Nanocomposites

Synthesis, characterization and drug release activity of poly(ε-caprolactone)/Fe$_3$O$_4$–alizarinred nanocomposites

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Abstract Applications of magnetic and fluorescent poly(ε-caprolactone) (PCL) is increased rapidly in the biomedical engineering field as a bioimaging probe. This urged us to do the present work. In the present investigation, the role of Fe$_3$O$_4$–AR dye nanohybrid on the ring opening polymerization (ROP) of CL was studied at different experimental conditions such as variation in [M] and [M/I]. Prior to ROP of CL, the nanohybrid was characterized by various spectral methods like FTIR spectroscopy, UV–visible spectroscopy, fluorescence spectroscopy, VSM and FESEM like analytical techniques. The Fe$_3$O$_4$–AR nanohybrid is used as an initiator for the ROP of CL. After the formation of PCL/Fe$_3$O$_4$–AR nanocomposite again the systems were characterized by FTIR spectroscopy, UV–visible spectroscopy, fluorescence spectroscopy, DSC, VSM and FESEM like methods. The interesting point noted in the present investigation is the size of Fe$_3$O$_4$ nanoparticle was found to be reduced after the nanohybrid and nanocomposite formation. The three functional groups of AR dye were involved in the ROP of CL. The binding constant and number of binding sites were determined.

Keywords Nanohybrid, ROP, Binding constant, Fe$_3$O$_4$, Alizarin red, HRTEM

Cite this article Balakrishnan Meenarathi, Ponpandian Siva, Shanmugavel Palanikumar, Lingasamy Kannammal and Ramasamy Anbarasan: Nanocomposites, doi: 10.1080/20550324.2016.1207009

Introduction

Poly(ε-caprolactone) (PCL) is an important biomedical plastic material that holds the potential to reduce the waste associated with the disposal of conventional polymers. The material scientists expect that synthesis of PCL by a bulk and single-step method without using any hazardous solvents and with luminescence and fluorescence properties since it is a biomedical candidate. This will increase the applications of PCL in the biomedical field. Various initiators are used for the synthesis of PCL. For example, in 2010 Ireland and co-workers reported about the cationic organomagnesium-initiated ROP of ε-CL. The biomedical PCL can be synthesized using functionalized initiators such as amine, hydroxyl, carboxyl, thiol, and amide. The biomedically valuable PCL can be synthesized using isobutyl alumoxane. Kinetics and mechanism of anionic ROP of ε-CL were explained in the literature. A novel Yttrium complex initiated ROP of ε-CL was done by Wu and research team. MWCNT-initiated PCL was synthesized and characterized by NMR and WAXS. Azemi et al. synthesized the solventless enzyme catalyzed ROP of ε-CL. Thiol functionalized, heteronuclear base functionalized, perfluoroalkane sulfonamide functionalized, and phosphoester functionalized PCL report is available in the literature. By thorough literature survey, we could not find any report based on the Alizarin red S (AR)-functionalized Fe$_3$O$_4$ initiated ROP of ε-CL and its drug release activity. The present methodology offers a solvent free ROP of ε-CL. Above all; PCL is an effective drug carrier material.

Magnetic nanoparticle particularly Fe$_3$O$_4$ has been effectively studied by various research team. Unfortunately, the application of Fe$_3$O$_4$ was restricted due to the absence of the functional group on the Fe$_3$O$_4$ surface. Recently, our research...
team reported about the functionalization of Fe<sub>3</sub>O<sub>4</sub> by different functionalities. The literature survey reveals that AR-functionalized Fe<sub>3</sub>O<sub>4</sub> report is not available. Recently, the polymer scientists are doing research with targeted drug delivery using Fe<sub>3</sub>O<sub>4</sub> particularly in the photodynamic therapy (PDT) field. This motivated us to do the present investigation because, after the utilization, it is not necessary to remove the iron from the system since it is a biometal.

