Original Article

Synthesis, Characterization and Comparison of Novel Poly (sebacic anhydride) Biopolymeric Implants and Microspheres for the Controlled Release of an Anticancer Drug

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ABSTRACT

Aim: The purpose of this study was to investigate the comparative drug release kinetics of implants and microspheres of an anticancer drug loaded onto a bio-degradable polymer. **Methods:** Poly (sebacic anhydride) was synthesized using a melt-polycondensation reaction, and its physicochemical properties were determined using gel permeation chromatography, nuclear magnetic resonance, differential scanning calorimetry, and Fourier transform infrared techniques. The polymer was used to encapsulate drugs via the melt moulding technique for implants and the solvent evaporation technique for microspheres. **Results:** *In-vitro* degradation of implants showed a 95% degradation rate in 6 days with the disappearance of the anhydride peak due to polymer hydrolysis. The microspheres of size 63 ± 3 μm were found to be spherical and porous in optical microscopy images. *In-vitro* drug release from implants (85 ± 3.5%) and microspheres (88 ± 4.5%) in pH 7.4 revealed similar sustained drug release following Higuchi kinetics. **Conclusion:** There was no significant difference observed in drug release patterns from implants and microspheres with the same quantity of polymer. Therefore, poly (sebacic anhydride) could become a successful candidate for controlling the release of a drug over a long period of time.

Key words: Implants, Microspheres, Drug delivery, Sustained release, Biodegradation.

INTRODUCTION

Drug delivery systems are commonly used to increase the pharmacological and therapeutic properties of drugs by modifying their pharmacokinetics. Among them, microspheres and implants could be used to monitor the amount of medication released over weeks or months.[1,2] Polymers may be natural, synthetic, or semi-synthetic in nature, which modulate drug release and allow for managed degradation.[3,4] Bio-degradable polymers were used to ensure that the end release of drug coincided with the end of polymer erosion.[5,6] Polyanhydrides are the most extensively studied biodegradable polymers,[7] with excellent biocompatibility and controlled release properties[8-12] and are widely used as a vehicle for anticancer drug delivery.[13] It has a reactive functional group available for passive hydrolysis[14] that degrades quickly in an aqueous environment.[15] They are simple to plan and manipulate to meet desired characteristics using readily available, low-cost technology.[15] These are surface eroding polymers,[16] which improve drug stability by reducing water contact with the drug prior to release. Poly-anhydrides have excellent controlled release properties[14] as a result of the hydrophobic backbone and the hydrolytically labile anhydride couplings[17] and do not display any signs of inflammation.[18] The exponential decline in

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the molecular weight (Mw) of polymers is frequently seen during the breakdown of poly-anhydride matrices.[3] Poly (sebacic anhydride) (PSA) is an aliphatic polyanhydride made up of sebacic acid monomer units (a dicarboxylic acid)[19-21] slightly soluble in water, but it's freely soluble in other organic solvents. Its molecular weight (Mw) can reach up to 137 kD depending on the length of time it takes to polymerize. Drug delivery systems prepared with this polymer will show a sustained drug release over weeks.

Bio-degradable polymeric microspheres for drug delivery have been extensively researched for the past 25 years[22] to customize release profiles with increased effectiveness, decreased toxicity and patient compliance.[23] The morphology, encapsulation effectiveness, and *in-vitro* release profile are all well-known.[24] To create bio-degradable microspheres various methods such as solvent evaporation[25] or solvent extraction method,[26] spray drying method[27] and using fluids under supercritical conditions without harmful residual solvents[28] can be used. Numerous approaches were made using PSA microspheres to deliver drugs like nifedipine[10] and p-nitroaniline.[4]

Bio-degradable polymeric implants are designed to deliver medication to the body in a consistent and regulated manner.[29] Implants are surgically put into the body cavity to retain them and deliver drugs.[30] Various methods are employed in preparing implants, e.g. melt molding, extrusion molding, and syringe extrusion. Various evaluation techniques are used to characterize implants e.g. surface morphology, surface area, weight, *in-vitro* dissolution rate,[31] drug loading capacity[32] etc. PSA implants have been used in a variety of ways to deliver drugs such as tamoxifen citrate[33] paclitaxel,[34] doxorubicin,[35] gentamycin,[36] salicylic acid.[37]

