Synthesis, characterization and sustainable drug release activity of drug bridged diblock copolymer

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Abstract

Ring opening polymerization of ϵ -caprolactone and tetrahydrofuran were carried out by bulk polymerization technique in the presence of a drug molecule as an initiator at 160 °C for 2 h under nitrogen atmosphere. The synthesized homo and diblock copolymer was characterized by various analytical techniques. Further, the sustainable drug release study was carried out at gastric pH of 7.2. The diblock copolymer formation was confirmed by the appearance of aromatic C=O stretching around 1680 cm⁻¹. Due to the hydrophilic nature the diblock copolymer exhibited lower melting temperature. The drug release study confirmed the first order drug release model.

Keywords ROP · Copolymer · FESEM · TGA · Tensile strength · Drug delivery

1 Introduction

Poly(ϵ -caprolactone) (PCL) has wide applications in bio-medical engineering field as a drug carrier material because of its bio-degradability and bio-compatibility. Such a bio-medically important candidate is prepared by ring opening polymerization (ROP) method through co-ordination insertion mechanism. For this purpose stannous octoate (SO) is used as a catalyst in the presence of different initiator species. ROP of CL was reported in the presence of n-butanol as an initiator [1, 2]. Terzopoulou et al. [3] reported the ROP of CL using SO as a catalyst and initiator. Similarly, other novel initiators such as benzylalcohol [4, 5], gelatin [6], lipase [7], mercaptohexanol [8], diethyleneglycol [9], bisphenolate ligand [10] and mPEG [11] were used for the ROP of CL. Due to the bio-degradability and bio-compatibility of PCL, it is used as a drug carrier material. Any drug molecule can be loaded on the backbone of PCL through a hydrogen bonding mechanism. But the drawback is it releases all the drug molecules immediately which lead to overdose of drug. This leads to the unwanted side effects

to patient sometimes. Hence, sustainable release of drug is essential. For this purpose, the drug molecule should be chemically conjugated using hazardous organic solvents. But, this technology is highly expensive. In 2013, Sawdon et al. [12] reported the guanosine, an antiviral acyclovir initiated ROP of CL. Folic acid initiated ROP of CL was reported [13]. The drug delivery study proved to be sustainable in release of drug in the given buffer medium. By keeping this idea in mind, the present investigation was made as a development of this idea. The literature survey reports that few reports are available on the drug initiated ROP of CL. This urged the authors to do the present investigation.

Poly(tetrahydrofuran) (PTHF) secured second rank in the polymer class in the bio-medical field because of its non-cytotoxic effect and bio-compatibility. PTHF can be synthesized by cationic ROP technique. In 2012, Nomura et al. [14] used V complexes as an initiator/catalyst for the ROP of THF. Different initiating systems such as keggins type heteropolyacids [15], cationic species [16], norbornyl cation [17], magamite-H⁺ [18], glycosyl [19] and aminoacids [20–22] were used for the ROP of THF. Recently, dye initiated ROP

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of THF was reported in the literature [23]. In 2015, folic acid initiated ROP of CL was reported by Kailash et al. [13]. The literature survey declares that no report on drug initiated ROP of THF is available in the literature except folic acid [13]. The novelty of the present investigation is drug molecules with different functional groups are used as an initiator for the ROP of THF with sustainable drug release.

In bio-medical engineering field, amoxicillin (amox) is used as an antibiotic particularly for the treatment of bacterial infection diseases. Time dependent release of amox was studied [24]. Controlled release of amox from modified cellulose was reported in the literature [25]. Gentamicin (gen) or garomicin is an antibiotic used for the treatment of pneumonia, urinary tract infections and bacterial infectious diseases. Controlled delivery of gen using poly(3-hydroxybutyrate) microspheres [26] was reported in the literature. Gentamicin sulphate release from PVA hydrogel was reported [27]. Neomycin (neo) is an antibiotic with two or more aminosugar which are connected through glycosidic linkages. Neomycin release from PVP hydrogel study was done by Choi et al. [28]. Chitosan nanofiber containing neomycin sulfate release study was reported in the literature [29]. The literature survey reported that drug bridged diblock copolymer based carrier material was not used for amox, gen and neo with sustainable releases. This tempted the authors to concentrate on sustainable release of the above mentioned drugs.