An organic dye is an important key element in the PDT for the production of reactive oxygen species (ROS) towards the apoptosis of cancer cells. In 2009, Kayrak et al. studied it is a biometal. In 2013, Demin et al. explained the interaction between the iron and the ferrite due to NaOH medium, the –OH group of AR may not be available. Recently, the polymer scientists are doing research on the functionalization of Fe<sub>3</sub>O<sub>4</sub> by different functionalities. The literature survey reveals that AR-functionalized Fe<sub>3</sub>O<sub>4</sub> report is not available. Recently, the polymer scientists are doing research with targeted drug delivery using Fe<sub>3</sub>O<sub>4</sub> particularly in the photodynamic therapy (PDT) field. This motivated us to do the present investigation because, after the utilization, it is not necessary to remove the iron from the system since it is a biometal.

An organic dye is an important key element in the PDT for the production of reactive oxygen species (ROS) towards the apoptosis of cancer cells. In 2009, Kayrak et al.26 studied the optimization of synthetic method for the production of fluorescent and conductive wool. In 2014, Kohila and research team27 studied the poly(congored) grafted silk fiber. On going through the literature, we could not find any report based on the AR-functionalized Fe<sub>3</sub>O<sub>4</sub> nanohybrid initiated ROP of CL. In the present investigation, we chose AR dye because of hydroxyl and –SO<sub>3</sub>Na like functional groups. The present investigation was done towards the synthesis and characterization of fluorescent dye functionalized magnetic nanohybrid. The novelty of the present methodology is an eco-friendly, biocompatible, economically cheaper and single-step preparation without any hazardous solvents.

Chemically conjugated drug delivery systems can be used in an effective way rather than the simply loaded drug delivery systems towards the sustainable release of drug and elimination of side effects in the pharmaceutical field. In this case, the rate of drug release is controlled by the rate of hydrolysis. In 2013, Khazaoi and co-workers28 reported the drug release behavior of poly(styrene-alt-maleicanhydride) system. Sultana et al.29 studied the ciprofloxacin hydrochloride release from Povidone K30 matrix. Drug release activity of aspirin loaded PLGA-PEG-PLGA/montmorillonite microparticles was reported in the literature.29 The other authors also reported about the drug release study.30,31 By thorough literature survey, we could not find any report on the Rif. loaded drug release activity of fluorescent and magnetic PCL. Hence, the drug release study is the main aim of the present investigation. In order to avoid the photodegradation of dye molecule during the PDT process, the dye is chemically conjugated with the PCL (as an initiator). Moreover, during the PDT application, lesser amount of dye is injected into the system in order to avoid the side effects and cytotoxic effects. For this purpose, we have considered the AR dye-functionalized Fe<sub>3</sub>O<sub>4</sub> nanohybrid as a chemical initiator for the ROP of ε-CL.

**Experimental**

**Materials**

e-caprolactone (CL, Across chemicals, USA), stannous-2-ethyl hexanoate (Sn(Oct)<sub>2</sub>, Across chemicals), FeCl<sub>3</sub>, FeSO<sub>4</sub> and NaOH were freshly purchased from s.d fine chemicals, India and used as such. Alizarinred S (AR) was purchased from Spectrum chemicals, India. Diethylether, non-solvent, was purchased from Aldrich chemicals and used as received. CHCl<sub>3</sub>, solvent was purchased from Aldrich chemicals, India. Rifabint (Rif, Ranbaxy Chemicals, India) was purchased in tablet form and used as such. Double distilled (DD) water was used for the preparation of reaction solutions.