Olaparib is indicated for ovarian, breast, pancreatic, and prostate cancer due to its high Poly (ADP-ribose) polymerase (PARP) inhibition[38] which plays an important function in single-strand deoxyribonucleic acid (DNA) break repair.[39] PARP inhibition causes cell death in cancers with genetic proclivity to repair damaged DNA[40] and improved outcomes in clinical trials for breast cancer, primarily those caused by gene mutations, which occur in 15% of patients.[41] Olaparib is available on the market as Lynparza® tablets, 300 mg given orally twice daily with or without food. It is a BCS class IV drug[42] that undergoes extensive CYP3A4 mediated hepatic metabolism[43] to produce primary metabolites such as monohydroxy metabolite (Mw 450) and a ring opening product (Mw 452)[44] resulting in poor oral bioavailability[45] with a half-life of 11.9 h[46] and being linked to severe anaemia and fatigue, myelodysplastic syndrome, acute myeloid leukemia and pneumonitis.[47,48] When it comes to oral medication, solubility, permeability, stability, and metabolism are all critical properties of the molecule that should be considered positive anti-cancer effects.[49] When the benefits of drug development are unfavourable, precise formulation tactics can be used to achieve maximum therapeutic progress.[49] Olaparib has been delivered in a different dosage forms, including lipospheres,[50] liposomes[51] and hydrogels.[52] In this study, we report a novel Olaparib bio-degradable PSA implant and microsphere *in-vitro* release comparison over a number of days, which could become a treatment approach for patients with breast cancer.

MATERIALS AND METHODS

Materials

Sebacic acid was obtained from Sebacic India Limited (Gujarat, India). Olaparib was supplied by MSN laboratories limited (Hyderabad, India). All the solvents were of analytical reagent grade and procured from SD Fine-Chem Ltd. (Hyderabad, India).

Methods

Polymer synthesis

Poly(Sebacic anhydride) was produced via melt condensation, utilizing sebacic acid as a monomer.[10,53-55] Sebacic acid (5 g recrystallized) has been combined with acetic anhydride (50 mL) and then agitated (40°C for 20 min) until a clear solution is formed. Following dehydration and acetylation of the diacid groups of sebacic acid monomer, excess acetic anhydride was removed by raising the temperature to 70–120°C under vacuum. The sebacic anhydride precursor polymerization was done at 150°C with continuous stirring for 2 hr. The concluding PSA was diluted in chloroform and recrystallized by means of an excess of ethyl ether and petroleum ether. The resulting suspension was centrifuged, dried and vacuum-sealed at 20°C under vacuum (Figure 1A). The obtained polymer's chemical identity was evaluated with suitable instruments to confirm its successful production.

Characterization of PSA

Characterization of the synthesized copolymer was done using different techniques.[56] The copolymers' number average molecular weight (Mn), weight average molecular weight (Mw), and polydispersity index (Mw/Mn) were measured using gel permeation chromatography (GPC) (Shimadzu, Nexera C190-E092D) linked to a refractive index detector (RID-20A) using LabSolutionsTM software with Shim-pack GPC-805C

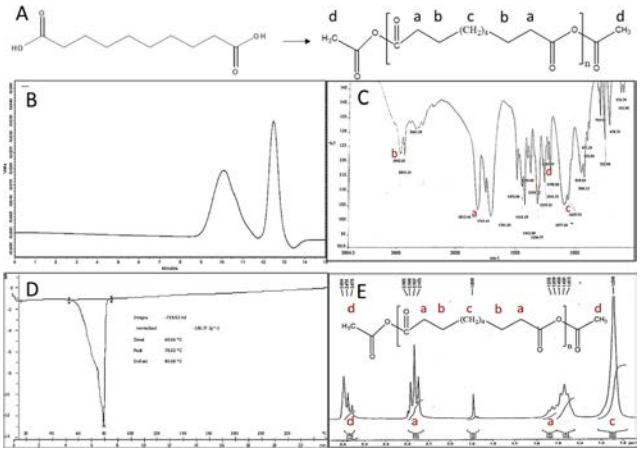

Figure 1: A. PSA polymer synthesis from sebacic acid monomer B. PSA GPC chromatogram with a single symmetrical unimodal peak, Mn as 1211 Da, Mw as 1283 Da, and Mw/Mn as 1.05 C. Typical FTIR spectrum of PSA showing a) carbonyl group of anhydride b) C-H stretch of CH_3 c) bending vibration of CH_2 group of unconjugated anhydride d) stretching vibration of the C-O group of -COOR D. DSC spectra of polysebacic anhydride show melting range of 78.65°C to 80.68°C E. NMR spectra of PSA showing the molecular weight of the polymer Mn = 1.23 kDa