2 Experimental

2.1 Materials

The monomers ϵ -caprolactone (CL, Sigma Aldrich, India) and tetrahydrofuran (THF, Ottokemi, India) and the

co-monomer phthalicanhydride (PAH, Loba Chemi, India) were purchased and used. Chloroform (solvent, Sigma Aldrich), diethyl ether (non-solvent, Spectrum Reagents and Chemicals), and stannous octoate (SO, catalyst, Sigma Aldrich) were used without any purification. Amoxicillin (amox), gentamycin (gen) and neomycin (neo) like drugs were purchased from Ranbaxy, India in the form of a tablet for drug delivery application. Double distilled (DD) water was used for making solution. The chemical structures of all the drug molecules are given in Scheme 1.

2.2 Synthesis of homopolymer and diblock copolymer

Synthesis of drug bridged diblock copolymer is a two step process [13]. In the first step: 1 g of CL monomer was taken in a 25 mL capacity round bottomed flask. With this 0.001 g SO [M/C = 1000] and 0.01 g drug [M/I = 100] were taken and degassed for 10 min. Then it is transferred to an oil bath and the temperature is maintained at 160 °C for 2 h. The reaction was arrested by the addition of 25 mL CHCl_3 . Further, it was precipitated by adding 200 mL diethylether. It was dried under fume hood for night. The dried sample was weighed (99% yield), stored under zipper lock cover and named as P1. This is the drug end capped homo polymer. The reaction is given in Scheme 2. The polymer obtained is in purest form. In the second step, 0.50 g of P1 was dissolved in 10 mL of THF. 0.01 g PAH was added and heated to 45 °C for 6 h under nitrogen atmosphere. After 6 h when the THF was evaporated. The product is named as P2, weighed [78% yield] and stored under zipper lock cover. The diblock copolymer formation is shown in Scheme 2.

Scheme 1 Structure of drug molecules

Scheme-1. Synthesis of PCL-Amox-PTHF

Scheme 2 Synthesis of PCL-Amox-PTHF

2.3 Characterization

FTIR spectra were recorded with the help of Shimadzu 8400 S, Japan model instrument by KBr pelletization method from 400 to 4000 cm^{-1} . 3 mg of copolymer was ground with 200 mg of spectral grade KBr and made into disc under the pressure of 7 tons. The melting temperature (T_m) of the polymer samples was determined using DuPont Thermal Analyst 2000 Differential Scanning Calorimeter 910S (USA) model instrument. All the measurements were made under N_2 atmosphere in the temperature range of RT to 100 $^{\circ}\text{C}$ with 10 $^{\circ}\text{C}/\text{min}$ heating rate. The NMR spectrum was recorded with the help of Bruker Biospin High Resolution Digital 300 MHz NMR Spectrometer (USA) using deuterated chloroform (CDCl_3) as the solvent and

morphological behavior of polymer with the help of FESEM (Hitachi S4800, Japan).

2.3.1 Drug release study

The drug release study was carried out for the homopolymer and diblock copolymer samples and the procedure is described in brief: [13] 0.50 g homopolymer or diblock copolymer was taken in disc form prepared under 7 tons of pressure. 500 mL of gastric pH solution was prepared and suspend the tablet in the medium, stirring. The drug released slowly and it was quantitatively measured at different interval of time by pipetting 2 mL of aliquot using UV-visible spectrophotometer. From the calibration curve, the % cumulative drug release (% CDR) was calculated as follows:

$$\% \text{CDR} = \frac{(\text{weight of standard}) \times (\text{sample absorbance}) \times (\text{sample dilution}) \times (\text{potency of standard})}{(\text{sample dilution}) \times (\text{sample absorbance}) \times (\text{label claim})} \quad (1)$$

tetramethyl silane (TMS) served as an internal standard. Thermal stability of polymer was measured using DuPont 951 thermo gravimetric analyzer (USA). Thermograms were recorded under air atmosphere in a temperature range of 30–800 $^{\circ}\text{C}$ at the heating rate of 10 $^{\circ}\text{C}/\text{min}$. Surface morphology of the sample was measured by JSM 6300 (Jeol product) SEM instrument. UV-visible spectrum was measured by using Shimadzu 3600 NIR spectrophotometer (Japan). Field emission scanning electron microscopy (FESEM) with EDX was used to examine

The following plots were made in order to determine the model of drug release model and their flow mechanisms which were drawn and their slope and intercept values were noted: zero-order model was the plot of (% CDR) versus time; first-order model was the plot of $\log(\% \text{ drug remaining})$ versus time; the Higuchi model was the plot of (% CDR) versus $(\text{time})^{1/2}$; the Hixson-Crowell model was the plot of $(\% \text{ drug remaining})^{1/3}$ versus time; and the Korsmeyer-Peppas model was the plot of $\log(\% \text{ CDR})$ versus $\log(\text{time})$.