**Synthesis of AR-functionalized Fe<sub>3</sub>O<sub>4</sub> nanohybrid system**

The novelty of the present investigation is the synthesis of AR-functionalized Fe<sub>3</sub>O<sub>4</sub> and the same is used as an initiator for the ROP of CL. The procedure in brief is mentioned here (Scheme 1). About 1 g AR dye was dissolved in 50 mL of DD water, taken in a 500 mL beaker under vigorous stirring conditions. About 2.5 g FeSO<sub>4</sub> and 5 g FeCl<sub>3</sub> were added inside the beaker under N<sub>2</sub> atmosphere at room temperature. Here, the Fe<sup>2+</sup> to Fe<sup>3+</sup> ratio was maintained at 1:2. Further, 100 mL of DD water was added and mixed for 10 min. 10 g NaOH in 100 mL DD water was prepared separately. Thus, prepared NaOH solution was added to the reaction mixture under vigorous stirring condition till the content became dark black. Once the permanent dark black color was obtained, further addition of NaOH solution was stopped. The reaction was allowed further for two hours with stirring. The added NaOH nucleated the formation of Fe<sub>3</sub>O<sub>4</sub>. After 2 h of mixing the excess NaOH was removed by placing the beaker on a magnetic bar. Under the influence of magnetic field the AR decorated Fe<sub>3</sub>O<sub>4</sub> molecules settled down, whereas the unreacted NaOH remained in the aqueous medium. The top aqueous layer was removed with the help of a pipette. The precipitate is washed with excess amount of DD water and placed on the magnetic bar. Under the influence of both gravitational and magnetic force, the AR-functionalized Fe<sub>3</sub>O<sub>4</sub> settled down and the liquid was removed. This washing process was continued till the supernatant liquid attains the pH 7.0 and colorless. Finally, the precipitate was freeze dried, weighed, and stored in a zipper lock cover. The same procedure was followed for the synthesis of pure Fe<sub>3</sub>O<sub>4</sub> in the absence of AR molecules. In the present investigation, AR contains two –OH groups and one –SO<sub>3</sub>Na group. Hence, the AR physically adsorbed on the surface of the ferrite molecules. In 2013, Demin et al.32 explained the interaction between the ferrite and alkoxysilane compound. But in the present study, already there are lot of –OH groups present on the surface of ferrite due to NaOH medium, the –OH group of AR may not interact with the ferrite surface. Hence, the only possibility is the interaction of –SO<sub>3</sub>Na with the metal surface.

**Synthesis of PCL/Fe<sub>3</sub>O<sub>4</sub>–AR nanocomposites**

A two-way necked 25 mL capacity round bottomed (RB) flask was taken and dried well. One neck acts as a sulfur free N<sub>2</sub> inlet, whereas the second one acts as a N<sub>2</sub> outlet. About 1 g CL was charged in the above said two way necked RB flask. With this 0.001 g Sn(Oct)<sub>2</sub>, (catalyst) was charged. Here, the [M/Cl] = 1000. ROP of CL was carried out under different experimental conditions such as [M]/[l] and monomer variation. Required amount of AR-functionalized Fe<sub>3</sub>O<sub>4</sub> was accurately weighed and mixed with the two-way necked RB flask. The contents were mixed for 10 min under N<sub>2</sub> purging at room temperature. After uniform mixing the two-way necked RB flask was kept in an oil bath at 160 °C. The ROP was allowed for 2 h under mild stirring condition.33 At the end of the reaction the N<sub>2</sub> purging was stopped and the highly viscous
liquid was dissolved in 25-mL CHCl₃ solvent. Thus, obtained polymer was purified by re-precipitation with the addition of diethyl ether. After the drying process for 6 h under fume hood, the Fe₃O₄/AR nanohybrid end capped PCL was obtained as a white crystalline powder. Thus, obtained white crystalline powder was weighed and stored in a zipper lock cover.