column at 30°C. The polymer was mixed in HPLC grade chloroform and filtered through a 0.45 µm filter of the cellulose nitrate type to make standards of polystyrene and samples (1 mg/2 mL). The sample was injected into GPC maintained at a flow rate of 1 mL/min using a Hamilton syringe and calibration curves were created using polystyrene standards to determine the molecular weight parameters. The Fourier transform infrared spectroscopy (FTIR) (Nicolet MAGNA-IR 560, Bio-Rad, US) spectrum was captured by mixing the polymer sample with KBr to form a pellet, which was then tested in the IR region (4000-400 cm^{-1}). Differential scanning calorimetry (DSC) (Model-204F1, Netzsch, Germany) thermogram values ranged from 25°C to 200°C were recorded at 10°C/min with a second scan in an inert environment. Thermal history wipe was achieved by doing rescans after each scan. Nuclear magnetic resonance spectroscopy (^{1}H NMR, Bruker 400 Ultrashied™) was used to analyze the synthesized polymer by dissolving it in $CDCl_3$ and the spectrum as chemical shift (δ) was recorded using tetramethylsilane as an internal standard. The polymer was analyzed in the range of 0 to 10 ppm and calculations for number average molecular weight were done based on the integral area under the peak.

Analytical Method development for drug

Previous publications on the development of a quantitative analytical approach for Olaparib have been slightly modified. Stock solution (1 mg/mL) containing medication was produced by dissolving it in acetonitrile. A series of standard solutions with concentrations ranging from 1 to 30 µg/mL were prepared and analyzed using RP-HPLC (Waters, USA) on a C_{18} column (Inertsil® ODS-3 V, 250 × 4.6 mm, 5 µm particle size) at 50°C. The mobile phase was made up of ACN (100%) and 10 mM ammonium formate in a 50:50 v/v ratio. The samples were evaluated using an isocratic method, at 1.2 mL/min flow rate, and injected 10 µL at 210 nm, using an optical spectrum detection system.

Preparation of implants

The implants have been prepared under sterile conditions using a melt-molding technique.[5] Briefly, PSA (85%, 680 mg) and drug (15%, 120 mg) were thoroughly blended and melted at about 80°C using a hot plate (Polymix-Px-Mst-2, Kinematica) to obtain a homogenous mixture of molten polymer. This uniform mixture was then poured into molds with a capacity of 180 mg each. The molds were covered in aluminum foil and kept in the refrigerator for about 2 hr. After a period of 2 hr, the implants were removed from the molds. Similarly, the blank implants were prepared without the drug.

Determination of drug content in the implants

The drug content was assessed by selecting ten implants. Each implant was ground with the help of a mortar and pestle using a phosphate buffer solution (PBS pH 7.4). The residue was subsequently dissolved in an ultrasonic water bath for 20 min. The suspension was then centrifuged for 10 min at 12,000 rpm. The HPLC was then used to analyze an aliquot of the supernatant (20 µL). The actual drug content was then determined for each implant.

In-vitro hydrolytic degradation of implants

For degradation studies of implants, 6 vials were taken with 20 mL of buffer solution (pH 7.4) and each implant, previously weighed, was placed in a vial and kept in a shaker bath at 37°C. Implants were removed from each vial at specific time intervals of 0 h, 12 hr, 1 day, 2 days, 4 days, and 6 days. The samples were dried for 24 hr at 40°C in a vacuum oven set at 700 mm Hg. Then the samples are analyzed by the FTIR technique.

$$\text{Erosion rate (\%)} = \frac{\text{Initial weight of PSA discs (Wo)} - \text{Weight of PSA discs after deg radation (W)}}{\text{Initial weight of PSA discs (Wo)}} \times 100 \quad (3)$$