Fig. 1 FTIR spectrum of a PCL-Amox, b PCL-Amox-PTHF, c PCL-Gen, d PCL-Gen-PTHF, e PCL-Neo and f PCL-Neo-PTHF systems

Table 1 FTIR data

Functional group	Wavenumber (cm ⁻¹)
N-H stretch	3445
O-H stretch	3340
C-H stretch	2855, 2948
C=O stretch	1729, 1687
C-O-C stretch	1041
C-H OPBV	723
Aromatic stretch	672, 803

2.3.2 Mechanical property

The mechanical properties were measured by Universal Tensile Tester, Deepak Polyplast, India. Three samples were measured according to the ASTM standard. The average is considered here.

3 Results and discussion

3.1 FTIR spectroscopy

Amox is an antibacterial drug with functional groups like -OH, -NH₂, -CO-NH₂, -C=O, C-S, -CO₂H and -C-N. Among the groups, the -OH is more active towards the ROP of CL. Hence, it is used here as an initiator for the ROP of CL. The [M/I] ratio was maintained as 10. The FTIR spectrum was recorded for the Amox functionalized PCL, Fig. 1a. A broad peak around 3340 cm⁻¹ is due to the O-H

stretching (Table 1). This -OH group arises from the PCL chain end. The -NH stretching is noticed at 3445 cm⁻¹ and the ester carbonyl stretching appeared at 1723 cm⁻¹. The ester C-O-C linkage appeared at 1194 cm⁻¹. The C-N stretching appeared at 1360 cm⁻¹. This is in accordance with Meenarathi et al. [30] report. The C-S stretching was noticed at 1421 cm⁻¹. The C-H out of plane bending vibration (OPBV) is seen at 725 cm⁻¹. Figure 1b indicates the FTIR spectrum of Amox bridged diblock copolymer (i.e.) PCL-Amox-PTHF. Here also the above said peaks were observed. Apart from those, some new peaks were also seen. Peaks at 2525 and 2650 cm⁻¹ are corresponding to the aromatic C-H symmetric and anti-symmetric stretching respectively. A doublet peak at 1696 cm⁻¹ is responsible for the carbonyl stretching of PAH (Table 1). The tetrahydrofuronium ion appeared at 1577 cm⁻¹ [31]. The aromatic stretching was noted at 615 and 789 cm⁻¹. The appearance of aromatic C-H stretching, carbonyl stretching and tetrahydrofuronium ion confirmed the ROP of THF in the presence of PAH.

The FTIR spectrum of Gen end capped PCL is shown in Fig. 1c. Table 1 shows the peak corresponding to PCL. A broad peak around 3560 cm⁻¹ accounts the O-H stretching of Gen. The C-H symmetric and anti-symmetric stretching appeared at 2865 and 2948 cm⁻¹ respectively. Peaks corresponding to PCL are also observed. The ester C-O-C linkage can be seen at 1187 cm⁻¹. Figure 1d indicates the FTIR spectrum of PCL-Gen-PTHF diblock copolymer (Table 1), and here also the above said peaks were observed. Apart from the regular peaks some new peaks were also observed. Peaks at 2524 and 2645 cm⁻¹ are due to C-H symmetric and anti-symmetric stretching respectively of aromatic phenyl ring. The carbonyl stretching at 1692 cm⁻¹ is due to the carbonyl stretching of PAH units. Another one important peak appeared at 1589 cm⁻¹ which is due to the formation of tetrahydrofuronium ion [31]. The aromatic C-H bending was noted at 662, 734, and 796 cm⁻¹. Thus the appearance of new peaks such as aromatic C-H, doublet formation, C-O-C stretching, and aromatic stretching confirms the ROP of THF in the presence of Gen end capped PCL as a chemical initiator.

Neo contains O-H, -NH₂ and ether like functional groups. The O-H group of Neo is more effective towards the ROP of CL. The FTIR spectrum of Neo end capped PCL is given in Fig. 1e. The O-H stretching, -CH stretching, C=O stretching, -C-N stretching, and C-H OPBV are observed at (3644 cm⁻¹, 2872 cm⁻¹ and 2955 cm⁻¹, 1731 cm⁻¹, 1361 cm⁻¹ and 728 cm⁻¹) (Table 1) respectively. The FTIR spectrum of PCL-Neo-PTHF diblock copolymer is given in Fig. 1f. Here also the above said peaks corresponding to PCL appeared (Table 1). New peak such as aromatic C-H stretching at 2533 cm⁻¹ and

2673 cm^{-1} , aromatic C=O stretching at 1693 cm^{-1} and aromatic C–H bending at 665 and 801 cm^{-1} appeared respectively. The aliphatic C–O–C linkage appeared at 1194 cm^{-1} [30]. Thus the FTIR spectrum confirmed the homopolymer and copolymer formation.