**Characterization**

Magnetic measurements were carried out with a superconducting quantum interference device magnetometer (Lakesore-7410-VSM, USA) with magnetic fields up to 7 T at 32 °C. FTIR spectra were recorded with the help of Shimadzu 8400 S, Japan model instrument by KBr pelletization method from 400 to 4000 cm⁻¹. Three milligram of polymer sample was ground with 200 mg of spectral grade KBr and made into a disk under the pressure of 7 tons. ¹H and ¹³C-NMR spectra of the polymer samples were recorded by using Bruker Biospin High Resolution Digital 300 MHz NMR spectrometer, USA. Dueterated chloroform (CDCl₃) was used as a solvent, and tetramethyl silane (TMS) served as an internal standard. UV–visible spectrum was measured by dissolving the sample in chloroform solvent. The instrument used here is Shimadzu UV-3600, Japan model instrument from 200 to 800 nm. The same sample solution was subjected to fluorescence emission measurement from 350 to 700 nm using Elico SL174 (India) instrument. The melting temperature ($T_m$) and the degradation temperature ($T_d$) of the polymer samples were determined by using Dupont Thermal Analyst 2000 Differential Scanning Calorimeter 910S, USA model instrument (simultaneous DSC and TGA analyzer). All the measurements were done under N₂ atmosphere in a temperature range of RT to 100 °C with 10 °C/min heating rate. Field emission scanning electron microscopy (FESEM) was used to examine the morphological behavior of the polymer with the help of FESEM – Hitachi S4800 Japan, instrument.

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\text{FTIR-RI of } [\text{C}=\text{O}/\text{C} - \text{H}] = A_{1726} / A_{1730} \tag{1}
\]
where $A_{1726}$ is corrected peak area of a peak at 1726 cm$^{-1}$ and $A_{720}$ is corrected peak area at 730 cm$^{-1}$. A Waters 2690 GPC instrument was used to determine the $M_w$ of the polymer samples using THF as an eluent at room temperature at the flow rate of 1 mL min$^{-1}$ against polystyrene (PS) standards.

**Drug release study**

The ultimate aim of the present investigation is the drug release activity of PCL. The drug release study was carried out for the above synthesized materials and the procedure in brief is given below: 0.50 g PCL was taken in a disk form prepared under 7 tons of pressure. About 500 mL of gastric pH solution was prepared and the tablet suspended in the medium with stirring. While stirring, the drug is slowly released and the same can be quantitatively measured at different intervals of time by pipetting 2 mL of aliquot by using UV-visible spectrophotometer. From the calibration curve, the % cumulative drug release (% CDR) was calculated as follows:

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

(2)

Various possible models were dried and the best fit models are explained in the present investigation. The drug release models were done in a universal standard model.

**Results and discussion**

**Characterization of Fe$_3$O$_4$/AR nanohybrid system**

The FTIR spectrum of pure Fe$_3$O$_4$ is given in Figure 1a. The spectrum shows two peaks. A broad peak around 3466 cm$^{-1}$ is due to the –OH stretching of Fe$_3$O$_4$. During the Fe$_3$O$_4$ synthesis some amount of water molecules are intercalated. The metal oxide stretching appeared at 603 cm$^{-1}$. Figure 1b represents the FTIR spectrum of AR decorated Fe$_3$O$_4$ nanohybrid. The –OH stretching appeared at 3444 cm$^{-1}$. The aromatic symmetric and anti-symmetric stretching was observed at 2889 and 2959 cm$^{-1}$, respectively. The bending vibration of –OH from AR appeared at 1637 cm$^{-1}$. The SO$_2$ stretching from AR appeared at 1216 cm$^{-1}$. The aromatic C–H stretching was observed at 870 and 920 cm$^{-1}$. The C–H out of plane bending vibration (OPBV) appeared at 719 cm$^{-1}$. The metal oxide stretching also appeared at 632 and 444 cm$^{-1}$. Hence, the appearance of new peaks such as –OH bending, SO$_2$ stretching, aromatic CH stretching, and C–H OPBV confirms the surface functionalization of Fe$_3$O$_4$ by AR dyes.

The UV–visible spectrum of AR before and after functionalization reaction confirms the interaction between Fe$_3$O$_4$ and AR dye. A broad peak at 418.7 nm (Figure 1c) is responsible for the AR dye. After the functionalization reaction the same peak was red shifted to 431.9 nm (Figure 1d). The red shift in the peak after the functionalization reaction confirms the existence of chemical interaction between dye and Fe$_3$O$_4$. The SO$_2$ group of AR dye might interact with the Fe$_3$O$_4$ through the secondary forces of attraction. As a result, the peak was red shifted. The red shift in the peak after the nanohybrid formation was explained in our earlier communication.

