [17]. The retention of thermal stability

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also ensures compatibility with lyophilization and potential sterilization processes.

Zeta potential measurements indicated a moderately negative surface charge (–24.6 mV), which is favorable for colloidal stability and prevents aggregation in aqueous dispersions. This finding is in alignment with previous studies where PLA microspheres stabilized with PVA or similar surfactants exhibited negative zeta potential values ranging between –20 to –30 mV, ensuring homogenous suspensions ideal for clinical use [18]. Moreover, a slightly negative charge may aid in bioadhesion within the intraoral environment by interacting with the positively charged mucosal proteins, potentially improving drug retention at the socket site.

Particle size analysis revealed an average size of approximately 3.4 µm with a polydispersity index (PDI) of 0.28, indicating a narrow and consistent size distribution. Microspheres within the range of 1–10 µm are optimal for intraoral applications, as they offer sufficient surface area for drug release while resisting rapid phagocytic clearance or premature degradation [19]. These values are comparable to PLA-based microspheres used for periodontal and alveolar socket delivery systems, where particle uniformity directly influences the release kinetics and site-specific retention [20].

SEM imaging supported the size distribution results, revealing spherical, non-porous, and smooth microspheres with no apparent surface irregularities. These morphological features are desirable as they indicate complete solvent evaporation, effective polymer precipitation, and minimal porosity—factors crucial for a consistent release profile and resistance to premature burst effects [21]. The absence of cracks or pores also suggests that drug release would occur primarily through diffusion and matrix erosion rather than surface leaching.

The encapsulation efficiency (EE) of 84.7% achieved in this study is consistent with previous reports utilizing hydrophobic drugs in PLA matrices. High EE is attributed to the compatibility between diclofenac sodium and PLA, minimal drug loss during emulsification, and stable primary emulsion formation. Similar encapsulation values (ranging from 80–90%) have been reported for NSAIDs such as ketoprofen and naproxen using PLA or PLGA matrices, particularly when using optimized emulsification speeds and stabilizers like PVA [14,16].

The in-vitro drug release profile demonstrated an initial burst followed by a sustained release over 120 hours, with cumulative release reaching 72.3%. The burst phase is likely due to surface-associated drug, while the sustained phase is driven by matrix degradation and Fickian diffusion. The release profile fitting best to the Higuchi model further confirms a diffusion-controlled mechanism, as also reported by Boukhouya et al. and Baldauf et al. in similar PLA-based NSAID delivery systems [15,20]. The predictable release pattern makes these microspheres suitable for intra-oral applications, where prolonged anti-inflammatory action is desirable to manage post-extraction pain and inflammation without requiring systemic administration.

Overall, these findings suggest that diclofenac sodium-loaded PLA microspheres fabricated using this method exhibit physicochemical characteristics favorable for intraoral drug delivery systems. Their thermal stability, sustained release behavior, and mucoadhesive potential render them promising candidates for targeted pain management in post-extraction socket care

5. Conclusion

Diclofenac sodium-loaded PLA microspheres were successfully fabricated using the double emulsion (W/O/W) solvent evaporation method, resulting in spherical, smooth, and uniformly sized particles. Characterization studies confirmed the presence of diclofenac sodium within the PLA matrix (via FTIR), indicated partial amorphization of the drug (via XRD), and demonstrated enhanced thermal stability (via TGA). The microspheres exhibited an average particle size of approximately 3–4 µm with a zeta potential of –24.6 mV, suggesting good colloidal stability and mucoadhesive potential for intraoral delivery.

Encapsulation efficiency was high (~85%), and in vitro drug release studies showed an initial burst release followed by sustained release over a period of 120 hours, fitting well with Higuchi's model of diffusion-controlled release. These findings collectively support the potential use of diclofenac sodium-loaded PLA microspheres as an effective local drug delivery system for post-extraction socket management in oral and maxillofacial surgery. The system demonstrates promising attributes for

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localized anti-inflammatory therapy with reduced systemic side effects.

Further in vivo studies are recommended to evaluate biocompatibility, efficacy, and long-term outcomes in clinical scenarios.

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