In-vitro release study of implants

For release studies of implants, 3 vials each containing 20 mL of buffer at pH 7.4 with 1% Polysorbate 80 were taken. One implant was added to each vial and the vials were placed in a shaking water bath at 37°C. At pre-set

time intervals, aliquots of dissolution medium (2 mL) were removed and filtered via a 0.45 µm millipore filter. By replacing the samples with a fresh medium (2 mL), the volume of the dissolution medium was kept constant. The drug concentrations have been analyzed using the above developed HPLC method with appropriate dilution. The cumulative drug release was evaluated with the DDSolver program.[57]

Preparation of microspheres

Microspheres were fabricated using an emulsion solvent evaporation technique. The drug solution (15%, 35.3 mg in 1 mL of DCM) was mixed with PSA solution (85%, 200 mg in 4 mL of DCM) to get the organic phase. PVA dispersion in water (1.0% w/v) was prepared by continuous stirring on a hot plate. For the preparation of microspheres, PVA solution (80 mL) was taken in a beaker (100 mL) and kept on a magnetic stirrer (IKA Labortechnik, Germany) with a bead size of C15 at 600 rpm. Then, using a 5 mL syringe, the organic phase was slowly added to the aqueous phase, keeping the needle inside the liquid to avoid air entrapment. The emulsion thus formed was kept for 4 h in order to allow solidification of microspheres by evaporation of organic solvent. A tabletop centrifuge (Jouan, MR 23i, France) was used to separate the microspheres that had formed and washed with water 2-3 times to remove unentrapped drug. In the vacuum oven, the microspheres were then dried to obtain dry microparticles. The blank microspheres used as a control were manufactured parallelly without any drug. The developed microspheres, were then characterized for drug loading, encapsulation efficiency and *in-vitro* drug release profile.

Determination of drug loading and encapsulation efficiency in microspheres

After preparation of the microspheres, the supernatant solution was collected and used for the determination of drug loading (DL%) using an indirect method. In this method, the amount of drug that remained unloaded from the initial amount (35.3 mg) was determined to get amount of the drug loaded into microspheres. The supernatant was diluted and the unloaded amount was determined using equation (1). The encapsulation efficiency (EE%) was evaluated by the 'indirect method' by subtracting the quantity of drug in washings from the total quantity of drug used in microsphere preparation and then calculating the encapsulation efficiency using equation (2). Although the data was obtained in triplicate, the average values were used to calculate the DL% and EE%.

$$\text{Drug loading (DL\%)} = \frac{\text{Amount of drug encapsulated}}{\text{Total weight of microspheres}} \times 100 \quad (1)$$

$$\text{Encapsulation efficiency (EE\%)} = \frac{\text{Weight of initial drug} - \text{Weight of free drug}}{\text{Quantity of drug taken initially}} \times 100 \quad (2)$$

Optical microscopy of microspheres

Microspheres were observed through an upright compound optical microscope. At 400x, the photo micrographs of microspheres were taken with an external camera to calculate the average size and size distribution, at least 100 vesicles were measured by the i-solution software. A particle Size distribution was plotted from the data obtained. Microspheres were examined for particle size and particle size distribution by mounting them on the slide with water as the mounting agent. Images of microspheres are shown in Figure 2C and 2D.

In-vitro release study of microspheres

Microspheres (50 mg) were put in 3 eppendorf tubes with PBS (1.5 mL, pH 7.4) added to each eppendorf and put in a shaking water bath (37°C at 100 rpm). An aliquot of dissolving medium (0.1 mL) was taken at pre-set time intervals, and filtered through a 0.45 µm millipore filter. The amount of drug released into the PBS medium was determined with the developed HPLC method. The samples were diluted to a suitable concentration and their absorbance at 382 nm was determined. The cumulative drug release was evaluated with the DDSolver program.[57]