The peculiar property of AR dye before and after surface functionalization reaction was tested by fluorescence spectroscopy. The fluorescence emission spectrum of pristine AR dye is shown in (Figure 1e) with the intensity of 806 cps. After the surface functionalization with Fe$_3$O$_4$ the FEI was suppressed to 606 cps (Figure 1f) without any shift in the peak. This confirms the quenching nature of Fe$_3$O$_4$.

The magnetic property of Fe$_3$O$_4$ was studied by VSM technique and is shown in Figure 1g with the magnetization value of 800 emu/g.

Figure 1 FTIR spectrum of a Fe$_3$O$_4$ and b Fe$_3$O$_4$–AR nanohybrid, UV–visible spectrum of c AR dye and d Fe$_3$O$_4$–AR nanohybrid, Fluorescence emission spectrum of e AR dye and f Fe$_3$O$_4$–AR nanohybrid, VSM of g Fe$_3$O$_4$ and h Fe$_3$O$_4$–AR nanohybrid, FESEM image of i Fe$_3$O$_4$ and j Fe$_3$O$_4$–AR nanohybrid system.
confirms the ROP of CL by the nanohybrid. In order to find out the efficiency of the nanohybrid towards the ROP of CL a log–log plot was made between [M/I] and RI(C=O/CH) (Figure 2f). This plot shows two regions. It means initially the ROP of CL was very fast and later it was found to be slow. While increasing the [M/I] the number of initiating sites were reduced. As a result the rate of ROP of CL was lowered. At the same time the molecular weight of the polymer was increased. From the plot, the slope value was determined as 0.25 which confirmed the 0.25 order of ROP CL with respect to the nanohybrid. (i.e.) R(ROP) \propto \text{[nanohybrid]}^{0.25}. This indicates that 0.25 mol of initiator is required to form 1 mol of PCL. The order of the reaction proved the initiating efficiency of nanohybrid towards the ROP of CL.

The MWCNT-NIR dye system exhibited 0.50 order of reaction towards the ROP of CL.38 When compared to the literature; the present system exhibited a good result.

The chemical structure of PCL was confirmed by NMR spectroscopy. Figure 3a represents the 1H-NMR and 13C-NMR spectrum of PCL/Fe3O4–AR nanocomposite synthesized at [M/I] = 100. The surface catalytic effect of nanohybrid towards the ROP of CL was tested at different [M/I]. While increasing the [M/I] from 10–400 the corrected peak area of carbonyl stretching of PCL was increased. The FTIR spectrum of PCL synthesized at various [M/I] is given in Figure 2a–e. The important peaks are characterized below: a broad peak around 3500 cm\(^{-1}\) explains the –OH stretching of PCL. The aliphatic C–H symmetric and anti-symmetric stretching was noted at 2860 and 2942 cm\(^{-1}\), respectively. The C=O stretching of PCL was noted at 1717 cm\(^{-1}\).34 The ester C–O–C linkage of PCL was identified at 1185 cm\(^{-1}\). The C–H OPBV could be seen at 729 cm\(^{-1}\). The M–O stretching was noted at 448 cm\(^{-1}\) as a small hump. From the FTIR spectrum it was found that, while increasing the [M/I], the ratio of FTIR-RI(C=O/C–H OPBV) was linearly increased. This confirms the ROP of CL by the nanohybrid. In order to find out the efficiency of the nanohybrid towards the ROP of CL a log–log plot was made between [M/I] and RI(C=O/C–H OPBV) (Figure 2f). This plot shows two regions. It means initially the ROP of CL was very fast and later it was found to be slow. While increasing the [M/I] the number of initiating sites were reduced. As a result the rate of ROP of CL was lowered. At the same time the molecular weight of the polymer was increased. From the plot, the slope value was determined as 0.25 which confirmed the 0.25 order of ROP CL with respect to the nanohybrid. (i.e.) R(ROP) \propto \text{[nanohybrid]}^{0.25}. This indicates that 0.25 mol of initiator is required to form 1 mol of PCL. The order of the reaction proved the initiating efficiency of nanohybrid towards the ROP of CL. The MWCNT-NIR dye system exhibited 0.50 order of reaction towards the ROP of CL.38 When compared to the literature; the present system exhibited a good result.