3.2 DSC study

The phase transition of the polymer can be altered by the initiator which is used for its polymerization to some extent. The DSC data is summarized in Table 2. The melting temperature (T_m) of semi-crystalline PCL was determined by DSC. Figure 2a indicates the DSC thermogram of PCL-Amox system with an endothermic peak at 67.3 °C corresponding to T_m of PCL [32]. Figure 2b indicates the DSC thermogram of PCL-Amox-PTHF system with an endothermic peak at 66.1 °C [30]. Appearance of single T_m confirmed the diblock copolymer formation without any simultaneous homopolymer formation of THF. While comparing the T_m values of homo polymer and diblock copolymer, the later system exhibited somewhat lower T_m due to the hydrophilic nature of PTHF segments. It absorbs moisture from atmosphere. As a result the flows of polymer chain are activated and hence there is a reduction in T_m value of the diblock copolymer. The DSC heating scan of Gen end capped PCL is given in Fig. 2c. The thermogram exhibits an endothermic peak corresponding to the T_m of PCL at 67.5 °C. The DSC heating scan of PCL-Gen-PTHF is given in Fig. 2d. The thermogram exhibits one endothermic peak at 65.1 °C corresponding to T_m of the diblock copolymer. In comparison, one can say that the diblock copolymer exhibited lower T_m corresponding to high moisture absorption nature. The moisture absorption nature is introduced to the diblock copolymer with the help of PTHF segments. The ROP of THF produced a linear structure without crosslinking. This leads to absorption of moisture and increases (i.e.) the hydrophilic nature. As a result, the T_m of the diblock copolymer was suppressed. The DSC of PCL-Neo and PCL-Neo-PTHF systems are given in Fig. 2 e, f respectively. The T_m of homopolymer PCL-Neo appeared at 68.2 °C whereas the PCL-Neo-PTHF exhibited the same at 66.1 °C. Moreover, the widening of peak confirms the

Fig. 2 DSC thermogram of a PCL-Amox, b PCL-Amox-PTHF, c PCL-Gen, d PCL-Gen-PTHF, e PCL-Neo and f PCL-Neo-PTHF systems

decrease in crystallinity of diblock copolymer. It means the amorphous character increased after the diblock copolymer formation in the presence of PAH as a co-monomer. The decrease in T_m value of diblock co-polymer is due to the increase in the hydrophilic nature of the polymer. The PCL-Neo system exhibited the highest T_m value.

3.3 TGA study

The thermal stability of homo polymer and diblock copolymer was tested by TGA under air atmosphere at the rate of 10 °C/min. The thermal property was studied between room temperature and 600 °C. The TGA thermogram of Amox functionalized PCL, the homopolymer is given in Fig. 3a. The thermogram exhibits two step degradation process. The first major weight loss around 400 °C is associated with the degradation of PCL backbone [30]. The second minor weight loss around 450 °C is due to the degradation Amox. Figure 3b represents the TGA thermogram of diblock PCL-Amox-PTHF copolymer. The thermogram exhibits three step degradation processes. The first minor weight loss around 220 °C is due to the degradation of

Table 2 T_m , molecular weight and mechanical property data

System	DR model	DR mechanism	T_m (°C)	M_w (g/mol)	TS (Kg/m ²)	%E (%)
Amox-PCL	First	Fickian	67.3	1483	5450	19.7
PCL-Amox-PTHF	First	Fickian	66.1	1647	5000	42.2
Gent-PCL	First	Fickian	67.5	3143	2358	32.6
PCL-Gent-PTHF	First	Fickian	65.1	5675	1762	59.8
Neo-PCL	First	Fickian	68.2	2236	2200	25.7
PCL-Neo-PTHF	First	Fickian	66.1	4375	2000	61.7

DR drug release, TS tensile strength, %E %elongation

Fig. 3 TGA thermogram of a PCL-Amox, b PCL-Amox-PTHF, c PCL-Gen, d PCL-Gen-PTHF, e PCL-Neo and f PCL-Neo-PTHF systems