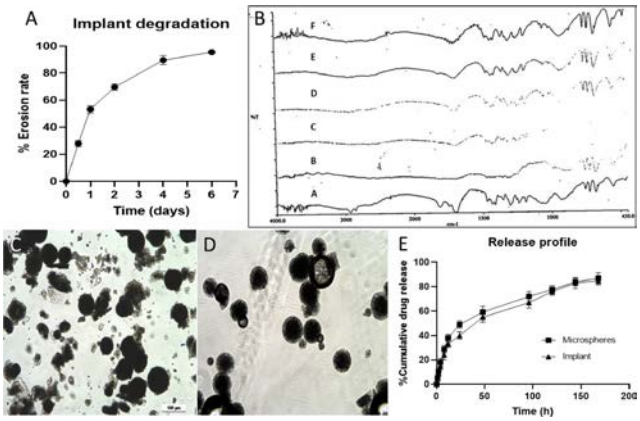

Figure 2: *In-vitro* degradation profiles of PSA implants B. FTIR spectra of PSA implants from bottom to top showing degradation. C. Microscopic images of blank microspheres at a scale of 100 µm D. Microscopic images of drug loaded microspheres show a spherical and porous surface at a scale of 100 µm E. *In-vitro* release profiles of implants and microspheres show comparatively similar release profiles following Higuchi kinetics. The release data was articulated as mean standard deviation (*n*=3).

RESULTS AND DISCUSSION

Characterization of polymer

The purity of the copolymers was verified by GPC, which revealed a single symmetrical unimodal peak with a narrow molecular weight distribution at a retention time of 10.0 min (Figure 1B). The synthesized polymer showed Mn as 1211 Da, Mw as 1283 Da and Mw/Mn as 1.05.

The FTIR spectrum of the synthesized polymer showed different functional groups (Figure 1C). As the given polymer is an anhydride, it is expected that there should be two bands, one at around 1812 cm^{-1} and another at around 1741 cm^{-1}. The spectra showed, the first band at 1812.46 cm^{-1} (symmetric stretching) and the second band at 1741.44 cm^{-1} (asymmetric stretching), which corresponds to the carbonyl group of anhydrides. The peak at 2932.23 cm^{-1} resembles the C-H stretch of CH_3 and the peak at 1039.75 cm^{-1} resembles to bending vibration of the CH_2 group of unconjugated anhydrides, while the peak at 1205.47 cm^{-1} corresponds to the stretching vibration of the C-O group of -COOR.

The DSC thermogram, showed the melting point of PSA is in the range of 78.65°C to 80.68°C (Figure 1D). The polymer, being hygroscopic, picked up moisture readily and hence showed an endotherm for the loss of moisture around 60-70°C. All the samples in the first heating scan were found to be crystalline and that Tm values of 70 to 85°C were equivalent to results reported previously.

The integrals of peaks corresponding to PSA were visible in the ^1H NMR spectrum (Figure 1E), which showed –C$\underline{H}_2$- groups of the central block (8H, δ 1.2348, intensity 8.08), –C$\underline{H}_2$- groups adjacent to the anhydride group (4H, δ 1.5252, intensity 0.98; 4H, δ 2.1965, intensity 3.00) and the terminal –OC$\underline{H}_3$ (6H, δ 2.4944, intensity 1.24) were used to calculate the Mn, based on the proton integral area and was found to be 1.23 kDa.

Calibration curve of drug

The developed RP-HPLC method showed a retention time of 10.523 min with a tailing factor of 1.00 and 9430 theoretical plates. The method showed linearity (R^2=0.9995) in the range of 1 to 30 µg/mL.

Preparation of drug-loaded implants

The implants for drug loading have been formed by mixing and melting the drug mixture with PSA. After that, the implants were made into tiny discs that were 0.5 mm in diameter with a 0.3 mm thickness on average. Moreover, the average weight of the implants was found to be 116.8 ± 3 mg (n=10), with a mean actual drug content (14.05% ± 0.15%), and was within the label claim of the drug (15.0%, w/w).

Weight loss studies of implants

Weight loss of the implant on degradation of the polymer at different time points was calculated and is shown in Figure 2A. The data exhibited that the erosion rate gradually increased up to 6 days.