The chemical structure of PCL was confirmed by NMR spectroscopy. Figure 3a represents the 1H-NMR spectrum of PCL/Fe3O4–AR nanocomposite system. Peaks corresponding to standard TMS and solvent appeared at 0 and 7.3 ppm, respectively. A signal at 4.2 ppm is corresponding to the –OCH3 proton. This is in accordance with our earlier publication.39 The –CO2–CH2 proton signal appeared at 2.4 ppm. The remaining methylene protons of PCL appeared between 1 and 2 ppm. The peak integration value confirmed the chemical structure and composition of PCL. Peaks corresponding to AR dye are not appeared due to non-solvation effect or lesser amount of AR dye used as an initiator (M/I = 100).
PCL was further confirmed by $^{13}$C-NMR spectroscopy (Figure 3b). Solvent peak appeared at 78 ppm. A signal due to the carbonyl carbon appeared at 173 ppm. Here, the aromatic and aliphatic carbonyl carbons are merged with each other and appeared as a single peak. Moreover, the quantity of AR taken was low ($M/I = 100$). The $–$OH and $–$CO$_2$–CH$_2$ signals appeared at 62 and 34 ppm, respectively. The methylene carbon signals appeared between 20 and 30 ppm. Thus, the NMR spectra confirmed the chemical structure of PCL.

The UV–visible spectrum was recorded for PCL, synthesized at various $[M]$ is shown in Figure 4a–e. The spectrum shows a peak at 446.4 nm. It was found that while increasing the $[M]$, the absorbance at 446.4 nm was found to be reduced. This can be explained as follows: While increasing the $[M]$ the number of monomers were increased at constant initiator concentration. The number of initiator shared by the monomer was reduced. As a result, the absorbance at 446.4 nm was reduced. Using the UV–visible spectroscopy one can find out the binding constant by plotting $1/[C_\text{L}]$ vs. $A_0/A - A_0$. Figure 4f indicates the same with a linear plot. The binding constant was determined from the $[I/S]$ as $0.28 \times 10^5$ M$^{-1}$. The binding constant value again confirms the existence of strong interaction between AR dye and PCL units. In comparison with the literature, we found that while changing the size and shape of the nanohybrid system, automatically the binding constant was changed.

While using a dye it is very important to find out the fluorescence property. Fluorescence emission spectrum was recorded for PCL samples synthesized at various $[M]$. It was found that while increasing $[M]$, the FEI was decreased and the spectrum is shown in Figure 5a–e. This is due to the increase in $[M]$, ultimately quenches the FEI of AR dye. In order to find out the number of binding sites involved in the ROP of CL and binding constant, the plot of log(weight of monomer) vs. $\log([I_0 - I]/I)$ (Figure 5f) was made and the slope value was determined as 1.06 and the intercept value was noted as 2.64. The slope value is the binding constant, whereas intercept value indicates the number of binding sites. This is in accordance with our earlier publication. In the case of AR dye; $2$–OH and $1$–SO$_3$Na groups are available. During the ROP of CL, the $–$OH group was actively involved in the ROP of CL. The $–$SO$_3$Na group was binded with ferrite through the physical forces. This physical force is very weak and it is cleaved when it is heated to higher temperature. Now the $–$SO$_3$Na group is attached with the PCL chain via secondary forces of attraction. The involvement of these 3 functional groups towards the ROP of CL was confirmed by FE spectroscopy.