the PTHF segments [22]. The second major weight loss around 425 °C is due to the degradation of PCL units. On comparison, the diblock copolymer exhibited the lower thermal stability due to the hydrophilic nature. Our results are in accordance with the literature report [21]. Figure 3c indicates the TGA thermogram of Gen initiated ROP of CL. The thermogram exhibited a two step degradation processes. The first major weight loss around 350 °C is due to the degradation of PCL backbone. The second minor weight loss around 450 °C, attributes to the degradation of Gen structure. The TGA of the PCL-Gen-PTHF diblock copolymer is shown in Fig. 3d with a three step degradation process. The first major weight loss around 220 °C is due to the structural degradation of PTHF segments. The second weight loss corresponds to the degradation of PCL backbone around 390 °C. As mentioned above, the third minor weight loss is ascribed due to the degradation of Gen. The TGA thermogram of PCL-Neo is given Fig. 3e with a single step degradation process. The major weight loss around 400 °C is due to the degradation of PCL backbone. Figure 3f indicates the TGA thermogram of PCL-Neo-PTHF diblock copolymer. The thermogram exhibited a two step degradation process. The first major weight loss up to 350 °C is due the degradation of PTHF segments. The second minor weight loss around 410 °C is associated with the degradation of PCL backbone. To conclude, the PCL exhibits higher thermal stability than the diblock copolymer. This can be explained as follows: Due to the hydrophobic nature, the PCL degradation occurred at higher temperature. Whereas due to the hydrophilic nature of PTHF, which absorbs larger amount of moistures, degrades at lower temperature. The TGA study proved that hydrophobic nature can increase the thermal stability of a polymer.

Fig. 4 SEM image of a PCL-Amox, b PCL-Amox-PTHF, c PCL-Gen, d PCL-Gen-PTHF, e PCL-Neo and f PCL-Neo-PTHF systems

3.4 SEM and FESEM image analysis

The surface morphology of Amox functionalized PCL is given in Fig. 4a. The image indicates the dried sky like morphology with some micro voids [33]. The micro voids are helpful for the drug carrying purpose. Hence, PCL is widely used in the bio-medical application. Figure 4b indicates the FESEM image of PCL-Amox-PTHF diblock copolymer. The surface morphology of the diblock copolymer is entirely different from the homopolymer. The surface morphology of diblock copolymer is having a cracked structure. The important point to be noticed here is after the diblock copolymerization, the surface becomes smooth in structure with some uniform distribution of nanoparticles. The nanoparticles are formed as a result of the combination of hydrophobic PCL and hydrophilic PTHF segments. The sizes of the particles were determined as 10 to 150 nm. The interface regions between hydrophilic and hydrophobic segments are responsible for the polymer nanoparticle formation. The formation of polymer nanoparticles is a key element for an effective drug carrier material [31]. The surface morphology of the polymer can be altered to certain level with the help of an initiator (or) a catalyst. In the

present investigation, the Gen end capped PCL exhibited broken stone like morphology [30] (Fig. 4c) with a length of approximately 1.5 μm and with breadth of 1 μm . The broken stone like morphology is peculiar for PCL [30]. The FESEM image of PCL-Gen-PTHF system is shown in Fig. 4d. The hydrophobic PCL and the hydrophilic PTHF were combined through the Gen. The image shows the presence of some nanosized particles. Obviously this is due to polymer nanoparticles. The sizes of micelles were determined as 100–130 nm. This polymer dispersion is due to the difference in the chain length of the diblock copolymer. If the chain length of the diblock copolymer is longer, the size of the micelles will reduce correspondingly. Again this can be explained on the basis of coiled structure of the polymer chains. The surface morphology of PCL-Neo system is given in Fig. 4e. The morphology confirms the gel like structure. The surface contains more number of micro voids [33]. The micro voids are useful for the drug carrying activity. Figure 4f represents the FESEM image of PCL-Neo-PTHF diblock copolymer. The image shows the agglomerate distorted spherical particle. The size of the particle varied from 300 to 600 nm.

3.5 EDX spectrum

The EDX spectrum of Amox functionalized PCL is given in Fig. 5a. Appearance of peak corresponding to C, N, S, and O confirmed structure of Amox functionalized PCL. The percentage of C was determined as 60.59%. The percentage of O, N, and S were determined as 17.21, 20.0 and 0.18% respectively. The element present in the PCL-Gen homopolymer was confirmed by EDX (Fig. 5b). The spectrum shows the presence of carbon (72.77%), oxygen (17.23%), nitrogen (7.2%) and sulphur (1.1%). The sulphur atom appeared in impurity. The EDX indirectly supports the structure of Gen end capped PCL. The EDX spectrum of PCL-Neo homopolymer is given in Fig. 5c. The spectrum shows peaks corresponding to N, C, and O with % content of 2.39, 80.61 and 17% respectively. The appearance of the peaks corresponding to N confirms the formation of Neo functionalized PCL.