In-vitro degradation study of implants using FTIR

The polymer degradation was studied using FT-IR based on the polymer quantity left at different time points, as shown in Figure 2B and Table 1. The FTIR data clearly showed the decrease and then complete disappearance of the characteristic anhydride peak as time passed and the intensification of the acid characteristic peaks. On the other hand, the strong carboxylic hydroxyl band, on the other hand, appears between 3300 and 2500 cm^{-1}, while the strong carboxylic carbonyl band appears at 1704 cm^{-1}, and their intensities increase with degradation time. The intensities of the anhydride bonding bands at 1816 cm^{-1} and 1740 cm^{-1}, as well as the C-O-C stretching bands at 1100 cm^{-1}, obviously decrease. This reveals that in the degradation process of PSA, the quantity of carboxylic groups in the PSA sample increases, and the number of anhydride bonds in the PSA sample decreases

Table 1: *In-vitro* degradation study of implants using FTIR at different time points.

S.no.	Time (h)	Anhydride peak 1810 cm^{-1}	Carboxylic acid 1700 cm^{-1}	OH Stretch 2929 cm^{-1}	Peak near -OH stretch
A	0	1807.0	1698.0	2929.2	3058.5
B	12	1813.6	1698.8	2929.8	3118.1
C	24	1811.9	1698.9	2929.8 & 2914.1	Not observed
D	48	1810.2	1704.4	2929.2 & 2851.3	Not Observed
E	96	Not observed	1738.1 & 1695.4	2933.7 & 2851.7	Not observed
F	144	Not observed	1738.3 & 1683.5	2934.3 & 2851.7	Not Observed

due to hydrolysis of the labile anhydride linkage present in the PSA.

Due to hydrolysis of the labile anhydride linkage present in the polysebacic acid, the free carboxylic acid amount increases with time. That is why the anhydride peak in the IR disappears. The anhydride peak shows a very small hump (compared to others). OH stretching becomes broader with increasing hydrolysis due to the formation of dimers.

Preparation of drug-loaded microspheres

The drug-loaded microspheres were fabricated with an emulsion-solvent evaporation technique and the average drug content determined using equation (1) was found to be 13.60% ± 1.05%, identical with the drug's label claim (15.0% w/w) and the encapsulation efficiency determined using equation (2) was found to be 90.65% ± 2.15%.

Optical microscopic study of microspheres

Microsphere morphology demonstrates spherical and porous surface drug loaded particles of size 63 ± 3 μm (Figure 2C, 2D), which further confirms the particles' integrity.

In-vitro drug release study of implants and microspheres

The release profile was evaluated with polyanhydride implants and microspheres containing drugs in PBS at 37°C. The drug demonstrated biphasic release behavior, with early rapid release trailed by sustained release for 7 days. The cumulative release data for implants and microspheres is calculated and compared. The release profile is shown in Figure 2E. About 85 ± 3.5% and 88 ± 4.5% of the drug were released from implants and microspheres respectively, in 7 days. It's worth noting that there are no major variations in release rates between implants and microspheres. The rate of drug release through bio-erodible systems is influenced by drug diffusion, polyanhydride degradation rate, and the solubility properties of the integrated drug, all of which play a role in the rate of drug release. Furthermore, surface erosion of anhydride blocks produces sebacic acid, which leads to the formation of low molecular weight polymer chains, which in turn leads to the formation of micelles, which prolongs the release. Different equations were used to analyze the release kinetics in order to calculate the drug release via polymeric matrices. Release profiles for implants fitted into kinetic models with correlation-coefficient (R^2) values revealed zero order (R^2=0.5162), first order (R^2=0.6930), Higuchi (R^2=0.7744) and Hixon-Crowell (R^2=0.2962). and the release profiles fitted in kinetic models for the microspheres characterized by correlation coefficient (R^2) values revealed zero order (R^2=0.4751), first order (R^2=0.6774), Higuchi (R^2=0.7331) and Hixon-Crowell (R^2=0.2658). The drug release profile from implants and microspheres was almost identical and followed Higuchi kinetics of drug release.