The phase transition of PCL during heating was analyzed by DSC. Figure 6a–e indicates the DSC thermogram of PCL.
In order to confirm the ROP of CL in the presence of Fe$_3$O$_4$–AR nanohybrid system the GPC analysis was used. Figure 7a and b indicates the GPC images of PCL synthesized at the [M/I] of 10 and 400, respectively. When the [M/I] was maintained at 10, the $M_w$, $M_n$, and polydispersity (PD) values were determined as 7535 g/mol, 3717 and 2.02, respectively. The PCL synthesized at the [M/I] value of 400, the $M_w$, $M_n$, and PD values were determined as 16412 g/mol, 9067 and 1.81, respectively. This indicates that while increasing the [M/I] ratio, the $M_w$ of the PCL was increased. This is due to the decrease in initiator concentration (i.e.) the number of initiating centers were reduced. The PD inferred that at higher [M/I] ratio, the polymer yielded a narrow molecular weight without any branching or cross linking. Hence, the GPC results proved that the Fe$_3$O$_4$–AR nanohybrid is an effective initiator towards the ROP of CL. This is in accordance with the literature report.34

Figure 8 shows the VSM loop of PCL/Fe$_3$O$_4$–AR nanocomposite system synthesized at [M/I] = 100. The VSM value was determined as 24.57emu/g. The VSM value of pristine Fe$_3$O$_4$ and surface-functionalized Fe$_3$O$_4$ were greater than that of the present system. The decrease in VSM value is due to the encapsulation of Fe$_3$O$_4$ by PCL chains. In our earlier publication.34 we explained the decrease in VSM after the in situ polymerization by four factors. The same four factors are suitable for the present investigation too.

Figure 9a shows the FESEM image of PCL/Fe$_3$O$_4$–AR nanocomposite synthesized at [M/I] = 100. The broken stone like morphology confirms the presence of PCL. The molecular weight of PCL is discussed in the forth coming session. The thermal stability of PCL/Fe$_3$O$_4$–AR nanocomposite systems was studied by TGA at the heating rate of 10 °C/min under nitrogen atmosphere (Figure 6f–j). Generally, the thermogram exhibited a two-step degradation process. The first minor weight loss below 200 °C is associated with the removal of moisture and cleavage of dye units from the PCL backbone. The second major weight loss around 310 °C is ascribed to the degradation of PCL backbone. The interesting point noted here is after the major degradation, the % weight residue remained above 400 °C is increased with the decrease of [M/I] ratio (i.e.) increase of Fe$_3$O$_4$–AR nanohybrid concentration. This confirmed that the nanohybrid was effectively initiated the ROP of CL under nitrogen atmosphere at 160 °C. Thus, both DSC and TGA explained the thermal properties of the PCL/Fe$_3$O$_4$–AR nanocomposite.
confirmed by UV–visible spectroscopy. It was found that while increasing the time the $\lambda_{\text{max}}$ value at 262.7 nm was increased (Figure 11a–h). Various drug release models like zero-order reaction, first-order reaction, Higuchi model, Korsmeyer and Peppas model and Hixson model were tried among which the first-order reaction exhibited the maximum $R^2$ value of 0.91. Figure 11i indicates the plot of log (%CDR retained) vs. Time. This indicates that the drug was slowly released into the medium via dissolution process in the gastric pH condition. The drug release mechanism was determined by using Korsmeyer and Peppas model (Figure 11j). From the plot, the slope value was calculated as 0.492 which is less than $n$ (i.e.) 0.89. This confirms the non-Fickian transport mechanism.

For the sake of comparison, the drug release mechanism of PCL nanocomposite was carried out by considering AR dye as a model drug. Here, also various drug models were tried. The UV–visible spectrum was recorded for different interval of time (Figure 12a–l). Among the models, the Korsmeyer and Peppas model exhibited the maximum $R^2$ value of 0.97. Figure 12m indicates the plot of log (%CDR) vs. log (Time). The slope
mechanism. The present investigation inferred that one can reduce the size of the material via thermal and mechanical treatment. In overall comparison, the present investigation yielded somewhat better results when compared with the literature particularly with the GPC results.

Acknowledgment

Mrs. G. Vijaylakshmi, Assistant Professor, Department of English is gratefully acknowledged for her valuable help during this manuscript preparation work.

Disclosure statement

No potential conflict of interest was reported by the authors.

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