3.6 GPC study

The ROP of CL and THF were confirmed by GPC technique. The GPC data is summarized in Table 2. The M_w , M_n and PD values were determined for PCL-Amox system as 1483.5 g/mol, 852.9 and 1.73 respectively (Fig. 6a). Figure 6b represents the GPC image of PCL-Amox-PTHF system and the data is given as follows: 1647.9 g/mol (M_w), 568 (M_n) and 1.9(PD). The increase in M_w is associated with the THF and PAH. The increase in M_w confirmed the ROP of THF in the presence of PAH as a co-monomer.

Fig. 5 EDX spectrum of **a** PCL-Amox, **b** PCL-Gen and **c** PCL-Neo systems

When compared with the Al complexes [34], the present investigation yielded low M_w . This is associated with the complexing nature of Al. Figure 6c indicates the GPC trace of Gen end capped PCL. The M_n , M_w and PD values were determined as 3143.0, 5675.3 g/mol and 1.80 respectively. The PD value confirms the absence of cross linked or branched structure of PCL. Figure 6d represents the GPC image of the PCL-Gen-PTHF system. Here the M_n , M_w and PD values were determined as 5636.18, 6613.5 g/mol and 1.17 respectively. Again it proves that the Gen-PCL initiated ROP of THF was successful with a linear structure. Moreover, the PD value was found to be reduced. This declared the typical polymerization of THF in the presence of Gen-PCL without any cross linkage. The M_w of the diblock copolymer is greater than that of

Fig. 6 GPC image of **a** PCL-Amox, **b** PCL-Amox-PTHF, **c** PCL-Gen, **d** PCL-Gen-PTHF, **e** PCL-Neo and **f** PCL-Neo-PTHF systems

M_w of PCL. Figure 6e indicates GPC image of PCL-Neo system. The M_w , M_n and PD values were determined as 2236 g/mol, 2089 and 1.07 respectively. The PD value confirms the formation of linear PCL. The GPC trace of diblock copolymer is given in Fig. 6f. In this system M_w , M_n and PD values were determined as 4375.6 g/mol, 3890.17 and 1.12 respectively. Among the drug molecules considered for the present investigation, the Gen is an efficient one towards the ROP of CL. This is proved by the M_w of PCL.

3.7 NMR study

The chemical structure of PCL-Amox-PTHF diblock copolymer was confirmed by 1H -NMR spectrum (Fig. 7a). Peaks at 0 ppm and 7.3 ppm are corresponding to standard TMS and $CDCl_3$ solvent respectively. Peaks between 7.72 ppm and 8.0 ppm are due to the aromatic protons of PAH. Peaks at 4.1 and 2.3 ppm are corresponding to alkoxy proton

and $-CO_2-CH_2$ protons of PCL. Figure 7b represents the ^{13}C -NMR spectrum of PCL-Amox-PTHF diblock copolymer. The carbonyl carbon signal appeared at 173.6 ppm. This is in accordance with Kannammal et al. [33]. Triplet peaks at 77 ppm are corresponding to $CDCl_3$ solvent. A sharp peak at 64.1 and 34.1 ppm are corresponding to alkoxy carbon signal and a methyl carbon signal nearer to CO_2 group. The aromatic carbon signals, PAH signals appeared around 130 ppm. The peaks corresponding to PTHF segments did not appear due to non salvation effect of $CDCl_3$ towards THF repeating units. The remaining carbon signals are matched with the structure of PCL. Figure 7c and d indicates the 1H and ^{13}C NMR spectra of the PCL-Gen-PTHF system respectively. Peaks at 0 and 7.3 ppm are corresponding to TMS and $CDCl_3$ solvent respectively. The aromatic proton signal between 7.6 and 7.9 ppm are due to PAH. A peak at 4.1 ppm is due to alkoxy proton [30] of PCL. The $-CO_2-CH_2$ attached with benzene ring appeared at 3.8 ppm. The $-CO_2-CH_2-$ protons from PCL appeared at 2.3 ppm. The methyl protons from Gen appeared at 1.3 ppm. The methylene protons of PCL appeared between 1.4 and 1.8 ppm. The chemical structure of PCL-Gen-PTHF was further confirmed by ^{13}C -NMR spectrum. The carbonyl carbon signals of PCL and PAH appeared at 173 ppm [31]. The aromatic ring carbon signals appeared at 129 ppm. A strong peak at 78 ppm corresponds to the solvent. The alkoxy carbon signal of PCL appeared at 64 ppm. The $-CO_2-CH_2$ carbon signal of PCL appeared at 33 ppm. The remaining carbon signals matched with the structure. Thus both 1H -NMR and ^{13}C -NMR spectra confirmed the chemical structure of PCL-Gen-PTHF system. Figure 7e indicates the 1H -NMR spectrum of PCL-Neo-PTHF. A peak at 7.2 ppm and 0 ppm are associated with $CDCl_3$ and TMS respectively. The alkoxy proton of PCL appeared at 4.1 ppm [30]. The $-CO_2-CH_2$ proton of PCL can be seen at 2.3 ppm. The proton signals matched with the chemical structure of PCL. Figure 7f represents the ^{13}C -NMR spectrum of PCL-Neo-PTHF system. The carbonyl carbon signal appeared at 173.5 ppm [30]. A sharp peak appeared at 77 ppm is ascribed to the solvent. Peak at 64 and 34 ppm are corresponding to the $-OCH_2$ and $-CO_2-CH_2$ carbon signals respectively. The appearance of these two peaks with the peak integration area of one confirms the chemical structure of PCL-Neo-PTHF.