DISCUSSION

The Melt-poly condensation method proves its simplicity in the preparation of PSA polymer with a single step reaction of conversion from acid to anhydride without the usage of multiple reagents. The degradation process of the polymer was better understood from the FTIR study and a good correlation was found between the spectra and the weight loss shown by the implants as the polymer was degraded into monomers and finally into sebacic acid. As the hydrophobic drug is entrapped and distributed in the polymeric matrix, the release profile was observed to be diffusion-like in a sustained manner. Microspheres prepared with the synthesized polymer using the emulsion solvent evaporation method have a particle size of 63 ± 3 μm with a spherical shape, porous and fractured rough surface because of the partial degradation of the polymer chains on the surface of the particle during the preparation process. There was a burst release observed in the microspheres, which may have been due to inhomogeneous and non-spherical particles distributed in the formulation. The two release profile curves of the dosage forms overlap each other virtually because of the similar diffusion-like release profile of the drug from the polymeric matrix.

CONCLUSION

Polysebacic anhydride polymer was successfully prepared and characterized by GPC, DSC, ^{1}HNMR, and FTIR. PSA has a lower melt temperature (Tm) and crystallinity, making it more suitable for use in controlled release systems. The model anticancer drug, olaparib was encapsulated in the implants and microspheres. Drug-loaded PSA implants were fabricated using the melt-molding technique and microspheres were fabricated using the emulsion solvent evaporation technique. A hydrophobic model drug was entrapped into a polymer with a size range of 63 ± 3 μm and an encapsulation efficiency of 90.55% w/w calculated using validated analytical methods. *In-vitro* release profiles showed 85 ± 3.5% and 88 ± 4.5% of drug from implants and microspheres respectively in 7 days following bi-phasic release behavior, with an initial rapid release accompanied by a sustained release characterized by the low dissolution of the drug crystals in aqueous

solutions with Higuchi controlled release kinetics and mainly controlled by diffusion of the drug through the polymeric matrix. The polymer in the implants showed degradation with time, which is evidenced by the FT-IR spectra, by the decrease in the intensity of the anhydride peak and the appearance of a boarder carboxylic acid peak. The main advantage of these polymers is their highly biocompatible degradation products. In conclusion, PSA has the potential to be applied in biomedicine as a new bio-degradable copolymer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HPLC: High pressure liquid chromatography; **PBS:** Phosphate buffer solution; **PVA:** Polyvinyl acetate; **RPM:** Rotations per minute; **BCS:** Biopharmaceutical classification system; **GPC:** Gel permeation chromatography; **NMR:** Nuclear magnetic resonance; **DSC:** Differential scanning calorimetry; **FTIR:** Fourier transform infrared; **PSA:** Polysebacic anhydride.

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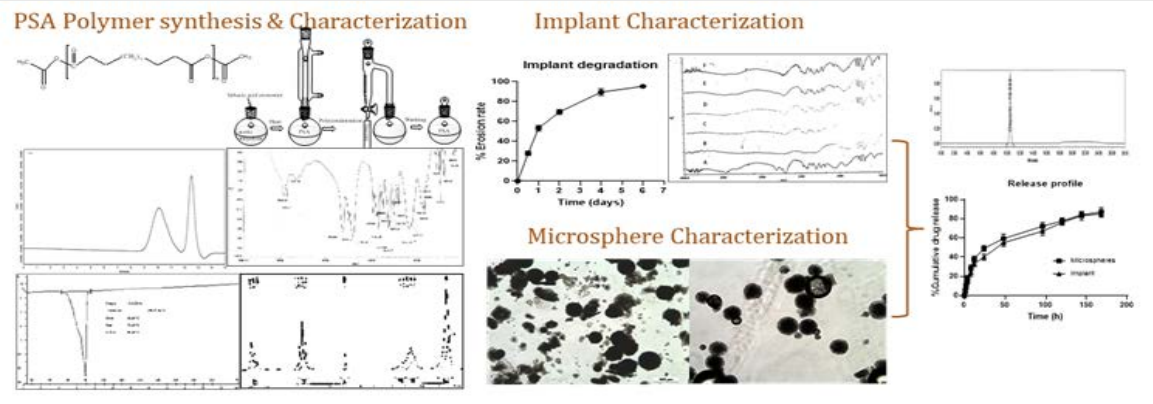
PICTORIAL ABSTRACT



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SUMMARY

In this study polysebacic anhydride polymer was prepared and characterized. Implants and microspheres were prepared using the synthesized bio-degradable polymer to obtain sustained drug release. The release profile comparison showed similar drug release pattern following Higuchi kinetics.

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