3.8 Tensile strength

The alternate aim of the current study is to test whether the polymer system is suitable for the splinting activity. The splinting activity needs good mechanical properties. The raw fabric exhibited the average tensile strength (TS) value of 1846.45 kg/cm² with 38.45% of elongation. In this case the homopolymer coated

Fig. 7 ^1H -NMR spectrum of **a** PCL-Amox-PTHF, **c** PCL-Gen-PTHF and **e** PCL-Neo-PTHF, ^{13}C -NMR spectrum of **b** PCL-Amox-PTHF, **d** PCL-Gen-PTHF and **f** PCL-Neo-PTHF systems

fabric exhibited a tensile strength value of 5450.68 kg/cm² with %elongation value of 19.72% (Table 2). After the coating the fabric exhibited 2.5 times higher tensile strength value due to the hydrophobic nature of

PCL. Unfortunately, the % elongation value dropped suddenly. This can be the brittle nature of the PCL coated fabric. The diblock copolymer coated fabric exhibited the tensile strength and % elongation values

Fig. 7 (continued)

of 5000 kg/cm² and 42.19% respectively. The present system yielded lower tensile strength value than the PCL coated fabric. This can be explained on the bases of increased moisture absorbing [20–22] capacity of diblock copolymer grafted fabric. The moisture content destabilized the tensile strength value. It means, after the diblock copolymer formation, the flexibility and amorphous characteristic of the polymer have increased. This leads to the increase in % of elongation [13].

3.9 Drug release study

PCL is a well known bio-degradable and bio-compatible polymer with less cytotoxicity. Recently, PCL is used as a drug carrier material and the drug release is purely based on the hydrogen bonding mechanism [35–37]. By keeping this idea in mind and in order to tackle the over dose drug release problem, the present investigation was made through sustainable drug release through hydrolysis mechanism. The sustainable drug release via hydrolysis

mechanism is the ultimate aim of the present investigation. The drug release activity of Amox-PCL system is quantitatively studied by UV–visible spectroscopy (Fig. 8a–k). It was found that while increasing the drug release time the λ_{max} value at 272 nm increased gradually. The various drug release model and drug release mechanism were determined from the UV–visible absorbance data. Table 3 indicates the maximum R^2 value for different models. Among the models the first order model [38] exhibited the maximum R^2 value of 0.8727 (Fig. 8l). This indicated the drug dissolution in a pharmaceutical dosage in the given gastric pH medium. It also indicates that the drug release depends mainly on the hydrolysis mechanism because Amox is chemically conjugated with PCL. In order to find out the real drug release mechanism, the plot of log (cumulative % of drug release) Vs log time, Fig. 8m was drawn and the slope value was determined to be 0.50. This confirms the Fickian transport mechanism of drug release. Thus the Korsemeyer and Peppas model confirms the drug release mechanism (Tables 2 and 3). The drug release activity of the diblock copolymer was also quantitatively

Fig. 8 UV-visible spectrum of Amox taken at 1 min time interval a-k First order plot l and Korsmeyer-Peppas plot for PCL-Amox system m

Table 3 Drug release data of PCL-Amox-PTHF system

System	Model	Slope(n)	Intercept	R ²
PCL-Amox	Zero order	0.02162	3.10637	0.8626
	First order	-1.23×10^{-4}	1.98946	0.8727
	Higuchi	0.04432	0.01046	0.6223
	K-P	0.50635	-0.7603	0.8396
	H-C	-3.93×10^{-4}	4.58928	0.8499
PCL-Amox-PTHF	Zero order	0.61971	35.303	0.7221
	First order	-0.0103	1.8740	0.9618
	Higuchi	0.08016	1.28725	0.7583
	K-P	0.45809	1.11576	0.9545
	H-C	-0.02139	4.15965	0.7990

K-P Korsmeyer-Peppas, H-C Hixon-Crowell

studied by UV-visible spectroscopy and mentioned in Fig. 9a-k. While increasing the time of drug release, the drug release activity also increased. The amount of drug released at different time interval was determined. Table 3 indicates the maximum R² value, intercept and slope value for the various drug release model. Among the models,

the First order model exhibited the highest R² value (0.96). Figure 9l. Indicates the plot of log (cumulative % drug remaining) Vs time. In order to find out the drug release mechanism, Korsmeyer and Peppas model plot was made and shown in Fig. 9m. The slope value was determined as 0.45 and confirmed the Fickian diffusion of drug release mechanism. The above drug release study indicated that both the homopolymer and diblock copolymer exhibited the same drug release mechanism via hydrolysis reaction.

Similarly, the other homopolymer and diblock copolymer systems having different drug molecules were subjected to drug delivery study and the data was summarized in Table 2. From the table it was found that all the drug bridged systems followed the first order model with Fickian drug transportation mechanism. This is purely based on the hydrolysis reaction because the drug molecules are chemically attached with the polymer backbones. The n values of PCL-Gen and PCL-Gen-PTHF systems, determined from the Korsmeyer and Peppas model plot was 0.47. This confirmed the Fickian diffusion mechanism. From the drug release study one can come to a conclusion that the Gen was released from the diblock copolymer backbone via

Fig. 9 UV-visible spectrum of Amox taken at 1 min time interval a-k First order plot l and Korsmeyer-Peppas plot for PCL-Amox-PTHF system m

hydrolysis reaction. The Gen was solubilized in the given medium and released from the diblock copolymer. The drug release activity of PCL-Neo and PCL-Neo-PTHF systems were studied under gastric pH. The data is given in Table 3. Various models were tried and the First order model exhibited the maximum R^2 value (0.988). The slope value of the Korsmeyer-Peppas model plot was found to be 0.35, which confirmed the Fickian drug transport mechanism. In the case of diblock copolymer system, again the First order model exhibited the max R^2 value. Further, the drug release mechanism was confirmed by drawing the Korsmeyer-Peppas model plot with the slope value 0.26. This explained the Fickian transport mechanism of drug. The present system concluded that both the homopolymer and diblock copolymer exhibited the Fickian transport mechanism of drug with First order drug release model. The drug release activity of diblock copolymer is induced through the soft segments like THF. Since it is a hydrophilic in nature there exist a thorough mixing with the drug

release medium. First, the hydrolysis started with THF segments followed by the junction of a drug and PTHF. Now the one end of the drug is free whereas the other end is conjugated with the PCL, is considered as a heterogeneous hard segment. Here the hydrolysis started with the junction of drug and PCL followed by the CL segments. The hydrolysis of PCL-drug takes some time to interact with the reaction medium. Finally, both ends of the drug are free from polymers and are released into the reaction medium. In the case of homopolymer, the hydrolysis starts at the junction of drug and PCL followed by the CL segments. The important point to be noted here is the drug release activity do not only depend only on the nature of the polymer but also depends on the molecular weight of the polymers. The coil like structure of polymer plays a vital role in the interaction with the reaction medium and finally the drug gets released. In such a way the sustainable drug release activity of diblock copolymer is attained through hydrolysis mechanism. In 2015, Kailash et al. [13] studied

the sustainable drug release activity of diblock copolymer, in which they reported the Hixon-Crowell model drug release with Fickian drug transportation mechanism. The present investigation is entirely different from the literature report [13]. This is associated with the nature, size and number of functional groups present in the drug as well as the pH of the drug release study.

4 Conclusions

The important points are summarized and presented as the conclusion. The FTIR spectrum showed a peak corresponding to the tetrahydrofuronium ion around 1580 cm^{-1} which confirmed the diblock copolymer formation. The ^1H -NMR spectrum showed a peak at 4.1 ppm corresponding to the $-\text{OCH}_2$ proton signal of PCL. The T_m of homopolymer is greater than that of diblock copolymer due to the hydrophobic nature of PCL. The diblock copolymer exhibited a two step degradation process due to the degradation of PCL and PTHF segments. The M_w of diblock copolymer is greater than that of homopolymer. The SEM image showed the broken stone like morphology for PCL. The EDX spectrum showed the presence of N and S which confirmed the presence of drug molecules in the diblock copolymer as an initiator species. The tensile strength of homopolymer is greater than that of diblock copolymer is due to hydrophobic nature. The diblock copolymer exhibited high % elongation value due to the hydrophilic nature. Both the homopolymer and diblock copolymer systems followed the first order drug release model with Fickian drug transportation mechanism.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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